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2014 Research DAY

24th Annual

USF Health Research DAY





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SCHOOL OF PHYSICAL THERAPY [&] REHABILITATION SCIENCES MORSANI COLLEGE OF MEDICINE





FRIDAY, FEBRUARY 21, 2014

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Proud Sponsors of the 24th Annual Research DAY

- Morsani College of Medicine
- ✤ College of Nursing
- ✤ College of Public Health
- School of Pharmacy
- School of Physical Therapy Rehabilitation Sciences
- MCOM Department of Internal Medicine

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A Special <u>Thank You</u> to Our Patron Sponsors:







Friday, February 21, 2014

Marshall Student Center

AGENDA

TIME	EVENT	LOCATION
4:00 pm – 6:00 pm	Presenters: Registration and Poster Set-up (Early registration: Feb 20 th , 4:00 pm– 6:00 pm)	Atrium/Ballroom
7:30 am - 9:30 am	Judges: Registration and Assignments	Atrium
8:00 am – 10:00 am	5th Annual Joseph Krzanowski, PhD USF Health Invited Oral Presentations	Oval Theater
10:00 am – 12:00 pm	Poster Judging Session	Ballroom
12:00 pm – 1:00 pm	Lunch Break	Atrium/ Ballroom
1:00 pm – 2:30 pm	 18th Annual Roy H. Behnke Distinguished Lectureship <i>Dr. James W. Simpkins</i> Director, Center for Basic and Translational Stroke Research West Virginia University <i>Title: "Wandering in Neurodegeneration</i> <i>Research: A Career of Running Against the Wind"</i> 	Oval Theater
1:00 pm – 3:30 pm	Posters Available for Viewing Sunshine ERC Posters	Ballroom/Plaza Room
2:30 pm – 3:15 pm	Awards Ceremony	Oval Theater
3:30 pm – 4:00 pm	Posters Removed	Ballroom
4:00 pm – 5:00 pm	Reception	Atrium/Ballroom



18th Annual

Roy H. Behnke Distinguished Lectureship

PLACE:

Marshall Student Center Oval Theater

TIME:

1:00 p.m.

SPEAKER:

James W. Simpkins, Ph.D. Director, Center for Basic Translational Stroke Research West Virginia University

TITLE:

"Wandering in Neurodegeneration Research:

A Career of Running Against the Wind"

Sponsored by: Department of Internal Medicine, Morsani College of Medicine, USF

18th Annual

Roy H. Behnke Distinguished Lectureship Keynote Speaker



James W. Simpkins, Ph.D. Director, Center for Basic and Translational Stroke Research

West Virginia University

James W. Simpkins received his Ph.D. degree under the mentorship of the pioneering neuroendocrinologist, Joseph Meites at Michigan State University in 1977. He then joined the University of Florida where he rose through the academic ranks to a full professorship in 1986. At the University of Florida, he was the founding director of the Center for the Neurobiology of Aging, served as Chair of two departments and was appointed the Frank Duckworth Professor of Drug Discovery in 1996. In 2000, he became the Professor and Chair of the Department of Pharmacology & Neuroscience and Founding Director of the Institute for Aging and Alzheimer's Disease Research at the University of North Texas Health Science Center at Fort Worth. In 2012, he joined the faculty of the Department of Physiology and Pharmacology of West Virginia University and currently serves as the Founding Director of the Center for Basic and Translational Stroke Research. In 2012, he received the Harman Award for Lifetime Achievement for Aging Research from the American Association of Aging.

The author of more than 370 publications, his research has focused on the discovery of novel compounds for the treatment of age-related brain disorders, with a particular focus on Alzheimer's disease and stroke. His body of research has resulted in 21 issued patents.

From the Desk of:

Phillip J. Marty, PhD Associate Vice President, USF Health Interim Chair, Department of Pathology and Cell Biology, Morsani College of Medicine & Professor, Public Health and Medicine



Dear USF Health/University Community:

This year marks the 24th "USF Health Research Day" Anniversary that highlights the research work of our students, trainees, staff and faculty across USF Health. This is another banner year for participation with 350 scheduled presentations submitted by students, staff, trainees and faculty.

An important aspect of our Research Day Program is the Annual Roy H. Behnke Distinguished Lectureship. This year, Dr. James Simpkins will be delivering the Distinguished Lecture titled "Wandering in Neurodegeneration Research: A Career of Running Against the Wind." Dr. Simpkins is Professor in the Department of Physiology and Pharmacology & Director, Center for Basic and Translational Stroke Research at West Virginia University.

With this 24th Anniversary of Research Day, we continue to acknowledge the importance and value of research to USF Health and the University. Our goal is to continue to recognize, grow and enhance the research efforts of our students, trainees, staff and faculty. **USF Health Research Day** is just one of those special events during the year that is part of **ResearchOne**, sponsored by USF Research and Innovation. USF Health Research Day recognizes the hard work of all our researchers and especially our students and trainees, and the great contributions they are making to the scientific advancement of their disciplines. It is an important day for this purpose and one we hope you will enjoy.



ADMINISTRATION

Donna J. Petersen, MHS, ScD, CPH

Harry R. van Loveren, MD

Interim Senior Associate Vice President and Dean, College of Public Health

Interim Dean, Morsani College of Medicine David W. Cahill Professor and Chair Department of Neurosurgery and Brain Repair

Dianne Morrison-Beedy, PhD, RN, FNAP, FAANP, FAAN

Kevin Sneed, PharmD

William S. Quillen, PT, PhD, SCS, FACSN

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Associate Dean and Director School of Physical Therapy and Rehabilitative Sciences

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Ralph Wilcox, PhD

Paul Sanberg, PhD, DSc

President, USF

Provost & Executive Vice President

Senior Vice President for Research & Innovation

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MORSANI COLLEGE OF MEDICINE

Committee on Research 2013-2014

Basic Scientists:		Term Expires
Wenlong Bai, PhD	Pathology & Cell Biology	2015
Jerome Breslin, PhD	Molecular Pharmacology & Physiology	2015
Vrushank Davé, PhD	Pathology & Cell Biology	2014
David Kang, PhD	Molecular Medicine	2014
Thomas Taylor-Clark, PhD	Molecular Pharmacology and Physiology	2015
Clinical Scientists:		
Timothy Friel, MD	LVHN	2014
Narasaiah Kolliputi, PhD	Internal Medicine	2015
Tuan Vu, MD	Neurology	2015
Mack Wu, MD	Surgery	2015
Ling Zhang, MD	Oncologic Sciences	2014
School of Physical Therapy & Rehabil	itation Sciences:	
Seok H. Kim, PT, PhD	Physical Therapy & Rehabilitation Sciences	2014
Dean's Appointments (At Large):		
Heather Agazzi, PhD	Pediatrics	2015
Brian Giunta, MD, PhD	Psychiatry & Behavioral Neurosciences	2015
Peter Nelson, MD	Surgery	2015
Hesborn Wao, PhD	Internal Medicine	2015
Other Committee Members	l	
Stephen B. Liggett, MD	Vice Dean for Research Ex-Officio, Non-Voting	Open



COLLEGE OF NURSING

Research Committee

Cindy Munro, PhD, RN, ANP-BC, FAAN, Associate Dean for Research and Innovation

Kevin Kip, PhD, Executive Director, Research Center

Susan Johanson, BS

Cathryn Branch, MPA

Paula Cairns, RN, BSN

Sue Ann Girling, BSAS

Mari Miranda, BA

Janice Walker, BA

Trudy Wittenberg, BS

Ming Ji, Ph.D.

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COLLEGE OF PHARMACY

Research Committee

Dr. Diane Allen-Gipson, PhD

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COLLEGE OF PUBLIC HEALTH

Research Committee

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Amy Alman, PhD

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Yangxin Huang, PhD

Russell Kirby, PhD

Etienne Pracht, PhD

Rene Salazar, PhD

Margaret Walsh, MPH

Kate Wolfe-Quintero, PhD

Administration/Staff Support

Wilbur Milhous, PhD Associate Dean for Research

Ellen Kent, MPH, CPH

Kay White

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STAFF ACKNOWLEDGEMENTS

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College of Pharmacy Thomas Rogers

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College of Public Health Ellen Kent

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USF Health Development Bari Becker Patrick Henry

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USF Health Communications

Alice Madsen Elizabeth Peacock Eric Younghans Sarah Worth

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School of Physical Therapy and Rehabilitation Sciences Samatha Lovari



POSTERBOARDS

Location:

Marshall Student Center 2nd floor Ballroom

Set up:

7:30a.m. – 9:30a.m.

10:00a.m. -12:00p.m.

<u>Judging:</u>

Tear down:

3:30p.m. – 4:00p.m.

Poster Size:

4 ft. high by 3 ft. wide

JUDGING OF POSTERS

Student posters will be judged by faculty members.

Students *must be present* at their poster to be eligible for judging.

Poster Presentations 10:00a.m. – 3:30p.m.

Posters will be judged on:

1. Presentation of poster

- Organization
- Readability
- Appearance
- Sense Appeal

2. Presentation of data

• Oral Communication

3. Knowledge of subject

• Question and answer presentation

AWARD CEREMONY

Student Winners will be announced at the Awards Ceremony following the USF Health Keynote Lecture



Listing of Presenters and Titles

Oral Presentations

Abs #	Name	Abstract Title
0-1	Ochotny, Misty	Role of sirolimus in post-cardiac transplantation when compared to standard immunosuppressive therapies: a systematic review
O-2	Acosta, Sandra	Combination therapy of human umbilical cord blood cells and granulocyte- colony stimulating factor exerts neuroprotection in a chronic TBI model
O-3	Cox, Ruan	Hyperoxia Exposure Results in Decreased Expression of Pro-Resolution Receptor ALX/FPR2
O-4	Franzen, Elisabeth	Preliminary Sexual Behavior and Contraceptive Differences among Youth Participating in a State-Wide Positive Youth Development Program Evaluation
O-5	Hudey, Stephanie	Persistently Activated CD27+CD80+ B cells Following ART Correlate with Macrophage Activation
O-6	Muhammad, Adnan	Outcome and Predictors of Survival after Transjugular Intrahepatic Portosystemic Shunt (TIPS) in patients with Cirrhosis and Portal hypertension
O-7	Rahman, Shams	Maternal Diabetes Mellitus and the Risk of Childhood Mortality among Children with Birth Defects: a Large Retrospective Cohort Study
O-8	Thompson, Erika	Theory-Based Determinants of Physical Activity during Pregnancy: A Systematic Review
O-9	Whelan, Jillian	Exploitation of the Host Ubiquitin System by Respiratory Syncytial Virus Nonstructural Protein
O-10	Wischhusen, Jonathan	Factors Associated with Health Literacy in a Community-based Sample of Older Blacks
O-11	Zhou, Zhiwei	Induction of Apoptosis and Autophagy and Suppression of EMT via Sirt1- Mediated Pathway by Plumbagin in Human Prostate Cancer Cells

	s Allerg	y, Immunology and Infectious Diseases
1	Balduzzi, Michael	Impulse Oscillometry (IOS) is Easier than Spirometry for Older Asthmatic and Non-asthmatic Subjects
2	Bellur, Adarsh	Naegleria fowleri Virulence Factor Nfa-1 is a Hemerythrin with NAD(P)H- dependent Oxidase Activity
3	Cheung, Michael	Suppression of the Immune Response Due to Respiratory Syncytial Virus Infection in Mesenchymal Stem Cells
4	Hudey , Stephanie	Persistently Activated CD27+CD80+ B Cells Following ART Correlate With Macrophage Activation
5	Laird, Chris	New potential transcriptional regulators of Bartonella henselae type IV secretion systems
6	Niebur, Hana	Intestinal Perforation and Non-tuberculous Mycobacterial Peritonitis in a Patien with Interleukin-1 Receptor Associated Kinase 4 Deficiency
8	Pemberton, Orville	Non-Covalent Inhibitors: A Novel Method of β-Lactamase Inactivation
9	Reiser, Michelle	LRBA Subcellular Localization: Evidence of LRBA's Role in Vesicle Trafficking fron the Golgi to Cell Membrane and Endocytosis
10	Rifkin, Eileen	Real-time PCR quantification of Virginia live oak (Quercus virginiana) pollen
11	Rogers, Elizabeth	Impact of Lupus on Lipid Handling in THP-1 Human Macrophages
12	Sampayo-Escobar, Viviana	Osteopontin (OPN) Plays a Critical Role in Respiratory Syncytial Virus (RSV) infection
13	Tabatabaian, Farnaz	Aggressive or Invasive Allergic Fungal Sinusitis?
14	Tu, Nhan	Identification of Bartonella-specific putative regulatory RNAs using RNA-Seq
15	Updegraff, Adam	Clinical Experience With Oxaliplatin (O) Desensitization (OD): A Case Series
16	Wang, Jia-Wang	LRBA Causes Immunodeficiency and Autoimmunity by Deregulating NFkB- mediated Multiple Immune Effectors Critical for B Cell Activation
17	Whelan, Jillian	Exploitation of the Host Ubiquitin System by Respiratory Syncytial Virus Nonstructural Protein
	କର୍ଗ	Cancer Biology Research
18	Das, Mahasweta	A "Nano-cell" strategy to treat lung cancer
19	Flaherty, Amber	IDH1 Mutation in Prostate Cancer: R132H and Beyond
20	Green, Ryan	Expansion of a Cancer Stem Cell Sub Population by Culture on a 3D Fibrous Scaffold
21	Hu, Chen	Ubiquitin Specific Peptidase 10 (USP10) Deubiquitinates and Stabilizes MutS Brotein Homolog 2 (MSH2) to Regulate Callular Sensitivity to DNA Damage
22	Hu, Chengbin	Protein Homolog 2 (MSH2) to Regulate Cellular Sensitivity to DNA Damage Targeting Epithelial-Mesenchymal Transition in the Treatment of Ovarian Cance
23	Kasiappan, Ravi	1,25-dihydroxyvitamin D3 increases cisplatin sensitivity in ovarian cancers
23		through microRNA-498

25	Kothari, Nishi	Aspirin as targeted therapy? Evaluating the PIK3CA mutation as a predictive biomarker in colorectal cancer patients.
26	Malaney, Prerna	Synergistic role of PTEN and Lkb1 loss in KRAS-driven lung cancers
27	Mauro, James	Functionally distinct gene classes as larger or smaller transcription factor traps
28	Nair, Sajitha	Identification & characterization of leukemia inducing factor: A novel diagnostic tool to identify acute lymphoblastic leukemia and diffuse lymphoma
29	Nelson, Nadine	The Role of Ikaros in Treg Development and Function in a Murine Pancreatic Cancer Model
31	Poff, Angela	Non-toxic metabolic therapy – ketosis and hyperbaric oxygen – elicit potent anti- cancer effects in vivo and in vitro
32	Quarni, Waise	VDR-RIPK1 Complex and its Implication in Vitamin D Action and Necroptosis
33	Reyna, Chantal	Axillary Burden of Disease Following False Negative Preoperative Axillary Evaluation
34	Suleiman, Yaman	The results of a phase I study of combination of gemcitabine plus pasireotide (SOM 230) LAR in metastatic pancreatic cancer (MPC).
35	Sun, Yuefeng	BMP4 Works through ID1 to Regulate FOXO1 Activity and Prostate Cancer Cell Growth and Invasion
36	Wells, Nicole	Roles of IL-10 and I-309 Cytokines in Reproductive Cancers
37	Xiang, Shengyan	HDAC6 deacetylates and ubiquitinates MSH2 to maintain proper levels of MutSa

	જા	Cardíovascular Research
38	Aslam, Sadaf	Selected Urinary Biomarkers as Early Risk Predictors of Renal Injury in Obese and Dysmetabolic Nonhuman Primates
39	Bettin, Margaret	Gender Differences in Presentation of Coronary Artery Disease in Patients Undergoing Stress Echocardiography and Nuclear Perfusion
40	Deng, Wei	Cardiomyocyte sialylation and complex N-glycosylation protect against dilated cardiomyopathy and heart failure
41	Doggett, Travis	Alcohol-induced endothelial hyperpermeability is diminished with inhibition of p38 MAP Kinase
42	Haines, Ricci	PTK6 mediates intestinal endothelial barrier dysfunction in response to TNF $lpha$
43	Harvey, Maria	Intramural hematoma of the aortic root and ascending aorta: A rare complication following transcatheter aortic valve replacement (TAVR)
44	Hooper, Justin	Arrhythmia evoked by airway nociceptive reflexes in healthy and cardiovascular diseased rats
45	Zhang, Xun	Sphingosine-1-Phosphate (S1P) enhances endothelial barrier function independently of Rac1
	ৰ্ণ্ড	Chart Reviews and Other Case Studies
46	Abboud, Elia Charbel	Do Silver-Based Wound Dressings Reduce Postoperative Pain in Colorectal Surgery?
47	Ahmad, Amier	Mucoepidermoid Carcinoma Arising in the Anophthalmic Socket: A Case Study
48	Baksh, Kathryn	Correlation between PET-FDG activity post-neoadjuvant chemoradiotherapy and tumor regression grade in locally advanced esophageal cancer

49	Black, Kaelan	Juvenile Ossifying Fibroma: Successful Endoscopic Gross Total Resection of a Rare Sinonasal Tumor in an Adolescent Male
51	Cameron, Michael	Node-Positive Papillary Thyroid Cancer: Predictive Factors for Recurrence after Surgery
52	Dalia, Samir	A New Prognostic Index In Diffuse Large B-Cell Lymphoma Using Serum Albumin: a pilot study evaluating the albumin adjusted-International prognostic index
53	Garrott, Ben	Incidental Colorectal Wall Thickening on CT: Evaluation of Prevalence, Significance, and Management
54	Gerardi, Diana	Serotonergic or Anticholinergic Toxidrome: Case Report of a 9 year-old Girl
55	Gillispie, Miriah	Rate of Remission in Polyarticular Juvenile Idiopathic Arthritits: A Practice Based Study
56	Grana, Alejandra	Need for Tube Thoracostomy Following Patent Ductus Arteriosus Ligation in Premature Infants
57	Grewe, Stefanie	A case of primary melanoma in situ without regression presenting as a depigmented patch
58	Hagele, Thomas	Bullous Morphea
59	Hernandez, Sarah	Dronabinol Treatment of Refractory Nausea and Vomiting Related to Peritoneal Carcinomatosis
60	Holdener, Stephanie	Chronic NK Cell Lymphoproliferative Disorder/Lymphocytosis, Nature of Disease and a Long-Run Follow Up
61	Kuk, Amber	Conservative Inpatient Refeeding Yields Modest Outcomes in Adolescents with Anorexia Nervosa and Eating Disorder Not Otherwise Specified
62	Manimala, Neil	Passing out from fatigue? Neurocardiogenic syncope as a presentation of chronic fatigue
63	Moore, Nerissa	Cystic Soft-Tissue Sarcoma Disguised as Chronic Hematoma: Complete Excision for Thorough Pathologic Examination is Crucial for Diagnosis
64	Ng, Emily	Does Socioecomomic Status Matter With Perioperative Outcomes After Robotic- Assisted Pulmonary Lobectomy?
65	Patel, Midhir	It's hard to see what's not there: A case of cryptorchidism that evolved into intra-abdominal metastatic seminoma
66	Patel, Ronak	Hurdling obesity in the road to renal transplantation
67	Patel, Rupal	Chronic opioid users are more difficult to sedate than alcoholics and non-
		substance users
69	Peir, Gene	substance users Safety and Efficacy of Bosentan in Infant Pulmonary Hypertension
69 70	Peir, Gene Posey, Lela	
		Safety and Efficacy of Bosentan in Infant Pulmonary Hypertension
70	Posey, Lela	Safety and Efficacy of Bosentan in Infant Pulmonary Hypertension Negative Pressure on Silver Nylon Dressings: Does it Reduce Infection Rates? Clinical Features And Outcome Of Clonal Mastocytosis Secondary To Chronic
70 71	Posey, Lela Rastogi, Prerna	Safety and Efficacy of Bosentan in Infant Pulmonary Hypertension Negative Pressure on Silver Nylon Dressings: Does it Reduce Infection Rates? Clinical Features And Outcome Of Clonal Mastocytosis Secondary To Chronic Myelomonocytic Leukemia (SM- AHNMD/CMML) Given Diverse Therapies Inter-Clavicular Stabilization with the Synthes Sternal Fixation System after

75	Soni, Kiran	Primary Cutaneous Fungal Infections in Oncology Patients
76	Thau, Matthew	Effect of body mass index on operative complications after robotic-assisted ivor- lewis esophagogastrostomy: Retrospective analysis of 133 cases
77	Vu, Kristie	High utilization of liver transplantation for hepatocellular carcinoma: Is it concerning?
78	Yesudas, Jeremy	Secondary Malignant Transformation of Giant Cell Tumor: Case Review of a Rare Occurence
79	Zayko, Olga	The surgical treatment of breast cancer in female veterans compared to the civilian population.
	ৰ্ম্	Clínícal Research
80	Abbott, Andrea	Vaginal and Vulvar Melanoma is Associated with a High Rate of Regional Nodal Disease
81	Atchsion, Christie	Development of New Risk Models for Hospital-Acquired Venous Thromboembolism in Children: Findings from a Large Single-Institutional Case-
82	Colizzo, Jason	Control Study Elevated intrabolus pressure on high resolution manometry distinguishes fibrostenotic and inflammatory esosinophilic phenotypes
83	Doren, Erin	Effects of Obesity on Satisfaction with Breast Cancer Operations: An Outcomes Study
84	Garate, Arantzazu	Follow-up Attendance among USF BRIDGE Physical Therapy Patients
85	Greenberg, Erin	Quantitative image analysis applied to the grading of vitreous haze
87	Hoggard, Timothy	Impaction Grafting for Repair of Proximal Humeral Fractures with Hemiarthroplasty: Thermal and Biomechanical Implications
88	House, Jarret	Diagnostic Digital Cytopathology: Are We Ready Yet?
89	Keene, Amanda	Preliminary Results from a Study Examining Sleep-Related Problems among Anxious Youth with Autism Spectrum Disorders
90	Klein, Aimee	A Biomechanical Analysis of the Relationship Between Hip Anatomy and Lower Extremity Musculoskeletal Injuries in Ballet Dancers
92	Mahmood, Umbareen	How Does Procedure Type Affect the Impact of Breast Cancer on Women's Lives
93	Mayer, John	Low Back Pain in the US Military: Epidemiology, Prevention, and Current Research
94	Muhammad, Adnan	Outcome and Predictors of Survival after Transjugular Intrahepatic Portosystemic Shunt (TIPS) in Patients with Cirrhosis and Portal Hypertension
95	Murphy, Travis	Variable Calcium Changes in Response to Surgery
96	Nguyen, Johnny	Practical Application of Next-Generation DNA Sequencing in Detection of ASXL1, RUNX1, EZH2, ETV6, and TP53 Mutations in Patients with Myelodysplastic
97	Patel, Priya	Syndrome Antibiotic Treatment Trial for the PANDAS/PANS Phenotype
98	Pavan, Reed	Postmortem Ultrasound and OCT Imaging of the Posterior Segment
99	Rigaud, Whitney	Evaluating the Recovery Curve for Clinically-Assessed Reaction Time Following Concussion Injury

100	Soto, Jose	Awareness of ongoing clinical trial information: physicians' and clinical trial administrators' perspectives
101	Taitano, Andrew	Bariatric Surgery Improves Histological Features of Nonalcoholic Fatty Liver Disease and Liver Fibrosis
102	Tao, Jiangchuan	Correlation of c-MYC, EZH2, IKZF1 and p-STAT5 Expression to the Prognosis of Adult B Lymphoblastic Leukemia
103	Teefey, Christina	Maternal serum galectin-3 is correlated with obesity
104	Tzekov, Radouil	Ocular changes in patients with Spinocerebellar ataxia type 7

	ର୍ଚ୍ଚ	Community, Family and Global Health Research
105	Ismail, Taheen	Underlying Causes of the Low Level of Fully Immunized Children in Rural Aligarh, Uttar Pradesh, India
106	Madow, Brian	Remote screening for Diabetic Retinopathy
107	Shamas, Eric	Voces de Cedro Galan: Community Based Participatory Research in a Resource Poor Region of Nicaragua
108	Wischhusen, Jonathan	Factors Associated with Health Literacy in a Community-based Sample of Older Blacks
	ৰ্ণ্য	Education Research
110	Burns, Jack	The Impact of Deliberate Practice in the Acquisition of Surgical Skills
111	Cronin, Kevin	What Factors Influence a 4th Year Medical Student's Rank Order List?
112	Goshev, Anastasia	Interprofessional - Interdisciplinary Education: Simulating the future of healthcare to prepare the Professionals of tomorrow
113	Horn, Gregory	Fundamentals of Laparoscopic Surgery Skill Acquisition: A comparison of blocked versus interleaved practice
114	Lozano, Aaron	Learning to be a First World Physician in a Third World Country
115	Merritt, Raymond	How Many Ultrasound Examinations Are Necessary To Gain Proficiency In Accurately Identifying The Nerves Of The Brachial Plexus?
116	Narayanan, Shreya	Nutrition Education: a curriculum to increase nutrition competency among medical students
117	Nguyen, Jacqueline	Neonatal abstinence syndrome management: A quality improvement (QI) initiative to educate caregivers, and providers in the outpatient setting.
118	Patel, Soha	Diabetic Ketoacidosis (DKA) in Pregnancy: A Comprehensive Simulation to Improve Patient Safety & Quality of Care
119	Pierce, Jacob	Examination of the factors influencing research efficiency
120	Raturi, Rita	Improving Collaborative Global Communications
121	Schutt, Charles	Anatomy and Physiology: A curriculum to increase medical competency of URM high school students and promote medicine as a possible career option.

	ର୍ଷ	Evídence-Based Study Desígn and Outcomes Research
122	Cain, Mary	Timing of delivery of a gastroschisis affected pregnancy and its impact on perinatal outcomes and hospital costs
123	Doepker, Matt	Predictors of improved survival in patients undergoing pulmonary metastasectomy for sarcoma
124	Gil-Herrera, Eleazar	An iOS-based Application for Pain Management
125	Govsyeyev, Nicholas	A Multi-Institutional Series of Pure Myxoid Liposarcomas of the Extremities and Torso
126	Konstantinovic, Monique	Sentinel node biopsy is indicated for thick clinically node-negative melanoma
127	Koscso, Jonathan	Factors associated with sentinel node positivity in patients with thick cutaneous melanoma (≥ 4 mm)
128	Lu, Samson	Culture Change in Trauma Surgery: Implementing a Standardized Handoff Checklist
129	Sutton, Sutton	Acute Appendicitis: Variation in Treatment and Outcomes by Insurance Status
130	Teefey, Patrick	Frozen-section reliability to identify endometrial cancer high-risk factors
	ৰ্ণ্ড	Molecular and Cellular Biology Research
132	Adderley, Shaquria	Variable roles of the H1-H3 receptors and PKC in histamine-induced barrier

	ത	Molecular and Cellular Dwwyy Research
132	Adderley, Shaquria	Variable roles of the H1-H3 receptors and PKC in histamine-induced barrier dysfunction in cultured endothelial cells from different sources.
133	Cox, Ruan	Hyperoxia Exposure Results in Decreased Expression of Pro-Resolution Receptor ALX/FPR2
134	DeForte, Shelly	Sequence-based classification of enzymes with an emphasis on the applicability of intrinsically disordered regions
135	DeNigris, John	Altered Dermal Fibroblast Behavior in a Collagen V Haploinsufficient Model of Classic Type Ehlers Danlos Syndrome.
136	Flowers, Antwoine	Impact of NT-020 treatment on gene expression in growth, survival, and senescence signaling pathways in an In-Vivo model of aging in the hippocampus.
137	Fukumoto, Jutaro	Deletion of ASK1 protects against hyperoxia-induced acute lung injury
138	Hamel, Laura	Screening for Chemical Modulators of Protein Palmitoylation
139	Ho, Shannon	From Proteomics to Personalized Medicine? The VEGFR-2 Protein Complexes in Human Placentas Near Term
140	Howell, Mark	In Vitro Anticancer Drug Screening Using a 3D Fibrous Scaffold
141	Huang, Kevin	Vascular Maturation and Cellular Infiltration of Electrospun Scaffolds for Fibrous Tissue Repair via VEGF and PDGF Delivery from Sacrificial Fibers
142	Johnson, Tamina	Development of Recombinant Functional Biomaterials for Neuronal Regeneration
143	Kesl, Shannon	Methods of Sustaining Dietary Ketosis in Sprague-Dawley Rats
144	Lee, James	Nrf2, Sirt1, and PGC1 α mediate improvements in oxidative stress after Roux-en-Y gastric bypass surgery

145	Liu, Wei	HDAC6 Ubiquitinates RIP3 and Stimulates Programmed Necrosis
146	Malipeddi, Jashwanth	Feature extraction of the palmitoylproteome through sequence-based analysis
148	Qin, Yiru	In vitro Immunotoxicity Evaluation of Graphene Quantum Dots
149	Reddy, Krishna	A putative molecular recognition feature in zDHHC S-palmitoyltransferase C- termini is essential for zDHHC9 and ERF2 function in vivo
150	Stojanovski, Bosko	Effect of pH and temperature on the structural integrity of 5-aminolevulinate synthase
151	Wang, Chunyan	Enhancing the Multilineage Differentiation of Bone Marrow Derived Mesenchymal Stem Cells in Three Dimensional PEG-Chitosan-Graphene Based Hydrogel
152	Wang, Miqi	Effects of local anesthetics on differentiation potential of human mesenchymal stem cells
153	Young, Ryan	The Use of Human Sweat Metabolites as Bait for Monitoring Vectors of Onchocercaisis in West Africa and Latin America
154	Yuan, Yuan	Elastin like Peptides (ELPs) Modulate Cellular Behavior through interaction with Cell Surface Glycosaminoglycans
	প্ট	Neuroscience Research
155	Acosta, Sandra	<i>Combination therapy of human umbilical cord blood cells and granulocyte-colony stimulating factor exerts neuroprotection in a chronic TBI model</i>
156	Ahmed, Jamileh	Analysis of iPSC-Derived Dopaminergic Neuron Susceptibility to Influenza and Excitotoxicity in Non-Affective Psychosis
157	Bastawrous, Marina	Dopaminergic Cell Loss as a Pathological Link between Traumatic Brain Injury and Parkinson's Disease
158	Blankenship, Stephanie	Novel Therapeutics Improve Motor Coordination and Seizure Activity in an Angelman Syndrome Mouse Model
159	Breydo, Leonid	Solvent Interaction Analysis of Intrinsically Disordered Proteins in Aqueous Two- phase Systems
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5THANNUAL

JOSEPH KRZANOWSKI, PhD

USF HEALTH

INVITED

ORAL PRESENTATIONS SESSION

Role of sirolimus in post-cardiac transplantation when compared to standard immunosuppressive therapies: a systematic review

<u>Misty Ochotny¹, Minal Shah¹, Alexis Ngo¹, Dr. Christina Doligalski², Dr. Kamila Dell³</u> ¹University of South Florida College of Pharmacy, ²Tampa General Hospital, ³USF College of Pharmacy, Department of Pharmacotherapeutics & Clinical Research

Keywords: sirolimus, cardiac allograft vasculopathy, post-cardiac transplant, renal dysfunction, calcineurin inhibitors

Objective: The primary objective was to evaluate the use and efficacy of sirolimus (SRL) in the reduction of the progression and prevention of cardiac allograft vasculopathy (CAV) when compared to standard immunosuppression for post-cardiac transplant (tx) patients. The secondary objective was to assess reduction in renal dysfunction (RD) in patients that used SRL instead of standard immunosuppression in post-cardiac tx.

Methods: A systematic review was conducted to evaluate randomized controlled trials, observational studies, review articles, and case reports involving SRL and CAV. Eligibility criteria included types of participants, exposure, outcomes, and inclusion and exclusion criteria. Primary and secondary outcomes assessed CAV-related events and renal function.

Results: The current standard of treatment for post-cardiac tx patients is CNIs that studies have shown to cause RD. Conversion to SRL as primary immunosuppression was shown to attenuate progression of CAV. SRL therapy post-cardiac tx was deemed safe and preferred in patients with RD. Patients who were converted to SRL and lowered or discontinued CNI doses post-cardiac tx were shown to have an improvement in renal function.

Conclusion: SRL can benefit cardiac tx rejection therapeutic treatments to reduce the progression and prevention of CAV and RD. There is a lack of literature regarding the use of SRL in post-cardiac tx patients. A future direction of research should include more longitudinal studies utilizing SRL as primary or adjunct treatment in post-cardiac tx recipients.

Presented by: Sandra Acosta, PhD, Postdoctoral Fellow

Combination therapy of human umbilical cord blood cells and granulocyte-colony stimulating factor exerts neuroprotection in a chronic TBI model

Sandra A. Acosta^{1,} Naoki Tajiri¹, Kazutaka Shinozuka¹, Hiroto Ishikawa^{1,} Shijie Song^{3,4}, Paul R. Sanberg^{1,2,4,5,} Juan Sanchez-Ramos^{3,4,5}, Yuji Kaneko¹, Cesar V. Borlongan^{1*} ¹Center of Excellence for Aging & Brain Repair, Department of Neurosurgery & Brain Repair, University of South Florida Morsani College of Medicine, ²USF Research & Innovation, ³James Haley Veterans Affairs Medical Center, ⁴USF Morsani College of Medicine, Department of Neurology, and ⁵Department of Molecular Pharmacology and Physiology

Keywords: TBI, G-CSF, hUCBCs

Objective: Traumatic brain injury (TBI) is associated with neuro-inflammation, and cognitive impairments. Cellbased therapies are currently being investigated in treating neurotrauma to regulate the hostile brain milieu found in TBI. In tandem, the stimulation/mobilization of endogenous stem/progenitor cells from the bone marrow through granulocyte colony stimulating factor (G-CSF) poses as an attractive intervention for chronic TBI. In this study, we tested the potential of a combined therapy of human umbilical cord blood cells (hUCB) and G-CSF to counteract the progressive secondary effects of chronic TBI

Methods: Four groups of rats were treated with saline alone, G-CSF+saline, hUCB+saline or hUCB+G-CSF at 7days post TBI. Eight weeks after TBI, hippocampal cell loss, neuroinflammatory response, and neurogenesis were analyzed using immunohistochemistry

Results: Results revealed that rats exposed to chronic TBI + saline exhibited widespread neuroinflammation, impaired endogenous neurogenesis in dentate gyrus and subventricular zone, and severe hippocampal cell loss. hUCB monotherapy suppressed neuroinflammation, nearly normalized the neurogenesis, and reduced hippocampal cell loss compared to saline alone. G-CSF monotherapy produced partial/short-lived benefits characterized by low levels of neuroinflammation, a modest neurogenesis, and a moderate reduction of hippocampal cells loss. On the other hand, combined therapy of hUCB+G-CSF displayed synergistic effects that robustly dampened neuroinflammation, while enhancing endogenous neurogenesis and reducing hippocampal cell loss

Conclusion: Combined treatment of hUCB+G-CSF rather than monotherapy appears optimal for abrogating chronic TBI associated impairments

Research supported by: Department of Defense W81XWH-11-1-0634

Abstract #: O- 3

Presented by: Ruan Cox Jr, MS, Graduate Student

Hyperoxia Exposure Results in Decreased Expression of Pro-Resolution Receptor ALX/FPR2

Ruan Cox Jr., Oluwakemi Phillips, Jutaro Fukumoto, Itsuko Fukumoto, Richard Lockey, Narasaiah Kolliputi University of South Florida Morsani College of Medicine, Department of Molecular Medicine

Keywords: Inflammation, Lung, Immunology, Resolution, Hyperoxia

Objective: Endogenously produced polyunsaturated fatty acids (PUFAs) are key mediators of the antiinflammatory response following acute injury. PUFA's such as resolvins and lipoxins have demonstrated potent proresolutionary effects in acute lung injury. These molecules have been shown to bind and exert their effects through g-coupled protein receptor Lipoxin A4/formyl peptide receptor 2 (ALX/FPR2). Previous reports have shown that various septic or sterile insults lead to an increase in ALX/FPR2 expression; however, the response of ALX/FRP2 to oxidative stress has not been elucidated. In this study we investigated the role of ALX/FPR2 in a murine model of hyperoxic acute lung injury (HALI).

Methods: C57BL/6 Mice were exposed to hyperoxic (50, 75, or 95% O2) or normoxic (≈ 21% O2) for 24, 48, or 72hrs. Following atmospheric treatment, mice were euthanized and bronchoalveolar lavage fluid as well as lung tissues were collected. Bronchoalveolar lavage fluid was used to assess alveolar protein leak. Lung tissue samples were used for histopathological analysis and to assess ALX/FPR2 protein and RNA expression following hyperoxia treatment.

Results: Results reveal that hyperoxia exposure results in a significant decrease in ALX/FRP2 expression in comparison to normoxia treated controls. This decrease was dose dependent and reduction in ALX/FRP2 was evident in as little as 24hrs following hyperoxia exposure.

Conclusion: Our results reveal, for the first time, a significant decrease in ALX/FRP2 expression which is not seen in other forms of acute lung injury. While the production of PUFAs in HALI may be normal, their proresolutionary effects may be blunted due to the decrease in receptor expression.

Research supported by: NIH RO1 AHA Joy McCann Culverhouse Endowment

Presented by: Elisabeth Franzen, BS, Graduate Student

Preliminary Sexual Behavior and Contraceptive Differences among Youth Participating in a State-Wide Positive Youth Development Program Evaluation

Elisabeth Franzen, BS, ¹; Elizabeth V. Powers, BA,^{1, 2}; Helen Mahony, MPH,¹; Sarah B. Maness, MPH,^{1;} Shireen <u>M. Noble, BASc,¹; Charlotte Noble, MA, MPH,^{1,2}; Ashley Singleton, MPH,^{1;} Wei Wang, PhD,³; Rita DeBate, PhD,¹; Stephanie L. Marhefka, PhD,¹; Ellen M. Daley, PhD,¹; Kay Perrin, PhD,¹; Eric R. Buhi, MPH, PhD,¹ ¹University of South Florida College of Public Health, Department of Community and Family Health, ²USF College of Arts and Sciences, Graduate Program in Applied Anthropology, ³USF College of Public Health, Department of Epidemiology and Biostatistics</u>

Keywords: Adolescents, Positive Youth Development, Sexual Behavior

Objective: The purpose of this research was to identify preliminary sexual behavior and contraceptive use differences between youth participating in an evidence-based positive youth development program (PYD), the Teen Outreach Program (TOP), and a matched control group, from baseline (time 1) to post-intervention (time 2).

Methods: This project involved a randomized controlled trial in 28 high schools in 12 Florida counties in the 2012-2013 academic school year. Treatment and comparison youth completed a survey at time 1 (n=1812 [82%] and 2177 [84%], respectively) and time 2 (n=1498 [68%] and 1909 [74%]). Participants were asked about sexual intercourse, sexual intentions, and contraceptive/condom use. Multilevel modeling was conducted and odds ratios (OR) and their corresponding 95% confidence intervals (CIs) were reported. The covariates of age, gender, and race/ethnicity were included in the model. Data were analyzed with S-PLUS version 8.1.

Results: After controlling for baseline risk, preliminary results showed youth in the treatment group were less likely to report ever having sex, compared to the control group (OR: 0.64, 95% CI: 0.48-0.86, p=0.0025). Treatment youth were less likely to report future intention, compared to control youth (OR: 0.71, 95% CI: 0.44-0.98, p=0.02). These results remained statistically significant after controlling for covariates.

Conclusion: Data support decreased incidence of sexual behavior and intentions of having sexual intercourse versus comparison group. Limitations include potential self-report bias and survey attrition. Strengths include large sample size and ethnic/racial diversity of participants. These preliminary findings lend support for PYD programs, such as the TOP.

Research supported by: Office of Adolescent Health, USDHHS

Presented by: Stephanie Hudey, MS, Med II Student

Persistently Activated CD27+CD80+ B Cells Following ART Correlate With Macrophage Activation

Stephanie N. Hudey¹, Bret J. Rudy², Xinrui Zhang³, Susan Lukas⁴, Maureen Goodenow³, John Sleasman⁵, ¹University of South Florida Morsani College of Medicine,Tampa, FL, ²New York University School of Medicine, New York City, NY, ³University of Florida, Gainesville, FL, ⁴USF Morsani College of Medicine Pediatrics, St. Petersburg, FL, ⁵Duke School of Medicine, Durham, NC

Keywords: HIV, macrophage activation, B cells, antiretroviral therapy (ART)

Objective: ART and control of HIV replication does not fully restore perturbations within resting and activated memory B cell compartments. This study was based on the hypothesis that ongoing macrophage activation and HIV-associated inflammation contributes to B cell abnormalities.

Methods: Cellular and plasma markers for inflammation were evaluated in 43 healthy controls and 17 HIV+ subjects. Flow cytometry analysis of B cell subsets and assessment of markers of macrophage (sCD163 and sCD14) and lymphocyte (sCD27) were measured by ELISA. Assays were performed prior to and at 24 and 48 weeks following ART. HCs and HIV+ treated subjects were also compared pair-wise and longitudinally at study entry (prior to ART), 24 weeks and 48 weeks on therapy by non-parametric rank sum.

Results: Control of viral replication failed to decrease the proportions of activated B cells or increase memory B cells after 48 weeks on therapy. sCD14, sCD27 and sCD163 all remained significantly elevated in HIV+ subjects at 48 weeks following therapy (p=0.0027, p<0.0001, and p=0.0142, respectively, Mann-Whitney). Regression analysis revealed a positive correlation between the decrease in resting memory B cells and levels of sCD14 at 48 weeks on therapy (r=0.51, p=0.038, Spearman test) Results also showed a positive correlation between the increase in activated B cells and the elevation of sCD14 24 weeks following therapy (r=0.54, p=0.028 Spearman).

Conclusion: Elevated levels of sCD14, a biomarker of macrophage activation, is the result of LPS binding to TLR4. Our results show that chronic B cell activation also reflects ongoing inflammation due to microbial translocation that may contribute to ongoing B cell dysfunction, even in HIV-infected subjects who control viral replication with ART.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Presented by: Adnan Muhammad, MD, Resident

Outcome and Predictors of Survival after Transjugular Intrahepatic Portosystemic Shunt (TIPS) in patients with Cirrhosis and Portal hypertension

Adnan Muhammad MD, Rafik Lababidi MD, Elaine Tan MD, Ambuj Kumar MD MPH, Yasser Saloum MD. Division of Gastroenterology, Department of Interal Medicine, University of South Florida Morsani College of Medicine

Keywords: TIPS Cirrhosis Portal hypertension Outcome

Objective: Cirrhosis of liver is the 10th leading cause of death in US. Major complications include variceal bleeding (VB) and refractory ascites (RA). Long-term treatment of VB and RA involves liver transplantation (LT) or transjugular intrahepatic portosystemic shunt (TIPS) in patients who are not candidates for LT. Aim: To determine the clinical outcome and predictors of survival after TIPS insertion.

Methods: This was a retrospective study. Data was collected on all consecutive patients with cirrhosis of liver who underwent TIPS insertion between Jan 2004 and March 2012. The KM method was employed to calculate survival and comparisons were made by log rank test. A multivariate analysis was carried out using the Cox proportional hazards model.

Results: Two hundred forty nine patients met the inclusion criteria. Mean age was 55 years (21-85). Baseline characteristics of the patients, etiology of cirrhosis, Child-Turcotte-Pugh (CTP) score, model for end stage liver disease (MELD) score, indication for TIPS and hepatic venous pressure gradient (HVPG) difference post TIPS were tabulated. HVPG difference was calculated by subtracting the post TIPS pressure gradient to pre TIPS pressure gradient. MELD score (p=0.017), CTP score (p=0.042) and TIPS indication (VB vs. RA) (p=0.004) were the significant predictors of survival. No significant difference in survival was noted in terms of age, gender, ethnicity, etiology of cirrhosis and HVPG difference post TIPS.

Conclusion: TIPS is a safe and effective way to manage the complication of portal hypertension. Mean survival was significantly lower in patients with VB and those with higher MELD and CTP scores. No significant difference in survival was seen in older patients (age \geq 65) when compared to younger age group.

Presented by: Shams Rahman, MD, Graduate Student

Maternal Diabetes Mellitus and the Risk of Childhood Mortality among Children with Birth Defects: a Large Retrospective Cohort Study

<u>Shams Rahman¹, Wendy N. Nembhard¹, Alfred Mbah¹, Mary K. Ethen², ¹University of South Florida, College of Public Health, Department of Epidemiology and Biostatistics, ²Birth Defects Epidemiology and Surveillance Branch, Texas Department of State Health Services</u>

Keywords: Maternal diabetes; birth defects; childhood mortality

Objective: To examine the association between maternal diabetes mellitus (DM) and the risk of childhood mortality among children with birth defects, and to assess whether this association varies by race/ethnicity.

Methods: This was a retrospective cohort study of mothers who gave birth to children with birth defects between Jan 01, 1999 and Dec 31, 2008 in Texas. All cases were ascertained from the Texas Birth Defect Registry. Maternal DM was ascertained from hospital, medical, and vital records.

Results: No significant difference for childhood mortality was observed among birth defect children of everdiabetic mothers compared to children of non-diabetic mothers Hazard Ratio Adjusted (HRa)=0.97; 95% confidence interval (CI) [0.87–1.08]. Maternal DM Type1 was associated with decreased risk of childhood mortality HRa=0.69[95%CI:0.47–1.01]. Maternal DM Type2 and DM unspecified was associated with insignificant elevated risk of childhood mortality among children with birth defects HRa=1.11 [95%CI: 0.72–1.71] and HRa=1.14; [95%CI: 0.88–1.46] respectively. We noticed a pattern of elevated risk for children with birth defects born to NH-black mothers in all groups of DM. Ever DM: HRa=1.05 [95%CI: 0.79–1.39]; DM Pre-pregnancy: HRa=1.50 [95%CI:0.21–10.73]; DM during Pregnancy: HRa=1.74 [95%CI: 1.00–3.03]; DM Type2: HRa=1.24 [95%CI: 0.31– 4.96]; and DM Unspecified: HRa=1.67 [95%CI: 0.94–2.97]. Birth defects count, maternal age, maternal education, infant sex and gestational age were significant predictors for childhood mortality among children with birth defects in our cohort.

Conclusion: Maternal DM (gestational and pre-gestational) did not significantly increase the risk of childhood mortality in our cohort. However, racial disparity may exist for this association.

Presented by: Erika Thompson, MPH, Graduate Student

Theory-Based Determinants of Physical Activity during Pregnancy: A Systematic Review

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Keywords: Pregnancy, Review, Physical Activity

Objective: National guidelines recommend that pregnant women engage in ≥30 minutes of moderate exercise most days of the week; yet only 14% report meeting this recommendation. Theory assists in identifying salient determinants of health behavior to guide interventions; however, the application of theory to physical activity among pregnant women has not been examined cohesively among the multiple levels of influence. This systematic review aims to examine the extent theory has been used to explain or predict physical activity during pregnancy.

Methods: The search produced 223 articles published before September 2013. Inclusion criteria applied: empirical-based; published in a peer-reviewed journal; measured predictors; comprised a pregnant sample; and guided by theory. Studies testing an intervention were excluded. The final sample included 12 studies.

Results: Multiple theories were utilized to explain/predict physical activity during pregnancy; however, the majority of these studies focused on intrapersonal level determinants. Seven studies aimed to predict physical activity based on theoretical constructs (i.e., intention, perceived behavioral control, self-efficacy). Five studies aimed to explain the behavior, identifying attitudes, beliefs, barriers, and benefits associated with physical activity.

Conclusion: This review found that previous research examining physical activity during pregnancy has focused primarily on intrapersonal theoretical determinants. Research examining factors at the interpersonal, community, and societal levels remain understudied. Future research should employ theory-driven multi-level determinants of physical activity to reflect the interacting factors during this critical period in the lifecourse.

Presented by: Jillian Whelan, MS, Graduate Student

Exploitation of the Host Ubiquitin System by Respiratory Syncytial Virus Nonstructural Protein 2

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Keywords: RSV, ubiquitin, host-pathogen interactions

Objective: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infection in young children worldwide. The RSV nonstructural protein 2 (NS2) is a multifunctional protein important for viral replication and disease pathogenesis and is essential for RSV-induced proteasomal degradation of host STAT2. We investigated the mechanism by which NS2 interacts with the host ubiquitin system during infection.

Methods: 293T cells were transfected with plasmid DNA. Co-IPs were performed for protein-protein interactions and western blotting for protein expression. A549 cells were infected with recombinant wild-type RSV (rA2) or mutated recombinant RSV at an MOI of 3 and harvested 16 hours post infection. NS2 mutations were designed using computational analysis and generated via site-directed mutagenesis. ImageQuant TL v2005 was used for densitometry analysis.

Results: Co-transfection of 293T cells with NS2 and ubiquitin increased ubiquitination of host proteins compared to ubiquitin alone. Similarly, A549 cells infected with rA2 increased ubiquitination compared to cells infected with recombinant RSV lacking the NS2 gene. Infected A549 cells treated with 10µM MG-132 for four hours did not result in a change in ubiquitin expression. NS2 co-immunoprecipitated with specific ubiquitin ligase complex proteins. Mutation of NS2 residues identified several residues that are vital to NS2-induced ubiquitination of host proteins.

Conclusion: Results indicate NS2 induces ubiquitination of an array of host proteins in a proteasome-independent manner, possibly via interaction with host ubiquitin ligase complex proteins. NS2-induced ubiquitination likely targets host anti-viral processes and can be limited by mutation of key NS2 residues.

Research supported by: SIPAIID NIAID USF

Presented by: Jonathan Wischhusen, MD, Med II Student

Factors Associated with Health Literacy in a Community-based Sample of Older Blacks

<u>Wischhusen J^{1,2}, Davis SN², Jackson B², Govindaraju S², Lin HY², Fulp W², Gwede CK²</u> ¹Moffitt Cancer Center, ²University of South Florida Morsani College of Medicine, Department of Oncologic Sciences

Keywords: Health Literacy, Colorectal Cancer Screening, Community Based Participatory Research

Objective: Colorectal cancer screening (CRCS) saves lives, but utilization rates are low, especially among ethnically diverse Blacks. Lower health literacy (HL) has been shown to be associated with decreased knowledge of CRCS modalities and more negative attitudes towards CRCS. This preliminary analysis examines factors associated with HL in a sample of ethnically diverse Blacks.

Methods: Participants were enrolled in a community based intervention trial designed to promote CRCS with immunochemical fecal occult blood test among average risk men and women aged 50 to 75 years. 158 participants completed baseline surveys assessing HL, CRCS awareness, cancer fatalism, Preventive Health Model (PHM) constructs and demographics. HL was measured using the eight item REALM-R measure; a score of 7 or greater is considered high health literacy.

Results: Majority of participants were female (55%), born in the US (93%), and made > \$10K per year (65%). The median age was 55.5 and 53% of participants had high HL. Bivariate analysis found high HL was significantly associated with CRCS awareness, PHM salience, PHM susceptibility, PHM social influence, PHM religious beliefs, cancer fatalism, gender, employment, education and income. Final multivariable logistic regression model found that high HL was significantly positively associated with awareness (OR=:1.6, p=<.001) and higher income (OR=:5.0, p=0.003) and negatively associated with PHM social influence (OR=:0.9,p=0.033) and cancer fatalism (OR=: 0.8, p=0.017).

Conclusion: Better understanding of HL will be beneficial in targeting appropriate media messages for CRCS screening education. Specifically, lower income medically underserved groups require low literacy materials addressing cancer fatalism and negative CRCS beliefs.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Presented by: Zhiwei Zhou, PhD, Postdoctoral Fellow

Induction of Apoptosis and Autophagy and Suppression of EMT via Sirt1-Mediated Pathway by Plumbagin in Human Prostate Cancer Cells

Zhi-wei Zhou, Xing-Xiao Li, Shu-Feng Zhou Department of Pharmaceutical Science, College of Pharmacy, University of South Florida

Keywords: Plumbagin; prostate cancer; apoptosis; autophagy; EMT; Sirt1

Objective: Plumbagin (PLB) has shown good anticancer activities, but the role of PLB in the treatment of prostate cancer is unclear. This study aimed to investigate the effects of PLB on the growth, apoptosis, autophagy, and epithelial to mesenchymal transition (EMT) of human prostate cancer PC-3 and DU145 cells and the underlying mechanisms.

Methods: Cell proliferation was evaluated by the MTT assay. Intracellular ROS level was measured using CM-H2DCFDA. Cell cycle distribution, apoptosis, and autophagy were determined using flow cytometry. Intracellular autophagy-associated signals were observed and quantified by confocal microcopy. The levels of proteins were quantified by Western blotting assay.

Results: The results showed that PLB had a potent growth-inhibitory, pro-apoptotic, pro-autophagic, and EMT inhibitory effects on both cells. PLB arrested PC-3 cell in G2/M and DU145 cells in G1 phase and significantly increased the intracellular level of ROS. PLB induced mitochondria-mediated apoptosis and autophagy in both cells. PLB suppressed PI3K/Akt/mTOR and p38 MAPK pathways and activated AMPK, contributing to the autophagy-inducing activities of PLB. Modulation of autophagy altered the apoptosis of both cells. Furthermore, PLB suppressed EMT-like phenotypes in both cells by restoring the balance of E-cad and N-cad. PLB down-regulated Sirt1 and inhibition of Sirt1 enhanced autophagy, whereas induction of Sirt1 abolished PLB-induced autophagy in both cells. In addition, inhibition of Sirt1 restored the balance of E-cad and N-cad. PLB also down-regulated PBEF in both cells.

Conclusion: These findings indicate that PLB promotes cellular apoptosis and autophagy but inhibits EMT in prostate cancer cells involving PI3K/Akt/mTOR and Sirt1-mediated pathways.



24th Annual Research DAY

USF HEALTH

ABSTRACT POSTER

SESSION

Impulse Oscillometry (IOS) is Easier than Spirometry for Older Asthmatic and Non-asthmatic Subjects Michael C. Balduzzi M.D., Adam Updegraff D.O., Kerri Rawson M.S., Brice Taylor M.D., Michelle Estevez M.D., Monroe J. King D.O., Richard F. Lockey M.D. University of South Florida Morsani College of Medicine Internal Medicine

Keywords: Impulse Oscillometry, Spirometry, Asthma,

Objective: Asthma is underdiagnosed in the elderly and some older persons find spirometry difficult. Therefore, a feasibility study comparing IOS and spirometry was performed in older asthmatics and non-asthmatics to determine patient acceptance and their ability to meet American Thoracic Society (ATS) and European Respiratory Society (ERS) standards.

Methods: Older subjects (age \geq 65) with physician diagnosed asthma and controls without asthma were asked to perform IOS and spirometry until they met ATS/ERS standards. They performed up to 8 trials of each unless they were unable to continue or required a rescue bronchodilator. They were asked to rate the ease of IOS and spirometry on a scale of 1-5 (easy-hard).

Results: Nineteen subjects meeting ATS/ERS standards completed IOS and spirometry. Ages ranged from 65-82 (M=74.05, SD=5.27) and 58% were female. No significant differences in age or gender were found between asthma (n=13) and control (n=6) groups. IOS ratings ranged from 1 to 3 (M=1.26, SD=.56) and spirometry ratings ranged from 1 to 5 (M=2.95, SD=1.39). Using Wilcoxon Signed Ranks Test, the IOS was rated significantly easier to perform than spirometry, z = -3.37, p = .001, r = -.55.

Conclusion: IOS was easier to perform than spirometry for older subjects with and without asthma and is a valuable option when patients can't perform spirometry.

Research supported by: USF Division of Allergy and Immunology, Department of Internal Medicine at USF Morsani College of Medicine

Abstract #: 2

Presented by: Adarsh Bellur, BS, Graduate Student

Naegleria fowleri Virulence Factor Nfa-1 is a Hemerythrin with NAD(P)H-dependent Oxidase Activity Adarsh Bellur, DeAndre Wells, Matthew Doenges, Andreas Seyfang Department of Molecular Medicine, University of South Florida Morsani College of Medicine, Tampa, FL

Keywords: pathogenic ameba, Fe-binding hemerythrin, oxidoreductase, virulence factor, drug screening.

Objective: Naegleria fowleri is a free-living pathogenic amoeba that can cause primary amebic meningoencephalitis (PAM) with a 98% fatality rate since no efficient drug treatment of PAM is currently available. N.fowleri Nfa-1 is a virulence factor recognized in patient antiserum and belongs to the Fe-binding hemerythrin protein family. Recombinant Nfa-1 protein was used for its biochemical and pharmacological characterization as potential novel drug target in this pathogenic ameba.

Methods: We cloned and expressed Nfa-1 as recombinant protein in E.coli as intein-chitin binding domain fusion protein in the pTwin vector system. Following purification by chitin-agarose chromatography, cleavage of the purified Nfa-1 protein was accomplished by thiol-induced activation of the intein protease.

Results: Nfa-1 has NAD(P)H-dependent oxidoreductase activity, using NADH or NADPH as substrate and ferricyanide as electron acceptor. Kinetic analysis revealed apparent Km and kcat values for NADH of Km = 65 microM and kcat = 4.4/sec, and for NADPH of Km = 22 microM and kcat = 3.3/sec, suggesting that both NADH and NADPH are substrates for this enzyme. This NADH:ferricyanide assay now opens the door for pharmacological drug screening against Naegleria Nfa-1 activity. Inhibitor studies in vitro with recombinant Nfa-1 enzyme showed inhibition by the NAD(P)H oxidase inhibitors DPI and Apocynin and by the xanthine oxidase inhibitor Allopurinol. Subsequent cytotoxicity assays using CHO cells co-cultured with N.fowleri amebae revealed strong protection from Naegleria cytotoxicity in vivo by Apocynin (IC50 = 15 microM), Allopurinol (IC50 = 48 microM), DPI (IC50 = 49 microM), and hypoxanthine (IC50 = 497 microM).

Conclusion: Revealing the enzyme activity of Nfa-1 and a set of lead inhibitors now provides the opportunity for drug screening against this *N.fowleri* virulence factor.

Presented by: Michael Cheung, MS, Graduate Student

Suppression of the Immune Response Due to Respiratory Syncytial Virus Infection in Mesenchymal Stem Cells Michael Cheung¹, Martin Moore², Subhra Mohapatra¹ and Shyam Mohapatra¹ ¹James A Haley VA Hospital and University of South Florida Morsani College of Medicine, Tampa, Florida, ²Emory University and Children's Healthcare of Atlanta, Atlanta, Georgia. University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: MSC, RSV, immune regulation

Objective: Respiratory syncytial virus (RSV) has been reported to infect human bone marrow cells but the consequences are poorly understood. RSV replicates readily in human mesenchymal stem cells (MSCs) and may affect their immunoregulatory functions and contribute to RSV-associated lung disease.

Methods: Human MSCs were infected with RSV expressing a fluorochrome and fluorescent microscopy, plaque assays, flow cytometry and reverse-transcription quantitative PCR (RTqPCR) of important regulatory cytokines were performed at 24, 48, and 72 hours post-infection (pi). In order to evaluate the effect of RSV infection on the immunoregulatory functions of MSCs an assay to measure the proliferation of human peripheral blood mononuclear cells (PBMCs) in response to mitogen stimulation was performed in the presence of conditioned media from infected MSCs. Controls for all experiments included mock-infection.

Results: RSV was found in infected human MSCs at 72 hours pi by fluorescence microscopy, flow cytometry, and plaque assays. The expression of IL6, IL8, and IL1β in RSV-infected MSCs was approximately 3-fold higher than in mock-infected MSCs while stromal cell-derived factor-1 (CXCL12) expression did not change. Culture supernatants of RSV-infected MSCs also significantly reduced the expansion of mitogen-activated PBMCs in a dose dependent manner.

Conclusion: Extrapulmonary RSV infection of MSCs could alter their function by upregulating IL6, IL8, and IL1β which affects immune cell proliferation and may account for the chronicity of RSV-associated disorders and the lack of RSV immunity. Alteration of MSC immunoregulatory function by RSV infection may also exacerbate RSV-associated lung disease.

Research supported by: VA Merit Review Grant and Career Scientist Award to Dr. Shyam Mohapatra.

Abstract #: 4	Presented by: Stephanie Hudey, MS, Med II
	Student

Persistently Activated CD27+CD80+ B Cells Following ART Correlate With Macrophage Activation

<u>Stephanie N. Hudey¹, Bret J. Rudy², Xinrui Zhang³, Susan Lukas⁴, Maureen Goodenow³, John Sleasman⁵, ¹University of South Florida Morsani College of Medicine, Tampa,⁴ St. Petersburg, FL, ⁵Pediatrics; ²New York University School of Medicine, New York City, NY, ³University of Florida, Gainesville, FL, ⁵Duke School of Medicine, Durham, NC</u>

Keywords: HIV, macrophage activation, B cells, antiretroviral therapy (ART)

Objective: ART and control of HIV replication does not fully restore perturbations within resting and activated memory B cell compartments. This study was based on the hypothesis that ongoing macrophage activation and HIV-associated inflammation contributes to B cell abnormalities.

Methods: Cellular and plasma markers for inflammation were evaluated in 43 healthy controls and 17 HIV+ subjects. Flow cytometry analysis of B cell subsets and assessment of markers of macrophage (sCD163 and sCD14) and lymphocyte (sCD27) were measured by ELISA. Assays were performed prior to and at 24 and 48 weeks following ART. HCs and HIV+ treated subjects were also compared pair-wise and longitudinally at study entry (prior to ART), 24 weeks and 48 weeks on therapy by non-parametric rank sum.

Results: Control of viral replication failed to decrease the proportions of activated B cells or increase memory B cells after 48 weeks on therapy. sCD14, sCD27 and sCD163 all remained significantly elevated in HIV+ subjects at 48 weeks following therapy (p=0.0027, p<0.0001, and p=0.0142, respectively, Mann-Whitney). Regression analysis revealed a positive correlation between the decrease in resting memory B cells and levels of sCD14 at 48 weeks on therapy (r=0.51, p=0.038, Spearman test) Results also showed a positive correlation between the increase in activated B cells and the elevation of sCD14 24 weeks following therapy (r=0.54, p=0.028 Spearman).

Conclusion: Elevated levels of sCD14, a biomarker of macrophage activation, is the result of LPS binding to TLR4. Our results show that chronic B cell activation also reflects ongoing inflammation due to microbial translocation that may contribute to ongoing B cell dysfunction, even in HIV-infected subjects who control viral replication with ART.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Presented by: Chris Laird, MS, Graduate Student

New potential transcriptional regulators of Bartonella henselae type IV secretion systems

<u>Chris Laird, Lisa Smith, Kellie Larsen, Burt Anderson</u> University of South Florida Morsani College of Medicine, Department of Molecular Medicine

Keywords: secretion systems, transcriptional regulation, DNA binding proteins

Objective: Type IV secretion systems (T4SSs) are virulence factors critical in establishing infections by the facultative intracellular pathogen Bartonella henselae. These macromolecular machines are compiled of several proteins related to ancient bacterial conjugation machinery and function in recognizing and invading host cells, establishing specific intracellular niches. B. henselae has two type IV secretion systems, one for each niche utilized in this organism's infection cycle.

Methods: We will experimentally test the physical binding interactions of T4SS promoter regions and associated potential interacting proteins by performing DNA and protein pull-downs, and electrophoretic mobility shift assays. Knock-out and over-expression mutants of these factors have been created to determine the effects on T4SS gene expression by qRT-PCR and subsequent endothelial and erythrocyte invasion assays to determine changes in virulence.

Results: A hypothetical DNA binging protein, BH11420, was discovered to specifically bind to the virB T4SS promoter region and a two-component system response regulator OmpR, which when knocked out of B. henselae causes increased trw gene expression.

Conclusion: Little is known about the transcriptional regulation of these secretion systems, currently only one identified regulatory circuit each although multiple levels of regulation likely exist to coordinate the infection of each niche. Our lab has preliminary data suggesting there are additional factors which may regulate the genes encoding these secretion systems.

Abstract #: 6

Presented by: Hana Niebur, MD, Resident

Intestinal Perforation and Non-tuberculous Mycobacterial Peritonitis in a Patient with Interleukin-1 Receptor Associated Kinase 4 Deficiency

<u>H. B. Niebur, N. Tang, J. W. Leiding</u> Division of Allergy, Immunology, and Rheumatology, Department of Pediatrics University of South Florida, St. Petersburg, FL, University of South Florida Morsani College of Medicine Department of Pediatrics

Keywords: IRAK4, non-tuberculous mycobacteria, peritonitis case study

Objective: Interleukin-1 receptor associated kinase 4 (IRAK-4) deficiency is an autosomal recessive immunodeficiency associated with recurrent invasive bacterial infections and impaired inflammatory response due to abnormalities in Toll-like receptor signaling. Infection severity and frequency typically decrease with age. Herein we describe a 16 year-old female with IRAK-4 deficiency that developed intestinal perforations, intra-abdominal abscesses, and non-tuberculous mycobacterial (NTM) peritonitis.

Methods: Bacterial cultures were performed at All Children's Hospital, St. Petersburg, FL with molecular identification of NTM performed by National Jewish Laboratories.

Results: This patient is a female with IRAK-4 deficiency who experienced life-threatening and invasive infections from 5 weeks to 7 years. She received IVIG from 7 to 10 years; subsequent infections were limited to chronic erosive sinusitis. At age 16, she experienced 2 spontaneous bowel perforations which led to recurrent intra-abdominal abscesses and peritonitis requiring numerous surgical interventions and broad-spectrum antimicrobial therapy over a 2-year period. Initial bacteria isolated included enteric flora and Pseudomonas. She developed Mycobacterium abscessus-induced peritonitis associated with severe protein losing enteropathy and intra-abdominal ascites.

Conclusion: Gastrointestinal disease has been reported in few cases suggesting this is an under- recognized feature of IRAK-4 deficiency. While NTM frequently causes peritoneal dialysis-associated peritonitis, Mycobacterium abscessus has not previously been described in IRAK-4 deficiency. This patient's clinical course challenges the previously reported natural history of IRAK-4 deficiency of less severe invasive infections after puberty.

Prevalence of Opportunistic Infections among HIV-infected Patients receiving Antiretroviral Therapy (ART) in Nakhon Nayok, Thailand

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Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 8

Presented by: Orville Pemberton, BS, Graduate Student

Non-Covalent Inhibitors: A Novel Method of β-Lactamase Inactivation

<u>Orville Pemberton, Yu Chen Ph.D.</u> University of South Florida Morsani College of Medicine, Department of Molecular Medicine

Keywords: beta lactamase, antibiotic resistance, penicillin, drug discovery, protein structures

Objective: The most widespread mode of β -lactam resistance involves the expression of enzymes called β -lactamases. Currently, many β -lactamase inhibitors work via an irreversible mechanism, covalently binding to the active site and permanently inactivating the enzyme. However, resistance to this mechanism is possible since these inhibitors structurally resemble the β -lactam antibiotics. Therefore, it is imperative that novel, non-covalent β -lactamase inhibitors be developed that are capable of restoring the effectiveness of the β -lactam antibiotics. This project will focus on the class D β -lactamase OXA-48 since it can degrade carbapenems, the drugs of last resort in the treatment of antibiotic-resistant infections.

Methods: The blaOXA-48 gene was obtained using custom gene synthesis. OXA-48 was then purified and crystallized. OXA-48 crystals complexed with imipenem were sent off to a synchrotron for structural analysis by X-ray diffraction. The DOCK computational program was used to dock commercially available compounds from the ZINC database into an OXA-48 model obtained from the Protein Data Bank (PDB).

Results: Compounds that could potentially bind to the OXA-48 active site were identified. For this project, these compounds will serve as potential leads in the development of compounds that are able to target conserved structural motifs that are shared by the serine β -lactamases. Currently, OXA-48/imipenem complex structure determination is underway.

Conclusion: This project demonstrates that it is possible to develop novel, non-covalent inhibitors that are able to target the serine β -lactamases. This would be crucial in determining how specific structural motifs and mutations play a role in β -lactam hydrolysis.

Research supported by: NSF Florida-Georgia LSAMP HRD #1139850, NIH

LRBA Subcellular Localization: Evidence of LRBA's Role in Vesicle Trafficking from the Golgi to Cell Membrane and Endocytosis

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Keywords: LRBA, Subcellular Localization, Vesicle Trafficking

Objective: Mutation or deletion of lipopolysaccharide responsive beige-like anchor (LRBA) gene causes common variable immunodeficiency, autoimmunity and chronic inflammation. However, the underlying molecular mechanism by which this occurs is unknown. LRBA is similar in structure to the lysosomal trafficking regulator gene. Therefore, it is hypothesized that LRBA may function as a regulator of vesicle trafficking. Its subcellular localization may help to decipher its function.

Methods: Immunofluorescent staining of cultured H293 cells was conducted using a polyclonal antibody to LRBA and monoclonal antibodies against various organelle-specific proteins. Confocal images were obtained with a multiphoton laser scanning microscope and the accompanied software was used for colocalization analysis. Time lapse video was obtained of live RAW264.7 cells stably transfected with LRBA-GFP using a Leica TCS SP2 laser scanning confocal microscope.

Results: LRBA is co-localized with three Golgi proteins (GM-130, P-230, and GS-28), early endosome antigen 1 (an early endosome marker), the RIIb and RIIc subunits of protein kinase A (PKA), and the microtubule protein, tubulin. A video of a live cell stimulated with LPS shows LRBA-positive vesicles budding from the Golgi and moving into the cell membrane.

Conclusion: LRBA is extensively associated with the endomembrane/vesicle trafficking system, which includes the Golgi complex, endosomes, lysosomes, plasma membrane and microtubules. LRBA also is associated with PKA. These results suggest that LRBA may play a role in membrane/vesicle trafficking and signal transduction required for the regulation and function of many immune molecules.

Research supported by: The Joy McCann Culverhouse Endowment to the Division of Allergy and Immunology

Abstract #: 10

Presented by: Eileen Rifkin, Staff

Real-time PCR quantification of Virginia live oak (Quercus virginiana) pollen

<u>Eileen Rifkin, Mark C. Glaum, MD, PhD, Jia-Wang Wang, PhD, Richard F. Lockey, MD, Dennis Ledford, MD</u> University of South Florida Morsani College of Medicine Internal Medicine

Keywords: pollen counting, qPCR, live oak, aeroallergens

Objective: Pollen counting methods require microscopic analysis that is prone to subjective variability. This investigation utilized quantitative real-time PCR (qPCR) to attempt to develop a more accurate and standardized method to quantitate aeroallergens.

Methods: Three types of qPCR standard curves were generated with species-specific primers and a TaqMan probe from the Quercus virginiana nitrate reductase gene. Grains were sonicated for DNA extraction prior to purification with silica spin-columns. The first curve was based on a serial dilution of DNA extracted from dry pollen to determine the efficiency and sensitivity of the qPCR. The second curve was based on a serial dilution of 100 mg of pollen to determine the reproducibility of the DNA extraction from decreasing pollen weights. The third curve was generated from absolute numbers of grains counted using a hemocytometer to establish correlation between the quantification cycles (Cq) and pollen number.

Results: The R-squared values for the first, second and third types of curves were 0.997, 0.982, and 0.990, respectively. The qPCR efficiency was 100%±10% with a qPCR detection range from a single to 10^7 pollen grains.

Conclusion: The R-squared values and qPCR efficiency indicate that the qPCR is highly specific and reproducible. The DNA extraction reproducibility and pollen count correlation are high. These techniques may be useful to count airborne oak pollen and other pollens.

Research supported by: 2013 ARTrust mini grant, The American Academy of Allergy, Asthma, and Immunology (AAAAI) The Joy McCann Culverhouse Endowment to the Division of Allergy and Immunology

Presented by: Elizabeth Rogers, BA, Med II Student

Impact of Lupus on Lipid Handling in THP-1 Human Macrophages

<u>Elizabeth Rogers¹, Allison B. Reiss², Steven E. Carsons², Joshua De Leon², Iryna Voloshyna². ¹University of South Florida College of Medicine, Internal Medicine, Tampa²Winthrop Research Institute, Winthrop University Hospital, Mineola, NY</u>

Keywords: Lupus, Lipid Handling, Cardiovascular Disease

Objective: Atherosclerotic cardiovascular disease (ASCVD) is a characteristic feature of systemic lupus erythematosus (SLE), resulting in severe complications such as myocardial infarction and stroke. Framingham risk factors or disease activity markers cannot predict CVD susceptibility. This study examines whether plasma from SLE patients modulates lipid uptake and processing in human monocytes/macrophages.

Methods: In an IRB approved study, cultured naïve THP-1 macrophages were exposed to 10% plasma from each of 21 healthy controls (HC) and 12 SLE patient \pm 5 µg/ml (Dil)-oxLDL. OxLDL accumulation was determined by fluorescent intensity. Following 18h incubation, RNA and protein were isolated. QRT-PCR and Western blotting techniques measured expression of scavenger receptors: CD36 and lectin-like oxidized low density lipoprotein receptor (LOX-1).

Results: Our results demonstrate that 10% SLE plasma elevates cholesterol influx proteins in THP-1 human macrophages, increasing CD36 mRNA to 189.4±6.9% and LOX-1 to 180.1±3.0% compared to HC (n=3, P<0.01). Protein expression of CD-36 was upregulated to 170.0±42.3% and LOX-1 to 271.4±69.5% of control. Macrophage oxLDL uptake in the presence of SLE plasma increased to 1608±108.7 fluorescent units [FU] (n=15) versus HC (1049±83.3FU, n=17, not statistically significant, p=0.08).

Conclusion: SLE plasma is atherogenic and promotes lipid uptake in human macrophages via upregulation of scavenger receptors CD36 and LOX1. These results may have predictive value for CV risk in this susceptible population. However, future investigations based on a larger cohort of SLE subjects is indicated to determine whether our preliminary finding of an upward trend is significant.

Research supported by: This research was supported by The AHA Medical 2013 Student Summer Research Award and the Scholarly Concentrations Program at USF MCOM.

Abstract #: 12

Presented by: Viviana Sampayo-Escobar, MS, Graduate Student

Osteopontin (OPN) Plays a Critical Role in Respiratory Syncytial Virus (RSV) infection

Viviana Sampayo-Escobar, Terianne Wong, Sandhya Boyapalle, Raminder Bedi, Subhra Mohapatra and Shyam Mohapatra James A Haley VA Hospital and University of South Florida Morsani College of Medicine, Tampa, Florida.

Keywords: Key Words: Respiratory Syncytial virus (RSV), Osteopontin (OPN), inflammation.

Objectives: Osteopontin (OPN) has been implicated in several inflammatory diseases including allergic diseases and influenza infection. However, the role of OPN in RSV infection is unknown. Since, OPN was one of the major genes that changed its expression in both RSV-infected and aged mice, we examined OPN as a potential risk factor during RSV infection.

Methods: RNA and protein isolated from Hep2 cells at various times after RSV infection (pi) were examined for OPN expression by qPCR and immunoblot. For OPN knockdown, Hep2 cells were transfected with shOPN or scrambled RNA and after 48 h, infected with RSV or mock-infected. At 96 h, mRNA for RSV-N (nucleocapsid protein) and OPN were analyzed. Wild-type and OPN knockout (KO) mice were compared for RSV infection following intranasal inoculation with 1 million pfu. Mice were examined on days 5 and 8 pi for expression of inflammatory lung and serum proteins.

Results: RSV-infected Hep2 cells showed increased OPN expression by 48 h pi that was maintained for 72 h pi. Cells transfected with shOPN, which down-regulated OPN prior to infection had a decrease in RSV titer. WT mice showed increased OPN expression at day 5 pi in lung sections immunostained with anti-OPN, and RSV-N expression and virus titer were reduced in OPN KO mice compared to WT rA2-L19F-infected mice.

Conclusion: Our results suggest that OPN plays a critical role in RSV infection in Hep2 cells and in RSV-infected mice. However, the mechanism underlying OPN-regulation of RSV infection, remains to be elucidated.

Research supported by: VA Merit Review Grant to SSM and Fulbright scholarship to VS

Presented by: Farnaz Tabatabaian, MD, Resident

Aggressive or Invasive Allergic Fungal Sinusitis?

Farnaz Tabatabaian, Hana Nieber, Panida Sriaroon, Mark Ballow, Mandel Sher. Division of Allergy, Immunology, and Rheumatology, Department of Pediatrics University of South Florida, St. Petersburg, FL University of South Florida Morsani College of Medicine Pediatrics

Keywords: Case report Allergic fungal sinusitis with Curvularia, epidural abscess.

Objective: Allergic fungal sinusitis is a form of chronic rhinosinusitis, which is associated with atopic individuals with nasal polyposis, characteristic CT findings, eosinophilic mucin on pathology, and positive fungal smear or culture. This is a case of allergic fungal sinusitis, a typically non-invasive disease with an uncommon complication of multiple epidural abscesses.

Methods: Imaging, pathology and bacterial cultures were performed at All Children's Hospital.

Results: A 16-year-old African American male with a history of anosmia developed severe headache, fever, and right sided facial numbness. He was initially diagnosed with acute sinusitis and was started on amoxicillin. After a week of therapy on re-evaluation the patient was noted to have evidence of nasal polyposis and left sided facial weakness. CT scan of the head illustrated extensive chronic rhinosinusitis, bony erosion with formation of bilateral frontal epidural abscesses and right temporal abscess. He underwent debridement of the bilateral frontal epidural abscesses and right temporal craniotomy removing the abscess. Microscopic analysis of mucosal fragments illustrated eosinophilic infiltration, chronic inflammation and branching septated melanin positive hyphae. Cultures from the sinus and abscesses grew Curvularia. IgE was significantly elevated at 4509 IU/ml. RAST specific testing for Curvularia illustrated elevated levels of IgE and IgG antibodies. Skin prick testing was positive for Curvularia. The Patient completed an extended course of antifungals as well oral steroids.

Conclusion: This patient illustrates a spectrum of disease that encompasses the progression of allergic fungal sinusitis to a more invasive process as demonstrated by the formation of epidural abscesses.

Abstract #: 14

Presented by: Nhan Tu, MS, Graduate Student

Identification of Bartonella-specific putative regulatory RNAs using RNA-Seq

<u>Nhan Tu¹, Ronan K. Carroll², Lindsey N. Shaw², Burt Anderson¹</u> ¹University of South Florida Morsani College of Medicine, Department of Molecular Medicine, ²University of South Florida College of Arts and Sciences, Department of Cell Biology, Microbiology and Molecular Biology

Keywords: RNA-Seq, Bartonella henselae, regulatory RNA, gene regulation

Objective: RNA-Seq is an increasingly utilized technique that employs next generation sequencing technology to study the transcriptome. RNA-Seq has been used to compare bacteria transcriptomes under various conditions resulting in improved genome annotation, novel regulatory RNAs and coding sequences, elucidated operon structures, and mapping of transcription start sites. Bartonella henselae is an emerging pathogen that infects humans scratched by an infected cat, which can cause cat scratch disease, fever with bacteremia, endocarditis, or bacillary angiomatosis. Several virulence-associated genes regulated by two component systems and alternate sigma factors have been described. To identify additional novel regulatory factors, we performed RNA-Seq using B. henselae Houston-1.

Methods: Total RNA was extracted and ribosomal RNA was removed. The enriched RNA was fragmented, converted into cDNA, and sequenced using an Ion Torrent PGM.

Results: Nine novel, highly expressed transcripts of 190-200 nucleotides were identified. These transcripts are either in intergenic regions or they overlap annotated genes that encode putative proteins of unknown function. A sequence alignment of the transcripts revealed 75-100% nucleotide identity. Based on their sizes and locations, we hypothesize that these transcripts may regulate gene expression in B. henselae. Bioinformatic analysis indicates that this family of putative regulatory RNAs is highly conserved in Bartonella species but not found in other alpha-proteobacteria.

Conclusion: We are using an anti-sense RNA approach and over-expression to determine their role in expression of virulence-associated genes. Identification of novel regulatory RNAs may provide potential drug targets against pathogenic Bartonella species.

Clinical Experience With Oxaliplatin (O) Desensitization (OD): A Case Series

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Keywords: Drug Allergy, Desensitization

Objective: Oxaliplatin is a platinum based cancer drug, and hypersensitivity reactions to O limit the ability to receive chemotherapy.

Methods: This is a retrospective analysis from May 2008 to October 2012 of patients who underwent OD after experiencing a hypersensitivity or severe adverse reaction to O. Each OD consisted of four infusions. Patients received intravenous (IV) diphenhydramine, 50mg; famotidine, 20mg; dexamethasone, 50mg; and oral acetaminophen, 625mg an hour prior to the OD. The total O dose was based on body surface area. Subsequently, 1/1000th of the total O was added to 100mL of 0.9% normal saline (NS) and infused over one hour; 1/100th of remaining O in 100mL NS was infused over the second hour; 1/10th of the remaining O in 100mL NS was infused over the second hour; 1/10th of the remaining O in 100mL NS was infused over the fifth and sixth hours. An additional dose of dexamethasone, 50mg IV was given prior to the final infusion.

Results: 29 patients underwent one or more OD (total, 85). One did not complete the OD due to flushing, tachycardia, and wheezing. The remaining 84/85 (99%) were successful. 60/85 (71%) reported no side effects. 24/85 (28%) experienced rash, flushing, palmar erythema or shortness of breath, all but one of which resolved following diphenhydramine, 50mg IV. One patient received epinephrine, 0.3mg IM, due to throat tightness and dyspnea with resolution of symptoms.

Conclusion: OD, using a standard protocol, provides a safe and effective method for patients with hypersensitivity or severe adverse reaction to O to receive chemotherapy.

Abstract #: 16

Presented by: Jla-Wang Wang, PhD, Faculty

LRBA Causes Immunodeficiency and Autoimmunity by Deregulating NFkB-mediated Multiple Immune Effectors Critical for B Cell Activation

<u>Jia-Wang Wang, PhD¹, Michelle Reiser, MS¹, Kunyu Li, BS¹, Eileen Rifkin¹, Bangmei Wang¹, Narasaiah Kolliputi, PhD¹, Richard F Lockey, MD^{1,2}. ¹Division of Allergy and Immunology, Department of Internal Medicine and Department of Molecular Medicine, University of South Florida Morsani College of Medicine, and ²James A. Haley Veterans' Hospital,, Tampa, FL</u>

Keywords: LRBA, Immunodeficiency, Autoimmunity

Objective: The absence of lipopolysaccharide-responsive beige-like anchor (LRBA) gene causes common variable immunodeficiency (CVID), autoimmunity and chronic inflammation. It is the only CVID gene that regulates vesicle trafficking and signal transduction, required for the regulation and function of many immune molecules. It is hypothesized that LRBA deficiency causes these medical conditions by deregulating multiple critical immune effectors.

Methods: LRBA was knocked down in Raji lymphoma cells by the short hairpin RNA (shRNA) technique. Antibodies to LRBA and dominant negative mutants also were used to repress LRBA. The levels of CVID receptors, toll-like receptor 4 (TLR4) and cytokines and the activation and nuclear translocation of AKT, nuclear factor kappa beta (NFkB) and mitogen-activated protein kinases (MAPKs) were analyzed by flow cytometry, enzyme-linked immunosorbent assay (ELISA) and Western blot.

Results: Knockdown of LRBA significantly increases cell survival and downregulates CD19, CD20, transmembrane activator and calcium modulator and cyclophilin ligand Interactor (TACI), TLR4 and p42/44. It also inhibits NFkB nuclear translocation and upregulates AKT, CD21, B cell-activating factor receptor, p38, Jun N-terminal kinase, tumor necrosis factor alpha (TNFa) and IL-10. Antibodies to LRBA in vivo also decrease the proinflammatory cytokines IL-6 and TNFa

Conclusion: Deregulation of these critical Immune effector genes and increased cell survival may contribute to CVID, autoimmunity and chronic inflammation caused by LRBA deficiency.

Research supported by: The Joy McCann Culverhouse Endowment to the Division of Allergy and Immunology.

Presented by: Jillian Whelan, MS, Graduate Student

Exploitation of the Host Ubiquitin System by Respiratory Syncytial Virus Nonstructural Protein 2

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Keywords: RSV, ubiquitin, host-pathogen interactions

Objective: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infection in young children worldwide. The RSV nonstructural protein 2 (NS2) is a multifunctional protein important for viral replication and disease pathogenesis and is essential for RSV-induced proteasomal degradation of host STAT2. We investigated the mechanism by which NS2 interacts with the host ubiquitin system during infection.

Methods: 293T cells were transfected with plasmid DNA. Co-IPs were performed for protein-protein interactions and western blotting for protein expression. A549 cells were infected with recombinant wild-type RSV (rA2) or mutated recombinant RSV at an MOI of 3 and harvested 16 hours post infection. NS2 mutations were designed using computational analysis and generated via site-directed mutagenesis. ImageQuant TL v2005 was used for densitometry analysis.

Results: Co-transfection of 293T cells with NS2 and ubiquitin increased ubiquitination of host proteins compared to ubiquitin alone. Similarly, A549 cells infected with rA2 increased ubiquitination compared to cells infected with recombinant RSV lacking the NS2 gene. Infected A549 cells treated with 10µM MG-132 for four hours did not result in a change in ubiquitin expression. NS2 co-immunoprecipitated with specific ubiquitin ligase complex proteins. Mutation of NS2 residues identified several residues that are vital to NS2-induced ubiquitination of host proteins.

Conclusion: Results indicate NS2 induces ubiquitination of an array of host proteins in a proteasome-independent manner, possibly via interaction with host ubiquitin ligase complex proteins. NS2-induced ubiquitination likely targets host anti-viral processes and can be limited by mutation of key NS2 residues.

Research supported by: SIPAIID NIAID USF

Abstract #: 18

Presented by: Mahasweta Das, PhD, Staff

A "Nano-cell" strategy to treat lung cancer

Mahasweta Das^{1,2}, Mark Howell², Shaily Sharma¹, Allison Nelson³, Swandharya R. Rajavel³, Subhra Mohapatra ^{1,2,4} and Shyam <u>S. Mohapatra ^{1,3,4}</u> ¹ USF Morsani College of Medicine, Nanomedicine Research Center, ²Department of Internal Medicine, ³Department of Molecular Medicine, ⁴James A Haley Veteran's Hospital and Medical Research Center, Tampa, FL

Keywords: Sertoli cell, lung cancer, Lipid Micelle Nanoparticles, Drug toxicity

Objective: To overcome the current limitation of drug delivery to lung and treat lung cancer, we have developed a "nano-cell" strategy using isolated rat Sertoli cells (SC) and Lipid Micelle Nanoparticles (LMNs).

Methods: SCs were isolated from rat pups and cultured. LMNs preloaded with doxorubicin (Dox; DLMN) were incubated with SCs. In vitro Dox uptake was studied using the confocal microscopy. C57/BL6 mice were injected with LLC1 cells through the tail vein (i.v.). 7 and 14 days after LLC1 injection, SCs loaded with Dox, LMN or DLMN were injected (i.v.) in each mouse. Mice were euthanized 21 days after LLC1 injection and blood, lung, heart, liver, kidney and spleen were collected and processed for future experiments. Mouse survival and body weight changes were used to evaluate the disease progression. Lung nodule area was measured from low magnification images using image J. H&E staining was performed to confirm the nodule formation inside the lung tissues. Cardiac Troponin Inhibitory subunit cTnI) was used as marker for the cardiac toxicity after drug treatment.

Results: Kaplan Meier survival analysis showed significant increase in survival of the mice after SC-Dox or SC-DLMN treatment. Area of tumor nodule was significantly decreased in the Dox or DLMN treated groups. cTnl expression was decreased in cardiac tissue of DLMN treated mice compared to that of Dox treated mice.

Conclusion: SCs successfully deliver payloads to the lungs without causing adverse effects. Dox or DLMN delivered to the lungs prevent the LLC1 induced tumor nodules in the lung. While efficacy of DLMN in reducing the tumor growth was comparable to that of Dox, DLMN shows advantage in causing significantly less cytotoxicity compared to Dox.

Research supported by: National Institute of Health R01CA152005

IDH1 Mutation in Prostate Cancer: R132H and Beyond

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Keywords: Prostate cancer, mutation,

Objective: Reports on mutations in the IDH1 gene in prostate cancer focus on the evolutionarily conserved residue R132. One study reported R132 mutations in 2/75 (2.7%) prostate cancers; the other study did not find R132 in 4 prostate cancers or the 2 prostate cancer cell lines. We studied the IDH1 mutations in our prostate cancer targeted exon sequencing database

Methods: Targeted exon sequencing was performed on 52 samples of prostate cancers as part of Moffitt Cancer Center's Total Cancer Care initiative. The coverage was set to be at least 50 fold. 51/52 samples are treatment naïve primary prostate cancer obtained during radical prostatectomy and 1 sample is a treatment naïve prostate cancer brain metastasis. Comparison was made to the 1,000 genomes project, Ployphen and COSMIC data to exclude likely polymorphisms.

Results: 1/51 (2%) primary prostate cancers harbor the R132H mutation, which is known to generate the oncometabolite, (R)-2-hydroxylutarate. Y183C was identified in 1/51 samples. This amino acid in exon 6 of IDH1 is predicted to be "damaging" by PolyPhen (2.89). Another prostate cancer had T325M mutation and is predicted to be "probably damaging" by Polyphen. V178I in IDH1 was also identified and is thought to be an inherited variant, given it has an allele frequency of 4% in 1000 Genomes, 5% in european, and 8% in african-american. Among the frequent gene mutations in metastatic prostate cancer, only a missense mutation in the androgen receptor (H875Y) was identified in the brain metastasis. This H875Y has been linked to androgen receptor.

Conclusion: Mutations in IDH1 R132H and Y183C are identified in prostate cancer. This holds further implications for future studies on prostate cancer, and may point to an interesting target in the disease.

Abstract #: 20

Presented by: Ryan Green, MS, Graduate Student

Expansion of a Cancer Stem Cell Sub Population by Culture on a 3D Fibrous Scaffold <u>Ryan Green, Mark, Howell, Chunyan Wang, Allison Nelson, Sowndharya, Rajavel, Mahmoud Alibrahim, Srinivas Bharadwaj,</u> <u>Shyam Mohapatra and Subhra Mohapatra</u> University of South Florida Morsani College of Medicine, Department of Molecular Medicine

Keywords: Cancer, Cancer Stem Cells 3D Culture

Objective: Cancer stem cells (CSCs) are a sub population of cells found within tumors possessing a phenotype of enhanced drug resistance and metastasis. These cells are thought to be the major contributors to the recurrence of cancer following initial rounds of treatment. However, CSCs represent a minority population in tumors and an expansion of these cells may be useful in screening of drugs with the potential to treat otherwise drug resistant forms of cancer. Since tumoroids grown on 3D scaffold rapidly develop an in vivo tumor like phenotype, we examined whether these cells possess CSC phenotype.

Methods: Mouse and human lung cancer cell lines; LLC and H1975, were cultured on this scaffold and compared to monolayer controls. Biopsies from subcutaneous murine LLC tumors were also cultured on scaffold. CSCs were identified by the presence of the stem cell transcription factors Oct-4, Sox-2, and NANOG and the surface receptor phenotype CD44high CD24low by immunostaining and flow cytometry, respectively. Side population (SP) analysis was performed by flow cytometry to identify the proportion of cells with active ABCG2 drug efflux transporter.

Results: Scaffold supported the growth of these cell lines and promoted the formation of tight aggregates, known as tumoroids. Immunostaining revealed a significant increase in CSC transcription factors and flow cytometry confirmed an increased number of CSCs in the tumoroids compared to monolayer. SP analysis revealed a greater number of drug effluxing cells in the tumoroids.

Conclusion: These results demonstrate that culturing tumor cells on fibrous scaffold results in an increase in the proportion of CSCs in the tumoroids of LLC and H1975 cell lines. Thus tumoroids can be used to screen for novel drugs targeting CSCs.

Presented by: Chen Hu, PhD, Postdoctoral Fellow

Ubiquitin Specific Peptidase 10 (USP10) Deubiquitinates and Stabilizes MutS Protein Homolog 2 (MSH2) to Regulate Cellular Sensitivity to DNA Damage

<u>Chen Hu¹, Mu Zhang¹, Wenlong Bai¹, Xiaohong Zhang¹, Dan Tong², Guo-Min Li², Zhenkun Lou³, ¹University of South Florida Morsani College of Medicine Department of Pathology and Cell Biology, ²College of Life Sciences, Wuhan University, Wuhan, China & Graduate Center for Toxicology, and, Markey Cancer Center and Department of Molecular & Cellular Biochemistry, University of Kentucky College of Medicine, Lexington, Kentucky, ³Division of Oncology Research, Mayo Clinic, Rochester, Minnesota</u>

Keywords: USP10, MSH2, Deubiqutinating enzymes, MSH2 Stability, DNA Damage

Objective: MSH2 protein level is regulated by ubiquitin-proteasome pathway. But the reversed process to counteract the ubiqintination of MSH2 remains unknown. Our objectives: 1. Identify MSH2's binding partner which regulate MSH2's stability 2. Understand how MSH2 is regulated upon DNA damage 3. Understand the potential roles of ubiquitin-proteasome pathway in cancer

Methods: Cell culture, Plasmids construction, Western blot and Immunoprecipitation, In vivo ubiquitination assay, In vitro ubiquitination and deubiquitination assay.

Results: USP10 deubiquitinates MSH2 leading to the MSH2 stablization and the sensitization of cells to DNA damage.

Conclusion: USP10 regulates cellular response to 6-TG and MNNG by stabilizing MSH2.

Research supported by: NCI R01CA164147 to Xiaohong Zhang

Abstract #: 22	Presented by: Chengbin Hu, PhD, Graduate
	Student

Targeting Epithelial-Mesenchymal Transition in the Treatment of Ovarian Cancer

<u>Chengbin Hu^{1,2} and Shu-Feng Zhou¹</u> ¹Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, ²Department of Molecular Medicine, USF Morsani College of Medicine

Keywords: Ovarian cancer; sodium-potassium ATPase; PBEF/NAMPT; EMT.

Objective: Epithelial ovarian cancer (EOC) is the most lethal cancer in women. The epithelial-mesenchymal transition (EMT) plays a crucial role in the initiation, growth, invasion and metastasis of EOC. The purpose of this study is to identify novel targets to reduce EMT for treatment of ovarian cancer. We hypothesize that Na+/K+ ATPase and nicotinamide phosphoribosyltransferase (PBEF/NAMPT) could modulate EMT of EOC and thus may represent new therapeutic targets.

Methods: ATPase and PBEF/NAMPT will be manipulated using pharmacological and biological approaches. The EMT markers of human EOC cell lines (OVCAR3-5 & SKOV3) and normal ovarian epithelial cell line will be monitored in the gain-of-function and loss-of-function assays. Other markers of cell cycle, apoptosis, autophagy, senescence, invasion & migration, chemoresistance, and stemness of cells will be determined. Na+/K+ Nude mice bearing xenograft tumor will be used in tumor growth inhibition and mechanistic study.

Results: Modulation of Na+/K+ ATPase and PBEF/NAMPT will alter EMT of EOC.

Conclusion: Na+/K+ ATPase and PBEF/NAMPT may represent novel therapeutic targets for ovarian cancer

Presented by: Ravi Kasiappan, PhD, Postdoctoral Fellow

1,25-dihydroxyvitamin D3 increases cisplatin sensitivity in ovarian cancers through microRNA-498

Ravi Kasiappan¹, Yuefeng Sun¹, Waise Quarni¹, Yin Xiong², Johnathan M. Lancaster², Xiaohong Zhang¹ and Wenlong Bai¹ ¹Department of Pathology and Cell Biology, University of South Florida Morsani College of Medicine and ²Department of Women's Oncology, H. Lee Moffitt Cancer Center and Research Institute

Keywords: Cisplatin, miR-498, ovarian cancer apoptosis and cell growth

Objective: Ovarian cancer is the deadliest gynecologic malignancy in women in the United States. Although cisplatin-based multi-modality treatment has prolonged survival, the development of chemo-resistance severely limits its success. The sensitization of cancer cells to drug-induced apoptosis has become an important strategy in overcoming chemo-resistance. Our recent studies have shown that 1,25-dihydroxyvitamin D3 (1,25D3) suppresses telomerase expression and cancer cell growth through microRNA-498 in ovarian cancers. The main objective of the present studies is to assess the effect of 1,25D3 in regulating cisplatin sensitivity and the involvement of microRNA-498.

Methods: Cisplatin sensitive (A2780) and resistant (A2780-CP) cells were used as the main cellular model to study the effect of 1,25D3 on cisplatin sensitivity. Molecular methods, including qPCR, flow cytometry, Western blot and confocal microscope were employed for different analyses

Results: Our studies found that pre-treatment of cells with 1,25D3 significantly increased cisplatin sensitivity and re-sensitized multiple cisplatin-resistant cells to the drug. Pre-treatment of 1,25D3 made cisplatin capable of inducing apoptosis in cisplatin resistant cells, which was blocked by calpain inhibitor PD151746. Depletion of vitamin D receptor by shRNA or miR-498 by sponges eliminated the effect of 1,25D3 on cisplatin-induced cell death. In cisplatin resistant cells, combination of 1,25D3 and cisplatin induced the mitochondrial release and nuclear translocation of AIF whereas cisplatin alone failed to induce these effects.

Conclusion: This study may lead to the development of novel strategy to overcome the cisplatin resistance and prolong the survival of ovarian cancer patients with active 1,25D3 compounds.

Abstract #: 24

Presented by: Jaymin Kathiriya, MS, Graduate Student

Identification of Structurally Disordered Kinases as Functional Kinome Hubs

Jaymin Kathiriya¹, Ravi Ramesh Pathak¹, Eric Clayman¹, Bin Xue⁶, Vladimir Uversky^{3,4,5}, and Vrushank Davé^{1,2} ¹University of South Florida Morsani College of Medicine, Department of Pathology and Cell Biology, ²Department of Molecular Oncology, H. Lee Moffitt Cancer Center and Research Institute, ³Dept of Molecular Medicine, ⁴USF Health Byrd Alzheimer's Research Institute ⁵Institute for Biological Instrumentation, Russian Academy of Sciences, Moscow, Russia, ⁶Department of Cellular, Microbiology, and Molecular Biology, University of South Florida College of Arts and Sciences

Keywords: Protein-protein interaction networks, intrinsically disordered proteins, network medicine, systems biology, kinase

Objective: Kinase inhibitors used for pharmacotherapy suffer from adverse off-target effects and elicit compensatory signaling. Thus, there is a need for a novel approach to inhibit multiple kinases with minimum side-effects. We aim to perform a systems level network analysis to reveal kinases central to a kinome network. Unique structural features of these modulators can be utilized for therapeutic interventions.

Methods: We use kinome-wide structural bioinformatics approach and identify a novel strategy to therapeutically target kinase cascades. We construct a network of kinase-kinase interactions to identify significant cross-talk in the kinome. Network analysis is used to identify kinome modulators.

Results: Structural disorder analysis on the entire kinome and its influence on multiple kinase interactions reveal that structurally disordered kinases are topologically significant kinome modulators. These kinome modulators engage in myriad kinase-kinase interactions, forming kinome sub-networks, and driving pathogenesis of cancer and other diseases. Biological validation of regulatory interplay between kinome modulators SRC and AKT kinases confirms the need for combination therapy.

Conclusion: Our findings identify novel kinome modulators driven by structural disorder. Kinase-kinase interactions underlie pathogenesis of cancer. Targeting regulatory cross-talk between disparate pathways controlled by kinome modulators can lead to reduced oncogenic potential in cancer cells.

Research supported by: This work was supported by American Heart Association Grant SDG-155-N (V.D.) and Moffitt Cancer Center Lung SPORE Career Development Grant (V.D.).

Aspirin as targeted therapy? Evaluating the PIK3CA mutation as a predictive biomarker in colorectal cancer patients.

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Keywords: Colorectal cancer, PIK3CA mutation, aspirin

Objective: Recent data has shown that regular ASA use improves overall survival in CRC patients with PIK3CA mutations. However, these studies have had limited mutant CRC patients and highly selected populations with earlier stage disease. We performed a collaborative study between two academic institutions to explore the association between regular ASA use and survival in unselected CRC patients.

Methods: Patients with PIK3CA mutated CRC were identified at Moffitt Cancer Center and Royal Melbourne Hospital. Prospective data (including age, sex, site of disease) and survival data were available. At MCC, PIK3CA mutations were identified by exome sequencing using an Illumina Next Generation Sequencing platform. At RMH, Sanger sequencing was used to identify PIK3CA mutations. Survival analyses were conducted using Cox logistic regression. ASA use data was collected through retrospective chart review.

Results: We identified 185 CRC patients with the PIK3CA mutation. In univariate analyses, regular ASA use was not associated with improved overall survival (HR 0.96, p=0.86) or improved cancer-specific survival. In patients with stage-2 or stage-3 disease, regular ASA use did not improve recurrence-free survival. In stage-4 patients, there was an association between regular ASA use and improved overall survival (HR 0.40, p=0.06). However, this was not sustained in multivariate analysis (HR 0.45, p=0.19).

Conclusion: In contrast to previously reported data, our work did not validate improved overall survival in PIK3CA mutant CRC patients who took aspirin. We also did not validate the recurrence free survival benefits to aspirin as adjuvant therapy. To our knowledge, this is the largest patient population examining ASA use in PIK3CA mutated CRC.

Research supported by: Moffitt Cancer Center

Abstract #: 26

Presented by: Prerna Malaney, BS, Graduate Student

Synergistic role of PTEN and Lkb1 loss in KRAS-driven lung cancers

<u>Prerna Malaney, Vrushank Davé,</u> Department of Pathology and Cell Biology, Morsani College of Medicine, USF, Tampa, FL, Department of Oncological Sciences, Moffitt Cancer Center, Tampa, FL

Keywords: non-small cell lung cancer, PTEN, KRAS, Lkb1

Objective: Lung tumors harboring co-mutations in the PI3K/AKT/mTOR or AMPK/mTOR and the RAS signaling cascades are often aggressive showing epithelial-mesenchymal transition (EMT) and metastasis leading to poor prognosis. KRAS remains undruggable while rapalogs targeting mTOR induce compensatory activation of AKT. Further, differential clinical outcomes are observed in patients having identical KRAS mutations due to secondary mutations in tumor suppressor genes.

Methods: To address the heterogeneity in mutant KRAS tumors to standard chemotherapy, we have developed two conditional inducible mouse models having loss of tumor suppressors PTEN and Lkb1 respectively in an oncogenic KRAS background. Both, the PTEN $\Delta\Delta$ /KRasG12D and the Lkb1 $\Delta\Delta$ /KRasG12D models use a lung specific CCSP-promoter and Cre/loxP technology to mediate deletion of PTEN or Lkb1 respectively.

Results: Microarray studies in PTEN-null lung epithelial cells reveal transcriptional activation of RAS pathway associated candidate genes. Both Dox-induced PTEN $\Delta\Delta$ /KRasG12D and Lkb1 $\Delta\Delta$ /KRasG12D lung tumors show induction of SNAIL1, SLUG, ZEB-2 and SOX2 genes. However, LkB1 $\Delta\Delta$ tumors show aberrant AMPK activity.

Conclusion: PTEN or Lkb1 loss accelerates KRAS-driven lung tumor progression, initiating EMT and increased stemness. Both models recapitulate features of human tumors and represent ideal preclinical systems to identify appropriate therapeutic regimens in genetically stratified tumor types.

Research supported by: AHA-SDG, NIH Lung Cancer Spore (Moffitt)

Presented by: James Mauro, BA, Med II Student

Functionally distinct gene classes as larger or smaller transcription factor traps

<u>James A. Mauro and George Blanck</u> Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL

Keywords: genomics, bioinformatics, apoptosis, transcription factors, gene size

Objective: In cancer biology, most molecular regulatory mechanisms are casually treated as on/off switches for specific cancer hallmarks, despite the lack of compelling evidence that cancer hallmarks can be exclusively attributed to specific regulatory proteins. To consider a novel paradigm for the basis of regulating a set of effector genes for proliferation, versus apoptosis-effector genes, we used a bioinformatics approach to ascertain differences between the transcription factor binding site occurrences in the two sets of genes.

Methods: Transcription factor binding sites, and open chromatin regions, were located in the human genome database using novel perl programs; and aligned with the proliferation and apoptosis-effector genes.

Results: Results indicated that there are more binding sites per gene, for transcription factors that regulate both proliferation and apoptosis, among the proliferation-effector genes than among the apoptosis-effector genes. Proliferation-effector genes also had more open chromatin regions. The larger number of open chromatin regions per gene, among the proliferation-effector genes, applied over a large number and very wide variety of cell lines and cell types. We also applied this "transcription factor trap" paradigm to the question of why p53 and interferon regulatory factor-1 (IRF-1) first activate cell cycle arrest genes followed by apoptosis genes, with results indicating the cycle arrest genes are larger p53 and IRF-1 traps.

Conclusion: These data support the idea that, as a set of transcription factors becomes active, there is a stochastic component leading to the accumulation of these transcription factors on genes that effect an initial phenotype before their accumulation on genes that effect a subsequent phenotype.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 28

Presented by: Sajitha Nair, PhD, Postdoctoral Fellow

Identification and characterization of 'leukemia inducing factor: A novel diagnostic tool to identify acute lymphoblastic leukemia and diffuse lymphoma

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Keywords: Acute lymphoblastic leukemia, diffuse lymphoma, pediatric cancer

Objective: The aim of this study was to confirm the prior in-vitro findings (Tebbi, CK US Patent # 8623647, article in preparation). This study will lead to a novel diagnostic method which identifies individuals susceptible to development of acute lymphoblastic leukemia and diffuse lymphomas. Additionally, characterize and identify the 'Protein complex X' by state of art knowledge of proteomics & genomics. The leukemia inducing proteins, designated 'Protein complex X' has shown to identify and separate these individuals from normal controls (Tebbi, C K article in preparation).

Methods: The human PBMCs were isolated from the normal individual/sickle cell anemia patients (controls) and those with ALL in remission. The PBMCs were exposed to the 'Protein X complex' for 72 hours at 370 C/5% CO2 were subjected to Immunophenotyping for the panel of ALL cells surface markers using flow cytometry. Simultaneously, the cells lysates were subjected to western blotting, RNA isolation followed by RT-PCR followed by critical analysis, in order to study the signaling cascade in the receptor –ligand interaction. Furthermore, the Protein X complex was characterized using FPLC and Laser spectrometry/Mass spectrometry, using proteomics techniques.

Results: The Protein X complex (leukemia inducing factors) was capable of re-inducing the ALL cell surface markers in the former ALL patients and patients with ALL in remission in-vitro and not in the normal individuals or sickle cell anemia patients. The control group developed no significant changes characteristic of ALL cell surface markers.

Conclusion: This discovery can potentially lead to the development and screening of the therapeutic vaccine for diffuse lymphoma and acute lymphoblastic leukemia.

Presented by: Nadine Nelson, MS, Graduate Student

The Role of Ikaros in Treg Development and Function in a Murine Pancreatic Cancer Model

Nadine D. Nelson¹ Shengyan Xiang², Xiaohong Zhang², Shari Pilon-Thomas³, Nasreen Vohra⁴ and Tomar Ghansah² ¹Department of Molecular Medicine, and ²Department of Pathology & Cell Biology, Morsani College of Medicine, University of South Florida, Tampa, FL, ³Immunology Program, H. Lee Moffitt Cancer Center, Tampa, FL, ⁴East Carolina University, Greenville, NC

Keywords: Regulatory T Cells, Ikaros, Signal Transduction, Transcription Factors, Tumor Immunity

Objective: The transcription factor Ikaros is critical for normal T cell development. In pancreatic cancer (PC) hosts, regulatory T cells (Tregs) are elevated and suppress anti-tumor immune responses. The transcription factor FoxP3 is key for Treg development and function. In this study, we aim to identify the role of Ikaros in regulating Tregs in a PC microenvironment.

Methods: Using our murine model of PC, we isolated splenocytes from tumor-bearing (TB) and control mice and performed western blot and quantitative real-time PCR analyses to evaluate Ikaros mRNA and protein expression. We also carried out in vitro degradation assays to determine a possible mechanism by which Ikaros is regulated in response to PC tumor-derived factors (TDF) using splenocytes. Flow cytometry analyses were also used to immunophenotype T cell populations in splenocytes from control and TB mice. Next, magnetic activated cell sorting (MACS) was used to sort CD3+ T cells from TB and control splenocytes for western blot analyses of Ikaros and FoxP3 expression.

Results: Our results showed no difference in Ikaros mRNA expression but reduced Ikaros protein expression in splenocytes from TB mice compared with controls. Our in vitro results suggest that PC-TDF cause proteasomal degradation of Ikaros. Analyses of T cells by flow cytometry revealed decreased CD4+ and CD8+ T cell percentages but increased CD4+CD25+ Tregs in TB splenocytes compared with controls. Also, Ikaros protein expression was downregulated while FoxP3 protein expression was upregulated in sorted TB T cells, compared with control.

Conclusion: These findings suggest that PC progression is associated with reduced lkaros expression, which may lead to loss of Treg homeostasis and function and dampened anti-tumor immune responses.

Abstract #: 30 withdrawn 1 30 14

Presented by: Brian Orr, MD, Resident

Perception and Utilization of Intraperitoneal Chemotherapy: A Survey of Florida's Gynecologic Oncologists

Brian Orr, MD', Patrick Teefey, MD', Sachin Apte⁺ ,Robert Wenham⁺ University of South Florida Morsani College of Medicine, Department of Obstetrics & Gynecology, ²Moffitt Cancer Center

Keywords: Ovarian Cancer Chemotherapy

Withdrawn

Methods: With permission from the Florida Society of Gynecologic Oncology, a voluntary email survey was distributed to the 59 physician members.

Results: We had a response rate of 44% (26/59). IP chemotherapy is used by 84.7% (22/26) however only routinely used by 69.3% (18/26). Of providers using IP chemotherapy, 73% modify the published regimen, and 42% provide treatment as an outpatient (GOG 172 protocol is inpatient). Providers in small practices, >20 years removed from training, and those without midlevel provider support were less likely to use IP chemotherapy.

Conclusion: Despite a proven survival benefit, improved toxicity profile and regimen tolerability, our survey suggests an underutilization of IP chemotherapy. Regimen modification and outpatient administration may improve treatment utilization

Presented by: Angela Poff, MS, Graduate Student

Non-toxic metabolic therapy – ketosis and hyperbaric oxygen – elicit potent anti-cancer effects in vivo and in vitro <u>Angela M. Poff¹,Nathan P. Ward¹, Thomas N. Seyfried²; Dominic P. D'Agostino¹</u>, ¹University of South Florida Morsani College of Medicine, Department of Molecular Pharmacology & Physiology, ²Department of Biology, Boston College

Keywords: Warburg effect, Cancer, Metastasis, Cancer metabolism

Objective: The Warburg Effect and tumor hypoxia underlie a unique cancer metabolism characterized by glucose dependency and mitochondrial dysfunction. This metabolic phenotype, exhibited by most if not all cancer types, offers promising new therapeutic opportunities. We hypothesized that we could exploit this phenotype by creating an unfavorable metabolic environment for cancer with a ketone-supplemented ketogenic diet. This diet restricts glucose availability to the tumor while elevating blood ketones, a protective and efficient energy source for normal cells that damage cancer. Simultaneous hyperbaric oxygen therapy can further damage cancer by inducing free radical production within tumors.

Methods: We hypothesized that this non-toxic combination therapy would be an effective treatment, so we tested its effects in the VM-M3 mouse model of metastatic cancer. To further characterize the effects of these therapies, we measured proliferation, viability, and ROS production in VM-M3 cells exposed to the following conditions: high glucose (control; 25mM), low glucose (LG; 3mM), ketone supplementation (β HB; 5mM), hyperbaric oxygen (HBOT; 90 min, 2.5 ATA), or combination therapy (LG+BHB+HBOT).

Results: Treated mice exhibited decreased tumor growth rate, decreased metastatic spread, and lived 103% longer than controls. Proliferation of all treated cells was significantly decreased from controls for up to 96 hours. Viability was decreased by 19% in LG, 13% in β HB, and 38% in LG+ β HB+HBOT treated cells. ROS production was increased by 47% in all HBOT treated cells.

Conclusion: This study strongly supports further investigation into the use of these non-toxic metabolic therapies as potential cancer treatments or adjuvants to standard care.

Research supported by: ONR and Scivation, Inc

Abstract #: 32

Presented by: Waise Quarni, MS, Graduate Student

VDR-RIPK1 Complex and its Implication in Vitamin D Action and Necroptosis

Waise Quarni, Ravi Kasiappan, Yuefeng Sun, Panida Webb and Wenlong Bai. Department of Pathology and Cell Biology, University of South Florida, Morsani College of Medicine Tampa, Florida

Keywords: Necroptosis, RIPK1, VDR.

Objective: 1,25-dihydroxyvitamin D3 (1,25VD3) and its receptor, vitamin D receptor (VDR), have long been studied for their growth suppressing activity in cancer cells. On the other hand, RIPK1-mediated necroptotic cell death pathway has a great potential in cancer therapy. So far, no studies have been done to investigate the crosstalk between necroptotic pathway and 1,25VD3 sensitivity in cancer cells. The purpose of the present study is to define the relationship between necroptotic pathway and 1,25VD3 induced cell death. Our main objective is to determine whether and how VDR and RIPK1 regulate each other's activity.

Methods: The complex formation between endogenous and transfected VDR and RIPK1 was investigated by coimmunoprecipitation. Levels of VDR and RIPK1 were determined by Western blot analyses in multiple cancer cell lines to identify candidate cell model systems. MTT and luciferase assays were employed to determine the roles of VDR and RIPK1 in growth suppression and the effects of RIPK1 on VDR transcriptional activity, respectively.

Results: Our co-immunoprecipitation studies had shown that VDR formed a complex with the RIPK1 through its Cterminus ligand binding domain. Luciferase reporter assays have shown that RIPK1 decreased VDR transcriptional activity, suggesting a negative role of RIPK1 in 1,25VD3 action. More importantly, our MTT analyses showed that the presence of VDR was crucial to RIPK1-mediated cell death. VDR and RIPK1 protein levels were found to be different in their respective wild type and knockout cells, suggesting a mutual regulation in expression.

Conclusion: We conclude that RIPK1 and VDR have a functional crosstalk and detailed mechanistic studies are needed to translate the crosstalk into novel strategies in cancer therapy.

Presented by: Chantal Reyna, MD, Resident

Axillary Burden of Disease Following False Negative Preoperative Axillary Evaluation

Chantal Reyna, Anne Frelick, Nazanin Khakpour, Christine Laronga, Marie Catherine Lee, John V. Kiluk H. Lee Moffitt Cancer Center and Research Institute, Tampa FL, USF Morsani College of Medicine, Department of Oncologic Sciences

Keywords: Axillary ultrasound Tumor Burden

Objective: Recent advances have impacted axillary management in breast cancer. Preoperative AUS and FNA have a sensitivity of 79-100% and specificity of 96-100% for axillary metastasis. We hypothesize that a false-negative AUS and FNA is predictive of minimal nodal disease at definitive surgery.

Methods: After IRB approval, a single-institution retrospective chart review of female breast cancer patients (pts) receiving AUS from 2004-2013 was performed. Preoperative chemotherapy, recurrent cancer, \geq T3 disease, palpable nodes, and inconclusive FNA were excluded. Pts with positive sentinel node biopsy(SLN) followed by completion axillary dissection(CALND) were evaluated for clinical, radiologic and pathologic data and analyzed by Chi-square using Fisher's exact test. Minimal nodal disease was defined as \leq 2 positive nodes.

Results: A total of 903 AUS were performed; 384 fit inclusion criteria. The false negative rate of AUS was 47% and 45% for AUS/FNA. The overall negative predictive value (NPV) of AUS/FNA was 78%. 73 pts had positive SLN followed by CALND: 55 invasive ductal carcinoma (IDC) and 18 invasive lobular or mammary carcinoma (ILC/IMC). No difference in AUS sensitivity was found (p=0.76). When stratified by histology, the NPV of AUS +/-FNA was 71% for minimal nodal disease in IDC compared to 44% in ILC/IMC. Only 16 IDC pts (29.0%) had \geq 3 positive nodes compared to 10 ILC/IMC pts (55.5%)(p = 0.05).

Conclusion: Preoperative AUS/ FNA use is increasing, as nodal disease remains an important prognostic factor. Our data shows a high NPV of AUS/FNA for IDC. In the majority of false negative evaluations, IDC had a low pathologic burden of axillary disease. Histology should be considered when contemplating CALND after negative AUS/FNA.

Abstract #: 34

Presented by: Yaman Suleiman, MD, Resident

The results of a Phase I study of combination of gemcitabine plus pasireotide (SOM 230) LAR in metastatic pancreatic cancer (MPC).

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Keywords: phase I, gemcitabine, pasireotide, metastatic pancreatic cancer (MPC).

Objective: Pasireotide is a cyclohexapeptide engineered to bind to multiple somatostatin(SST) receptor subtypes to mimic the action of natural somatostatin and is potent inhibitor of insulin-like growth factor-1(IGF-1). SST receptors and IGF receptors are highly expressed in pancreatic cancer, therefore potentially making it a valuable target.

Methods: A 3+3 dose escalation design was used; pts with previously untreated MPC were eligible for the trial. Patients received GEM 1000 mg/m2(weekly IV for 3 out of 4 weeks) and pasireotide according to dose escalation. Two dose levels were planned, 40mg IM and 60 mg IM once a month. Cohort was expanded to 10 more patients at the highest tested dose to further access safety and efficacy. IGF-1, IGFBP, and IGFBP-3 were measured at baseline and with each restaging.

Results: 20 patients enrolled with this study were treated and evaluable for safety and efficacy. No dose limiting toxicities were observed with the two used doses. 12 %(2/16) of pts had partial responses(PR), 56%(9/16) had stable disease(SD) as best response. Median PFS was 4.1 months (range 1 to 16 months) and median overall survival was 6.8 months. Most common grade 3 or 4 toxicities were neutropenia(n=1), and thrombocytopenia(n=1). Median baseline IGF-1 level was lower in pts with SD than in PD (63 vs.71 ng/mL), the median drop in the level of IGF-1 between the first cycle and the last cycle was more prominent in the SD than PD (16 vs. 28 ng/mL).

Conclusion: Pasireotide in combination with gemcitabine was well-tolerated. The disease control rate (56%SD+12%PR)in patients with MPC. Baseline IGF-1 level may potentially be a prognostic and predictive biomarker for pasireotide. These results are promising and warrant further evaluation.

Research supported by: Novartis Pharmaceuticals

Presented by: Yuefeng Sun, PhD, Postdoctoral Fellow

BMP4 Works through ID1 to Regulate FOXO1 Activity and Prostate Cancer Cell Growth and Invasion

<u>Yuefeng Sun, Yonghua Yang, Ravi Kasiappan, Panida Lungchukiet, Waise Quarni, Xiaohong Zhang and Wenlong Bai</u> University of South Florida Morsani College of Medicine Pathology and Cell Biology

Keywords: Prostate Cancer, BMP4, Metastasis

Objective: FOXO transcription factors control the expression of genes involved in apoptosis, cell cycle, and stress responses etc. Our published studies have identified FOXO proteins as the converging nuclear target for steroid hormones and growth factors in prostate cancer cells and shown that they play an essential role in the antagonistic crosstalk between the PTEN and the androgen receptors. A role of FOXO factors in prostate cancer invasion has been suggested but the mechanisms are unclear. The present study defines how FOXO1protein is involved in BMP signaling and prostate cancer invasion through a novel family of binding proteins, the inhibitor of DNA binding (ID) proteins that are known to control tumor invasion and metastasis.

Methods: Yeast 2-hybrid screening was performed to identify new FOXO binding proteins. Multiple human prostate cancer cell lines were used to investigate the FOXO activity and the expression of inhibitor of DNA binding (ID) proteins. Co-immunoprecipitations, MTT, luciferase reporter, siRNA knockdown and trans-well assays were performed to study FOXO-ID interactions and their roles in prostate cancer growth and invasion.

Results: FOXO1 was used as a bait to screen a cDNA library from human prostate cancer and identified ID proteins as novel FOXO interacting proteins. ID1 was shown to be expressed at high levels in androgen-refractory C4-2 and CWR22RV1 cells. Its expression was low in androgen-sensitive LNCaP and CWR22 cells but induced by BMP4. Through ID1, BMP4 decreased FOXO1 activity and promoted prostate cancer cell growth, migration and invasion.

Conclusion: Our data identified new FOXO1 interacting proteins and a new pathway for BMP4 to promote prostate cancer invasion through FOXO inhibition by ID1 binding.

Abstract #: 36

Presented by: Nicole Wells, MS, Graduate Student

Roles of IL-10 and I-309 Cytokines in Reproductive Cancers.

<u>Nicole Wells, Kimberly Dobrinski, Santo Nicosia, Patricia Kruk</u>, Department of Pathology and Cell Biology, University of South Florida Morsani College of Medicine, Tampa, FL

Keywords: ovarian cancer, endometrial cancer, IL-10, I-309, drug resistance

Objective: Endometrial (EC) and ovarian cancers (OC) are leading causes of gynecological death. Understanding mechanisms underpinning cancer could provide new therapies. This study seeks to understand roles for I-309 and IL-10 cytokines in reproductive cancers.

Methods: Protein arrays were carried out on serum (OC patients), urine (EC patients). Student's T test determined significant differences. Western blots and ELISAs were performed using normal and OC cell lines. Western blots of cell lysates were performed using antibodies for I-309, IL-10 and actin. IL-10 ELISA was performed on cell lysates and conditioned media.

Results: Protein arrays for urine of EC patients showed increased I-309 while serum from OC patients had increased IL-10 compared to controls. Western blots confirmed I-309 in OC cell culture lysates and ELISA validated increased IL-10 levels OC cells.

Conclusion: All OC cells exhibited increased I-309 compared to controls and drug resistant cells demonstrated elevated protein levels compared to their drug sensitive counterparts. There are conflicting reports as to the source of I-309 from white blood cells within cancer tissues or from cancer cells themselves, so this study is the first to show that I-309 may be produced by OC cells. Though the anti-inflammatory T-cell inhibitor, IL-10, has been found in reproductive cancers, excretion of IL-10 within OC has not been shown. The present study verified elevated levels of IL-10 within OC cells and future studies will investigate its secretion by OC cells. OC cells, then, produce both cytokines and I-309 may to contribute to drug resistance. Future research will ascertain the subcellular localization of these cytokines within reproductive cancers tissues.

Research supported by: DOD grant W81XWH-10-1-0177

Presented by: Shengyan Xiang, PhD, Postdoctoral Fellow

HDAC6 deacetylates and ubiquitinates MSH2 to maintain proper levels of MutSa

Shengyan Xiang §, Mu Zhang §, Lei Wang, Kendra Williams, Wei Liu, Chen Hu, Joshua Haakenson, Santo V. Nicosia, Wenlong Bai and Xiaohong Zhang §These authors contributed equally to this work. Department of Pathology and Cell Biology, University of South Florida Morsani College of Medicine

Keywords: Histone deacetylase 6 (HDAC6), MutSa, MSH2, Mismatch repair, deacetylation, E3 ubiquitin ligase ubiquitination. **Objective:** To understand the mechanism of regulating the level of MutSa by Histone deacetylase 6 (HDAC6) in mammalian cells upon DNA damage response.

Methods: Immunoprecipitation and Western blotting analyses were performed to analyze protein expression.

Results: MSH2 is a key DNA mismatch repair protein. It forms the MSH2/MSH6 (MutSa) and MSH2/MSH3 (MutSa) heterodimers, which help to ensure genomic integrity. MutSa not only recognizes and repairs mismatched nucleotides, but also recognizes DNA adducts induced by DNA-damaging agents, and triggers cell cycle arrest and apoptosis. Loss or depletion of MutSa from cells leads to microsatellite instability (MSI) and resistance to DNA damage. Although the level of MutSa can be reduced by the ubiquitin-proteasome pathway, the detailed mechanisms of this regulation remain elusive. Here we report that histone deacetylase 6 (HDAC6) sequentially deacetylates and ubiquitinates MSH2. HDAC6 deacetylates MSH2, MutSa disassociates, and monomeric MSH2 is ubiquitinated and degraded by the proteasome pathway. Although HDAC6 is able to markedly reduce the levels of the MSH2 monomer, it can only modestly down regulate the level of MutSa. Nevertheless, absence or depletion of HDAC6 significantly increases apoptosis in cells exposed to the DNA damaging agents: 6-thioguanine (6-TG) and N-methyl-N'-nitro-N-nitrosoguanidine (MNNG).

Conclusion: Overall, we report for the first time that HDAC6 harbors intrinsic E3 ubiquitin ligase activity, and suggest that HDAC6 increases cell tolerance to DNA damage by exerting both E3 ligase and deacetylase activities that promote MSH2 degradation. In addition, our results indicate that HDAC6 is also involved in the in the ubiquitin-proteasome pathway.

Research supported by: Grant support: NCI R01CA164147 to Xiaohong Zhang.

Abstract #: 38

Presented by: Sadaf Aslam, MD, Faculty

Selected Urinary Biomarkers as Early Risk Predictors of Renal Injury in Obese and Dysmetabolic Nonhuman Primates Sadaf Aslam¹, Jennifer D. Newcomb¹, Ellen H. Linden¹, Qi Jiang², and Barbara C. Hansen¹, ¹Obesity, Diabetes and Aging Research Center and Department of Internal Medicine, University of South Florida Morsani College of Medicine, Tampa, FL, and ²David H. Murdock Research Institute, Kannapolis, N.C

Keywords: Urinary biomarkers, GFR, AER, BUN, Creatinine, Diabetes, Nephropathy

Objective: -To evaluate the role of renal injury biomarkers in nephropathy associated with obesity and metabolic dysfunction.

Methods: Renal function parameters such as Albumin Excretion Rate (AER), Glomerular Filtration Rate (GFR) and the renal injury biomarkers; Neutrophil Gelatinase-Associated Lipocalin (NGAL), Kidney Injury Molecule -1 (KIM-1), Monocyte Chemoattractant Protein-1 (MCP-1, Cystatin-C (Cys-C) and Tissue Inhibitor of Metalloproteinase -1 (TIMP-1) were evaluated in a colony of 87 (50 male) rhesus monkeys (Macaca mulatta). Monkeys ranged in age from 8.5 to 40 yrs and in weight from 4.6 to 25.5 kg and were grouped according to metabolic status (normal, dysmetabolic, diabetic) and weight (lean, overweight, obese).

Results: NGAL in overweight monkeys was significantly higher than in lean monkeys (p=0.003) while KIM-1 in obese monkeys was significantly higher than lean monkeys (p=0.015). NGAL and TIMP-1 were significantly higher in dysmetabolic monkeys than insulin-treated diabetics (p=0.05 and p=0.004, respectively). Dysmetabolic monkeys had significantly higher AER (p=0.03) and BUN/Creat ratio (p=.007) than obese normal and diabetic group. MCP-1, TIMP-1, Cys-C and KIM-1 all increased significantly with AER (all p<0.05).

Conclusion: Renal injury biomarkers were correlated with established renal function parameters (AER, BUN/Creatinine) indicating development of chronic kidney disease due to obesity and/or metabolic dysfunction. TIMP-1 appeared to have predictive ability of kidney pathology in dysmetabolic monkeys. There are strong associative relationships between obesity, metabolic dysfunction and nephropathy which should be considered in the development of obesity and diabetes.

Research supported by: National Institute of Aging

Presented by: Margaret Bettin, BA, Med II Student

Gender Differences in Presentation of Coronary Artery Disease in Patients Undergoing Stress Echocardiography and Nuclear Perfusion Testing

Margaret Bettin, Aarti A. Patel, Maleeha Haq, Ryan Martin, Brendan Malik, Michael Scholfield, Bonnie Kirby, Lisa Miller, Arthur Labovitz, University of South Florida Morsani College of Medicine, and, Department of Cardiology, Tampa, FL

Keywords: women, gender, stress test, coronary artery disease, atypical

Objective: We aim to clarify the differences in indications for stress testing between women and men with coronary artery disease upon ischemic evaluation.

Methods: Data was gathered retrospectively from patients who underwent outpatient stress echocardiography or nuclear perfusion testing. Frequencies and student t-tests were used to describe normal versus abnormal stress tests among patients presenting with and without typical symptoms. This data was further stratified by gender.

Results: Of the 131 studies reviewed, 71 were female and 60 were male. Twenty-four females (18%) and 14 males (11%) presented with atypical symptoms (dyspnea, fatigue, poor exercise tolerance, musculoskeletal pain) and underwent stress testing. There was a significant difference (p=0.008) in atypical symptoms prompting a stress test in females over males. There was no significant difference between the two groups for overall positive stress test (p=0.404) or those with positive stress test presenting with atypical symptoms (p=0.09). Interestingly, of those presenting with atypical symptoms and positive stress test, only women, and not men, demonstrated coronary artery disease on LHC.

Conclusion: Women may not manifest coronary artery disease with typical chest pain as demonstrated by our study. In our population, atypical symptoms more often prompted a stress test in women than compared to men, which was found to be statistically significant. Moreover, of those with positive stress tests it was suggested that women were more likely than men, although not statistically significant, to have coronary disease on LHC. These results suggest that women with cardiac disease may present differently than men and that evaluation should include symptoms other than chest pain.

Abstract #: 40

Presented by: Wei Deng, MS, Graduate Student

Cardiomyocyte sialylation and complex N-glycosylation protect against dilated cardiomyopathy and heart failure Wei Deng, Andrew R. Ednie, Eric S. Bennett, Department of Molecular Pharmacology and Physiology, Morsani College of Medicine

Keywords: Glycosylation, Cardiovascular, dilated cardiomyopathy, heart failure

Objective: Human congenital disorders of glycosylation are characterized by variably reduced glycoprotein glycosylation resulting in multi-system effects, including cardiac dysfunction. Here we questioned whether cardiomyocyte-specific (α MHC-Cre) deletion of mannosyl (alpha-1,3-)-glycoprotein beta-1,2-N-acetylglucosaminyltransferase, Mgat1, responsible for initiating synthesis of complex and hybrid N-glycans, contributes to the onset of dilated cardiomyopathy.

Methods: Cardiac-specific Mgat1 conditional knockout mice (Mgat1fx/fx/αMHC-Cre) were generated by breeding Mgat1fx/fx with Mgat1fx/+/αMHC-Cre.

Results: At age 16 weeks (earliest time point tested), Mgat1F/F α MHC-Cre, showed significantly reduced ejection fraction (EF) and fractional shortening (FS) compared to littermate controls (in %, for controls (n=8), EF = 73.8 ± 2.1,FS = 42.5 ± 1.8; for Mgat1F/F α MHC-Cre mice (n=7), EF = 61.4 ± 2.3; FS = 32.8 ± 1.6; p<0.002). Systolic function of Mgat1F/F α MHC-Cre mice, but not of control mice, continued to deteriorate with age (at 30 weeks, Mgat1F/F α MHC-Cre mice (n=5) in %: EF = 38.2 ± 4.5; FS = 18.8 ± 2.5; p<0.0005). Mgat1F/F α MHC-Cre mice presented with apparent dilated cardiomyopathy indicated by reduced systolic function, a thinner wall and larger internal diameter of the left ventricle (p<0.0005) with no apparent increase in left ventricular mass index, and marked right and left ventricular dilatation observed during necropsy.

Conclusion: Together, our data suggest complex N-glycosylation are necessary for normal cardiac function, and reduced cardiomyocyte N-glycosylation contributes to the onset of significant ventricular systolic dysfunction consistent with dilated cardiomyopathy leading to heart failure.

Research supported by: Supported by NSF grant # IOS-1146882

Presented by: Travis Doggett, BS, Graduate Student

Alcohol-induced endothelial hyperpermeability is diminished with inhibition of p38 MAP Kinase

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Keywords: VE-Cadherin, Endothelial, Permeability

Objective: We hypothesized that alcohol-induced endothelial hyperpermeability occurs via a mechanisms involving activation of p38 MAP kinase, Rac1 inactivation, and disruption of VE-cadherin binding at junctions.

Methods: Transendothelial electrical resistance (TER) of human umbilical vein endothelial cell monolayers and integrated optical intensity (IOI) of extravasated FITC-albumin via intravital microscopy of conscious rats receiving 2.5 g/kg alcohol or isovolumic water via pre-implanted gastric catheters served as an index of barrier function. VE-cadherin localization was determined by immunofluorescence labeling of fixed cells expressing VE-cadherin-GFP. GTP-bound Rac1 was determined by ELISA.

Results: The results show that alcohol at concentrations greater than 20 mM significantly decreases TER, disrupted VE-Cadherin continuity, and significantly decreased GTP-bound Rac1 ($53\% \pm 5.8$ of control, p<0.01). Overexpression of Rac1 failed to attenuate the EtOH-induced drop in TER however, addition of 100 µM 8-CPT-2'-O-Me-cAMP, an indirect activator of Rac1, post alcohol caused a significantly faster return to baseline TER (14.9 ± 0.5 min vs. 59.1 ± 1.5 without activator, p<0.01). Addition of 6 µM of SB203580, a p38 MAP kinase inhibitor, 30 min before addition of alcohol significantly blunted the maximum decrease in TER (-14.9% ± 1.9 vs. -36.8% ± 1.8, p<0.001). Alcohol increases microvascular leak (max IOI 300.6 ± 50.96 vs. 78.92 ± 12.86, p<0.01).

Conclusion: These results suggest that alcohol-induced increase in endothelial permeability occurs due to activation of ump38 MAP kinase and disruption of junctional VE-Cadherin, Rac1 may also be involved but its role remains uncertain.

Research supported by: Supported by NIH R01HL098215, R21AA020049, and ABMRF/Foundation for Alcohol Research.

Abstract #: 42

Presented by: Ricci Haines, PhD, Postdoctoral Fellow

PTK6 mediates intestinal endothelial barrier dysfunction in response to TNFa

<u>Ricci Haines¹, Sarah Yuan², Mack Wu¹</u> ¹ University of South Florida, Morsani College of Medicine, Department of Surgery, and ² Department of Molecular Pharmacology and Physiology

Keywords: endothelial, PTK6, barrier function

Objective: A key event in the progression of systemic inflammation resulting from severe trauma or shock involves hyperpermeability of the intestinal endothelium. The signaling events leading to increased endothelial permeability in these disease states are incompletely understood. Although the role of protein tyrosine kinase 6 (PTK6, also known as breast tumor kinase BRK) has been primarily studied in mechanisms underlying metastasis and cancer, it has also been shown that PTK6 participates in mediating colonic epithelial barrier dysfunction. In this study, we hypothesized that PTK6 is 1-expressed in intestinal endothelial cells, and 2- contributes to endothelial hyperpermeability in response to inflammation.

Methods: To this end, we investigated the role of PTK6 in mediating the disruption of intestinal endothelial barrier function.

Results: Results showed that PTK6 was detected in intestinal endothelial cells at the level of protein and mRNA. In addition, PTK6 knockdown attenuated decrease in transendothelial electric resistance (TER) as measured by electric cell-substrate impedance sensing (ECIS) of intestinal endothelial monolayers in response to inflammatory factors including TNF α . Furthermore, we showed that TNF α increased activity of PTK6 as evidenced by increased phosphorylation at Y342, supporting the hypothesis that this kinase plays a role in endothelial inflammation. We further studied the potential targets of PTK6 including junctional structure proteins to determine the molecular mechanism of its role in regulating endothelial barrier function.

Conclusion: Our study explores a potential implication that targeting PTK6 may serve as a novel therapeutic strategy in treating diseases characterized by hyperpermeability of the intestinal endothelium.

Intramural hematoma of the aortic root and ascending aorta: A rare complication following transcatheter aortic valve replacement (TAVR)

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Keywords: Aortic stenosis, intramural hematoma, TAVR, aorta, case report

Objective: Demonstrate a rare complication of a transcatheter aortic valve replacement(TAVR), a noninvasive aortic valve replacement alternative to open surgery

Methods: Case report

Results: Imaging findings will demonstrate this rare complication with CT imaging of the chest

Conclusion: Well described complications from TAVR include aortic rupture, valve malpositioning, aortic regurgitation, valve embolization, coronary compromise, conduction abnormalities, cardiac tamponade, kidney injury and stroke. The overall incidence of intramural hematoma following TAVR is unknown, with very few cases reported. Intramural hematoma after TAVR is usually demonstrated with echocardiography. Our case illustrates this rare complication of TAVR with cardiac CT angiogram. Intramural hematoma after TAVR is thought to be associated with female gender, advanced age, and frailty, demographics reflected in this patient. The natural course of aortic intramural hematoma is along the spectrum of aortic dissection. Non TAVR patients with ascending aortic hematoma are often managed surgically at our institution. However, this patient was deemed a high surgical risk prior to TAVR. Intramural hematoma was demonstrated to the level of the aortic root. Therefore, surgical management would include re-performing aortic valve replacement. Consultation with cardiothoracic surgery was sought. The calculated risk of mortality with an open surgery was estimated at 65% using the Society for Thoracic Surgery criteria. Therefore, our patient was managed with close observation and follow up CTA. Follow up CTA four days later demonstrated chronicity of the intramural hematoma without progression. The patient was discharged home. Long term follow-up is currently pending.

Abstract #: 44

Presented by: Justin Hooper, MS, Graduate Student

Arrhythmia evoked by airway nociceptive reflexes in healthy and cardiovascular diseased rats Justin Shane Hooper, Thomas Taylor-Clark University of South Florida Morsani College of Medicine, Department of Molecular Pharmacology & Physiology

Keywords: Arrhythmia, Particulate Matter, Nociception, Pulmonary-Cardiac reflex

Objective: To determine the contribution of afferent pulmonary C-fibers in arrhythmias evoked by particulate matter (PM) inhalation.

Methods: Selectively activate pulmonary C-fibers via gating of the ion channel TRPA1 (shown to be activated by PM) using the agonist AITC. In order to measure cardiovascular effects, we implanted 15 week old Sprague-Dawley (SD) and Spontaneously Hypertensive (SH) rats with a radiotelemetric ECG device. ECG was recorded for 30 minutes during exposure of the rats to ambient air, nebulized vehicle, and AITC (30 mM).

Results: We found an increase in dropped beats and arrhythmias (second-degree AV block and premature ventricular contractions) in both SD and SH rats upon irritant inhalation. Furthermore, SH rats had a significant increase in brady/tachy events upon irritant inhalation.

Conclusion: We conclude that lung C-fiber reflexes evoke arrhythmias, which in cardiovascular disease may contribute to morbidity and mortality.

Presented by: Xun Zhang, MD, Graduate Student

Sphingosine-1-Phosphate (S1P) enhances endothelial barrier function independently of Rac1

Xun E. Zhang, Shaquria P. Adderley and Jerome W. Breslin, Department of Molecular Pharmacology and Physiology, University of South Florida Morsani College of Medicine, Tampa, FL

Keywords: S1P, Rac1, cytoskeleton, endothelial barrier, permeability

Objective: We hypothesized that S1P mobilizes local lamellipodia to enhance endothelial barrier integrity and we tested the role of Rac1 in this process.

Methods: P1-P5 Human Umbilical Vein Endothelial Cells (HUVECs) were used for the studies. Trans-endothelial Electrical Resistance (TER) served as an index of barrier function and time-lapse live cell imaging was also employed to study local lamellipodia protrusions. HUVECs were transfected with siRNA sequences to knockdown Rac1 expression or with plasmids to yield cells overexpressing Rac1 (Wild-type, dominant negative) or expressing GFP. Additionally, HUVECs expressing GFP-actin were used for the lamellipodia imaging study.

Results: The results show that S1P (2µM) caused brief coordinated membrane protrusions of individual cells that coincided with increased TER. There was no difference in baseline TER between controls and Rac1 knockdown groups at 24, 48 and 72h time points. In addition, S1P treatment resulted in a sharp, significant increase in TER in all groups, with similar magnitudes. Likewise, baseline TER was not different between GFP-Rac1 wild-type, Rac1 dominant negative and GFP control groups, and S1P treatment produced a similar significant increase in TER in all three groups.

Conclusion: Our data suggests that S1P endothelial barrier protection is associated with a rapid protrusion of local lamellipodia that does not require Rac1.

Research supported by: Supported by NIH R01HL098215

Abstract #: 46

Presented by: Elia Charbel Abboud, MD, Postdoctoral Fellow

Do Silver-Based Wound Dressings Reduce Postoperative Pain in Colorectal Surgery?

<u>Elia Charbel Abboud, Timothy Legare, Judson Settle, Amir Boubekri, Jorge Marcet, Jaime Sanchez.</u> University of South Florida Morsani College of Medicine, Department of Surgery

Keywords: Silver Pain Chart Review

Objective: To evaluate postoperative pain in patients using silver-nylon dressings vs standard gauze dressings following elective colorectal surgery.

Methods: We performed a post-hoc analysis of pain scores and analgesic use in patients who participated in a previous silver-nylon dressing trial looking at surgical site infection rates following elective colorectal operations. 110 patients were randomized to receive either a silver-nylon or gauze dressing. Postoperative pain scores were prospectively measured, and analgesic use was documented. We completed our study with a literature review of the effect of silver on pain

Results: In the silver group, there was a statistically significant decrease in the self-reported pain scores from postoperative days zero to nine. All p values, calculated using the Mann-Whitney U Test, were <0.02. This was independent of SSI status (p>0.21). Post-hoc analysis of analgesic use revealed a total average morphine equivalent of 4,428.87 in the control group and 3,069.80 in the silver group. However, this difference was not statistically significant (p=0.78). Our literature review revealed both supporting and conflicting evidence on the efficacy of silver in reducing pain in various wounds.

Conclusion: Anecdotal evidence and clinical experience suggest that silver-based dressings may reduce pain, in addition to having antimicrobial properties. Unfortunately, studies that support this assertion are limited by size, poor design, non-control of potential confounding factors, and the examination of pain as a secondary, rather than the primary, outcome measure of the research. More rigorous prospective randomized controlled trials looking at pain as the primary endpoint are needed.

Presented by: Amier Ahmad, BS, Med III Student

Mucoepidermoid Carcinoma Arising in the Anophthalmic Socket: A Case Study

<u>Amier Ahmad BS¹, Ilya M. Leyngold MD^{1,2}</u> ¹University of South Florida Morsani College of Medicine, ²University of South Florida Morsani College of Medicine, Department of Ophthalmology, Oculoplastic Surgery Service, Tampa FL

Keywords: Case Study, Ophthalmology, Mucoepidermoid Carcinoma

Objective: Mucoepidermoid carcinomas are the most common malignant salivary gland tumors in adults and children, and generally arise from the major or minor salivary glands located in the mouth and upper aerodigestive tract. Mucoepidermod carcinoma arising from ocular adnexa is very rare, but has been reported in the presence of an intact globe. To our knowledge, we describe the first case reported in literature of a mucoepidermoid carcinoma arising from an anophthalmic socket.

Methods: A case of a 48 year old male who was initially evaluated at the USF Eye Institute with a mucoepidermoid carcinoma of the left anophthalmic socket extending intracranially is presented. His clinical course, treatment, and outcome are described.

Results: The patient underwent surgical excision, radiation therapy, and chemotherapy. Despite aggressive surgical and medical treatment the patient expired from metastatic disease within 6 months of presentation.

Conclusion: Mucoepidermoid carcinoma arising from an anophthalmic socket may carry a more dismal prognosis than tumors arising with the intact globe, and those arising from salivary glands. Absence of an eye may allow for a more rapid intracranial tumor spread and decreased survival.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 48

Presented by: Kathryn Baksh, MD, Resident

Correlation between PET-FDG activity post-neoadjuvant chemoradiotherapy and tumor regression grade in locally advanced esophageal cancer

Baksh K, Fulp W, Coppola D, Meredith K, Hoffe S, Shridhar R, Almhanna K University of South Florida Morsani College of Medicine, Department of Oncologic Sciences

Keywords: Esophageal Carcinoma, Neoadjuvant chemoradiotherapy, Tumor regression grade

Objective: We set out to determine whether there was a correlation between metabolic tumor response (i.e the change in the standard uptake value measured pre and post neoadjuvant CRT) and tumor regression grade in our patient population.

Methods: A retrospective review of 56 patients with stage II-III esophageal cancer treated with neo-adjuvant CRT followed by surgery was performed. Pre- and post- treatment PET scans were reviewed. Maximum SUV at the site of the primary tumor was recorded. Upon completion of surgery, tumor regression grade was determined by a specialized pathologist. Spearman correlation was used to compare pre, post, and change in max SUV, to the 4 level TRG variables.

Results: The median follow-up was 24 months. No significant correlation was found between pre-treatment or post treatment SUV and TRG with p value of 0.73 and 0.94 respectively. There was no significant correlation between decreased FDG uptake following CRT and TRG with p value of 0.82. Consistent with previous data, TRG predicted the therapeutic efficacy and prognosis for patients with locally advanced esophageal carcinoma treated by neoadjuvant chemotherapy.

Conclusion: Our results are preliminary and retrospective in nature. A larger sample is needed to confirm these findings. Decreased FDG uptake in sequential PET scans strongly correlates with tumor response, but is not accurate enough to predict pathological response.

Research supported by: Dr. Khladoun Almhanna, H. Lee Moffitt Cancer Center

Juvenile Ossifying Fibroma: Successful Endoscopic Gross Total Resection of a Rare Sinonasal Tumor in an Adolescent Male

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Keywords: Juvenile Ossifying Fibroma.

Objective: Objectives: To report a rare case of juvenile ossifying fibroma in a child with extension into the orbit and anterior cranial fossa successfully removed by an endonasal endoscopic approach.

Methods: Methods: PubMed search and case report.

Results: Results: The endonasal endoscopic approach was successful in obtaining a gross total resection of this large tumor that extended lateral into the orbit and superiorly into the anterior cranial fossa across the midline. Endoscopic office evaluation and follow-up CT scan is consistent with no evidence of recurrent disease at more than six months.

Conclusion: Conclusions: Juvenile ossifying fibroma is a rare tumor of the sinonasal cavity and even more unusual in the pediatric age group. Large tumors involving the orbit and cranial fossa have traditionally been resected using an open transnasal/ transcranial approach, with an open transcranial and endonasal endoscopic approach for smaller tumors. We describe a case in which visualization with straight and angled telescopes and endoscopic instrumentation allowed high confidence resulting in a gross total resection of this very large tumor. We believe this approach by an experienced endoscopic can offer equal success in treatment outcome with lower morbidity and quicker recovery than the traditional approaches for this tumor.

Abstract #: 50

Presented by: Beth Byron, MD, Postdoctoral Fellow

Somatostatin analogs (SSA) in patients with diffuse idiopathic pulmonary neuroendocrine cell hyperplasia: a case series

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Keywords: Diffuse interstitial pulmonary neuroendocrine cell hyperplasia

Objective: To assess changes in symptoms as well as pulmonary function tests (PFTs) in response to somatostatin analog (SSA) treatment.



patients complained of chronic cough and dyspnea; two of the patients were asymptomatic. Most of the patients had received previous treatment with steroids and/or inhalers; however their symptoms did not improve. The patients were started on treatment with octreotide LAR 20-30mg or depot lanreotide 120mg every 4 weeks. Since initiation of therapy, fourteen of the sixteen symptomatic patients have noticed a subjective improvement in their cough and dyspnea. Additionally, seven of the eight patients in whom PFTs were checked were noted to have an improvement in FEV1 following treatment.

Conclusion: Octreotide LAR treatment may improve chronic respiratory symptoms and PFTs in patients with DIPNECH. Prospective trials focusing on symptom-control and monitoring of pulmonary function tests are warranted.

Node-Positive Papillary Thyroid Cancer: Predictive Factors for Recurrence after Surgery

Michael Clark Cameron, BS, University of South Florida Morsani College of Medicine Oncologic Sciences

Keywords: papillary thyroid cancer recurrence thyroidectomy

Objective: To evaluate relationship between pathology of node-positive papillary thyroid cancer and patterns of failure after surgery.

Methods: Records of patients with node-positive papillary thyroid cancer treated surgically between 1998 and 2012 were reviewed. Patients without positive nodes, distant metastases at presentation, or who received external beam radiation were excluded. 235 remained for analysis. Recurrences were scored if biopsy-proven or radiographic/clinical evidence initiated change in management. Locoregional recurrence (LRR) was assessed via Kaplan-Meier analysis. Potential predictors were compared via log-rank. Variables with prognostic potential on univariate analysis were subjected to multivariate analysis with Cox proportional hazards regression.

Results: 18.3% had recurrence. Local recurrence developed in 2.6%, regional in neck/upper mediastinum in 17.4%, local and regional in 18.7%, distant in 1.3%. Regional recurrence was more likely in lateral neck (63%) than central (36.6%) or mediastinal (9.8%); failure occurred in more than one compartment in 2.1%. Of the 43 recurrences, 34 were salvaged surgically. Actuarial risk of LRR was 82% at 3 years, 78.4% at 5 years, and 67.1% at 10 years. LRR risk at 3 years was elevated in T2-4 (75.5%, p<0.001), N1B (78.7%, p=0.027), extracapsular extension (75.2%, p=0.006), and increasing positive nodes (68.7%, p<0.001 for \ge 5 vs <5). On multivariate analysis, \ge 5 LN (HR 0.272, 95% CI 0.14 - 0.52, p<0.001) remained significant for LRR.

Conclusion: At median follow-up of 40 months, patients with node-positive papillary thyroid cancer are most likely to recur in neck rather than thyroid bed or distantly. Increasing nodal burden is associated with significantly increased risk of locoregional recurrence.

Abstract #: 52

Presented by: Samir Dalia, MD, Resident

A New Prognostic Index in Diffuse Large B-Cell Lymphoma Using Serum Albumin: A pilot study evaluating the albumin adjusted-International Prognostic Index

Samir Dalia MD¹, Julio C Chavez, MD¹, Celeste M. Bello, MD¹, Paul A. Chervenick, MD¹, Najla H Al Al¹i, Lubomir Sokol, MD, Ph.D, ¹, Eduardo M. Sotomayor, MD¹, Ji-Hyun Lee, PhD², Kate Fisher, MA², Zachary Thompson, PhD², Bong-jin Choi, MA² and Bijal D. Shah, MD¹ ¹University of South Florida Morsani College of Medicine Oncologic Sciences and the Department of Malignant Hematology, H. Lee Moffitt Cancer Center & Research Institute, ²Biostatistics, H. Lee Moffitt Cancer Center & Research Institute,

Keywords: Chart Review, Lymphoma, Albumin

Objective: To identify if serum albumin (SA) can be incorporated into a prognostic index for diffuse large B-cell lymphoma (DLBCL)

Methods: Patients with DLBCL treated between 2007-2010 with RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) were identified using the Moffitt Total Cancer Care platform. Age, ECOG performance status, LDH, extranodal sites of disease, stage, and albumin were collected and analyzed using Random Forest Modeling. Significant variables led to the creation of a new algorithm, the Albumin Adjusted International prognostic index (A-IPI). This score assigned a point for SA <3.7g/dL, LDH >the upper limit of normal, ECOG performance status >=2, and Ann Arbor stage III-IV. Progression free and overall survival was compared by the risk groups using Kaplan-Meier curves along with the log rank test. Statistical analysis was done using R statistical software.

Results: A total of 124 patients were identified. Median age was 58 years with 62% male. 46% were over the age of 60 at diagnosis and 63% were Ann Arbor stage 3 or 4. The A-IPI score identified three groups of patients (Very good: A-IPI=0, Good: A-IPI=1-2, Poor: A-IPI=3-4). OS was 95%, 64%, and 44% (P=0.001) in each A-IPI group respectively and was 93%, 64%, 52% (P=0.021) in each Revised-IPI (R-IPI) group.

Conclusion: In comparison to the R-IPI, the A-IPI appears to better define poor risk patients while retaining the ability to discriminate well between low ("Very Good") and intermediate ("Good") risk groups. Confirmation in an large prospective cohort is indicated, however, these data suggest SA may be a better surrogate for co-morbid status, pro-inflammatory states, and worse disease biology than age in patients with DLBCL.

Research supported by: Moffitt Cancer Center

Incidental Colorectal Wall Thickening on CT: Evaluation of Prevalence, Significance, and Management Ben Garrott, Melanie Francis, Leena Kamat MD, Joseph R. Grajo MD, University of South Florida Morsani College of Medicine Radiology

Keywords: Colon, Wall thickening, Computed Tomography

Objective: 1. To examine the frequency of incidental colorectal wall thickening (CRWT) on CT and the prevalence of underlying pathology 2. To review how CRWT is managed

Methods: All radiology reports from CT scans of the abdomen and pelvis performed at TGH between October 2011 and March 2012 were reviewed. Reports mentioning CRWT were collected. Patients with current or prior gastrointestinal disease were excluded to isolate patients with "incidental" CRWT. The data was analyzed to calculate: (1) Frequency of incidental CRWT (2) Clinical method of follow up (3) Percentage of colonoscopies resulting in a diagnosis of malignancy or colitis (4) Frequency of management based on the wording of radiology reports.

Results: A total of 3364 cases were reviewed, 129 of which met inclusion criteria, resulting in a 3.8% rate of incidental CRWT. Of these, 22% (29/129) led to colonoscopy, 40% (51/129) were followed with repeat CT, 16% (20/129) were managed with both colonoscopy and repeat CT, 2% (2/129) were evaluated with barium enema, and 4% (5/129) were clinically managed with a GI clinic visit. The remaining cases demonstrated no evidence of specific follow up according to charts. Of the patients who had colonoscopy, only 1 (3%) had cancer, 7 (24%) had colitis, 4 (14%) had erythema/hyperemia, 6 (21%) had polyps, and 8 (28%) were normal. Rates of follow up were 73% if mentioned in the Body of the report, 66% if mentioned in Body and Impression, and 75% if mentioned in Body and Impression with specific management recommendations.

Conclusion: Incidental colorectal wall thickening on CT is a rare finding that is almost always benign. Clinicians manage patients with colonoscopy and/or repeat imaging in 2/3 to 3/4 of cases regardless of how they are reported by the radiologist.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 54

Presented by: Diana Gerardi, MA, Graduate Student

Serotonergic or Anticholinergic Toxidrome: Case Report of a 9 year-old Girl

<u>Diana M. Gerardi, MA; Tanya K. Murphy, MD, MS; Megan Toufexis, DO; Camille Hanks, BA</u>. University of South Florida Morsani College of Medicine, Rothman Center for Pediatric Neuropsychiatry, Department of Pediatrics

Keywords: anticholinergic toxidrome; serotonin syndrome; pediatric toxidromes; case study

Objective: To report an acute onset of symptoms erroneously attributed to serotonin syndrome in a child who had been given both anticholinergic and serotonergic agents.

Methods: Case Summary: A nine-year old female with chronic anxiety and gastrointestinal problems was prescribed oral sertraline 6.25 mg daily, as well as hyoscyamine, ondansetron, montelukast, and a course of nitazoxanide. She was also routinely given diphenhydramine and omeprazole.

Results: Three days after increasing sertraline to 12.5 mg, she presented to the emergency room with altered mental status, hallucinations, mydriasis, tachycardia, and pyrexia. She was admitted to the pediatric intensive care unit (PICU), and subsequently treated unsuccessfully for serotonin syndrome, with blurred vision and clonus persisting at discharge, four days after admittance. Upon follow-up with her outpatient clinic, all anticholinergic agents were discontinued, and symptoms slowly resolved.

Conclusion: This case illustrates the importance of differential diagnosis between toxidromes, and how clinical presentation can be altered by preexisting conditions as well as the use of medications that affect multiple neurotransmitter systems.

Presented by: Miriah Gillispie, MD, Resident

Rate of Remission in Polyarticular Juvenile Idiopathic Arthritis: A Practice Based Study

<u>Miriah C Gillispie, MD¹, Teresa Hennon, MD², James Jarvis, MD², ¹Department of Pediatrics University of South Florida</u> Morsani College of Medicine, ²Department of Pediatrics, University of Buffalo and the Women and Children's Hospital of Buffalo

Keywords: polyarticular juvenile idiopathic arthritis; remission; TNF-inhibitors; methotrexate; chart review

Objective: To determine the feasibility of attaining prolonged disease-free periods (clinical remission on medication (CRM) in children with juvenile idiopathic arthritis (JIA) in the routine clinical setting. We also sought to determine whether there are inter-institutional differences in practice that might affect the frequency or time course for reaching the CRM milestone.

Methods: We performed a retrospective chart review of 45 children with the polyarticular form of JIA seen at two pediatric rheumatology centers; those seen at Site 1 from 2003-2010 and those at Site 2 from January 1st, 2010 to September 1st, 2013.

Results: Overall, 76% of the children in this study achieved the CRM state, those at Site 1 in a mean time of 22.33 + 3.64 months and those at Site 2 with a mean time of 14.75 + 1.22 months. We observed inter-institutional variations in practice that appeared to contribute to the length of time to CRM. Furthermore, longer time periods to CRM were associated with longer time periods from diagnosis to initiation of anti-TNF therapies. We also observed a temporal trend in the time to achieving CRM at each of the two sites, a trend associated with earlier initiation of anti-TNF therapy.

Conclusion: The majority of children with polyarticular JIA can experience prolonged periods without disease activity. There is a trend in pediatric rheumatology practice toward earlier initiation of anti-TNF therapies, which is associated with shorter time periods from diagnosis to attainment of CRM.

Research supported by: Ephraim P. Engleman Endowed Resident Research Preceptorship awarded by the American College of Rheumatology

Abstract #: 56

Presented by: Alejandra Grana, BS, Med I Student

Need for Tube Thoracostomy Following Patent Ductus Arteriosus Ligation in Premature Infants Alejandra Grana MS, Kristen Marcet MS, Anthony A. Sochet MD, Jennifer Leshko RN BNS, Jeffrey P. Jacobs MD, Gul H. Dadlani MD University of South Florida Morsani College of Medicine Cardiology

Keywords: Chart Review, Patent Ductus Arteriosus, Thoracostomy Tube, Cardiology, Premature Infants

Objective: We performed a single institution retrospective review of the mortality and morbidity associated with thoracostomy tube placement in premature infants undergoing surgical ligation of a patent ductus arteriosus.

Methods: An IRB approved single institution retrospective review of all neonates undergoing surgical ligation of a patent ductus arteriosus prior to two months of life from January 2007 to December 2011 was performed using the CardioAccess Database. Patient demographics, anthropometric data, operative details and preoperative comorbidities were recorded. Mortality was assessed intraoperatively and at discharge. Postoperative morbidities analyzed included: length of stay, duration of mechanical ventilation, postoperative pneumothorax and the need for late thoracostomy tube placement. Statistical analyses were completed using Fisher's exact test and Wilcoxon signed-rank sum test.

Results: There were 125 premature infants who underwent surgical ligation of a patent ductus arteriosus, 44 had a tube thoracostomy and 81 did not. No statistical difference was seen between those with and without thoracostomy tube placement for length of stay (111 vs. 92 days, p = 0.36), duration of mechanical ventilation (31 vs. 33 days, p = 0.77), incidence of post-operative pneumothorax (1 vs. 6 patients, p = 0.42) and discharge mortality (2 vs. 7 patients, p = 0.49). There was no need for late thoracostomy tube placement in either cohort.

Conclusion: PDA ligation with placement of a tube thoracostomy was not associated with statistically increased mortality or morbidities. Subsequently, our center no longer places a thoracostomy tube in premature infants after surgical ligation of a PDA.

Research supported by: All Children's Hospital, Johns Hopkins Medicine

A case of primary melanoma in situ without regression presenting as a depigmented patch

<u>Stefanie Grewe, Brooke Baldwin MD, Kristine Poyner, PA-C, Christopher Ewanowski MD</u> University of South Florida Morsani College of Medicine

Keywords: melanoma, vitiliginous patch, case study, depigmented

Objective: Malignant melanoma is a deadly type of skin cancer often characterized by the manifestation of unusual pigmentation deposited by melanocytes.

Methods: Here we present a rare case of melanoma in situ presenting as a vitiliginous patch. Vitiligo, appearing in a classic symmetric, apical distribution in areas other than the site of a malignant melanoma, has been reported as a precursor to or after the diagnosis of primary or metastatic melanoma as a result of immune attack on melanocytes. Depigmentation can also be seen at the site of primary melanoma in cases of tumor regression. Our case is distinct from these instances of depigmentation; this is a primary melanoma in situ with no histopathologic evidence of regression that presented as a vitiliginous patch. A 43 year old female patient presented to our clinic with a 1.2 x 1.0cm white patch with background erythema on her right anterior thigh. She stated that it had doubled in size over a month and that there was no previous pigmented lesion at this site. A 2mm punch biopsy was performed and pathology revealed melanoma in situ with no significant regression or inflammation.

Results: Following a literature search only two other reported cases of primary melanoma in situ presenting as cutaneous vitiliginous patches were described, confirming the rarity of this clinical presentation. In our case the depigmented lesion was completely excised with 1cm margins and no further depigmented patches occurred on the patient.

Conclusion: Melanoma in situ presenting as a vitiliginous patch is an entity of which dermatology providers should be aware as to broaden the perspective of what constitutes an abnormal lesion and a potential malignant melanoma.

Abstract #: 58

Presented by: Thomas Hagele, MD, Resident

Bullous Morphea

Thomas Hagele, Jennifer Harb, Mary Lien, University of South Florida Morsani College of Medicine Dermatology

Keywords: Morphea, Bullous Disease, Dermatology

Case Report: Morphea is an inflammatory disease that is histologically similar to progressive systemic sclerosis (PSS) but presents with distinct clinical features. An asymmetric patchy or linear distribution favors morphea, while systemic sclerosis typically starts as symmetric tightening of the distal extremities. Most commonly, morphea presents as an erythematous slightly elevated plaque with a violaceous border. Over time, central sclerosis and poikilodermatous changes occur, resulting in a shiny and atrophic clinical appearance. Bullous morphea is a rare morphea variant which is associated with bulla formation within a morpheaform plaque. Currently, the pathogenesis of this variant is poorly understood. Current theories suggest lymphatic obstruction due to the underlying sclerosis may obstruct lymph flow resulting in dermal edema and bulla formation. Others have suggested that eosinophils may be involved, given the association of eosinophilia and the presence of Major Basic Protein in tissues specimens. Here, we present a case of bullous morphea and discuss treatment options in addition to the clinical, histological, and laboratory findings of this rare entity.

Presented by: Sarah Hernandez, MD, MBA, Resident

Dronabinol Treatment of Refractory Nausea and Vomiting Related to Peritoneal Carcinomatosis Hernandez SL, Sheyner I, Stover KT, Stewart JT, University of South Florida Morsani College of Medicine

Keywords: dronabinol, endocannabinoids, nausea, cancer, vomiting

Objective: In recent years, cannabis alkaloids including dronabinol have been shown to have antiemetic effects, acting as agonists at endocannabinoid receptors. Dronabinol is well studied, and FDA approved, for refractory chemotherapy-related nausea and vomiting. However, to date, there have been only 3 reports of the use of cannabinoids in nausea and vomiting unrelated to chemotherapy. Our objective is to explore further uses of dronabinol in patients with nausea and vomiting refractory to other agents.

Methods: A previously healthy 49-year-old woman was diagnosed with stage IV high-grade serous ovarian adenocarcinoma with peritoneal carcinomatosis and malignant ascites. She was ultimately referred to Hospice and Palliative Care Unit (HPCU) with refractory abdominal pain and nausea related to the peritoneal carcinomatosis. She vomited as much as 10 to 20 times/d and rated her nausea at 9 or 10/10. The vomiting failed to respond to ondansetron IV, dexamethasone IV, metoclopramide, and haloperidol IV, with patient ratings still in the 7 to 9/10 range Ultimately, dronabinol was added and titrated to a maximal dose of 5 mg orally twice a day.

Results: The dronabinol was well tolerated and was dramatically effective, with prompt resolution of the vomiting after the 15 mg/d dosage was reached; she rated nausea at 0 or 1/10. For the subsequent 6 weeks she did well, had no further vomiting, minimal nausea. She ultimately died peacefully.

Conclusion: Refractory nausea and vomiting are often encountered in a hospice setting and can be a source of intense suffering. Dronabinol may be a novel alternative to conventional antiemetics for some patients. Further investigation will be necessary to elucidate its range of efficacy and its tolerability in this population.

Abstract #: 60

Presented by: Stephanie Holdener, BS, Med II Student

Chronic NK Cell Lymphoproliferative Disorder/Lymphocytosis, Nature of Disease and a Long-Run Follow Up <u>Stephanie Holdener¹, Prerna Rastogi², Johnny Nyugen¹, and Ling Zhang², ¹University of South Florida Morsani College of Medicine, Department of Pathology and Cell Biology, Hematopathology, ²Moffitt Cancer Center, Tampa, FL</u>

Keywords: Chronic Natural Killer Cell Lymphocytosis

Objective: Chronic natural killer cell lymphoproliferative disorders/ lymphocytosis (CLPD-NK) have been included as a provisional entity in 2008 WHO classification of hematologic neoplasms. It is characterized by a persistent (>6 months) increase in peripheral blood NK cells (>2 109/L) without a definitive etiology and may be related to a sustained reactive process or a potential neoplasm.

Methods: Cases with a diagnosis of CLPD from 01/1999 to 12/2012 were retrieved from MCC. Cases with chronic virus infection (eg. EBV or CMV), drug induced transient NK cell proliferation , de novo aggressive NK cell leukemia or leukemic phase of extranodal NK cell lymphoma were excluded.

Results: 15 cases of CLPD-NK (9M: 6F) with median age of 74 +/- 10.5 years were identified. Follow up was between 20 and 158 months. All patients presented with lymphocytosis, variable degree of anemia and neutropenia and a subpopulation showed thrombocytopenia. Four of 13 (without prior treatment) had severe neutropenia (<0.5 k/µL) and one had Hgb <10 g/dL. Median lymphocyte count was 7.78 k/µL +/- 4.72 and NK cell was 5814/uL +/- 3283/uL. All cases with CLPD-NK were phenotypically surface CD3-/CD16+/CD56(+/-)/CD57(+/-)/CD4(-)/CD8(-/+)/CD7(+/-)/TCR $\gamma\delta/\alpha\beta$ (-).TCR gene rearrangements were negative besides 3 cases with coexisting clonal LGL proliferation. Six patients were on immunomodulant therapies and two have experienced splenectomy. Median survival was 59 +/- 45 months.

Conclusion: CLPD-NK is clinically indolent disease. FCM data requires careful analysis to delineate NK cell population from a clonal T cell LGL, particularly $\gamma\delta$ variant. Sustained cytopenia and increasing splenomegaly might predict a disease progression.

Research supported by: Moffitt Cancer Center

Conservative Inpatient Refeeding Yields Modest Outcomes in Adolescents with Anorexia Nervosa and Eating Disorder Not Otherwise Specified

Amber Kuk, Amy Weiss University of South Florida Morsani College of Medicine Pediatrics

Keywords: Chart Review, Eating Disorder, Anorexia Nervosa, Refeeding Syndrome

Objective: Maximizing weight gain in hospitalized eating disordered patients has been associated with long-term weight restoration, improved cognitive and physical functioning, and decreased anorexic thinking. However, rapid weight gain can be difficult to attain as patients with anorexia nervosa become hypermetabolic during refeeding. Recent studies have begun to challenge the traditional means of slow refeeding and are showing more rapid weight gain without detrimental effects. Our aim was to evaluate current refeeding practices at our institution.

Methods: We performed a retrospective chart review of adolescents, ages 12 to 21 years, diagnosed with either anorexia nervosa (AN) or eating disorder not otherwise specified (ED NOS) admitted for inpatient refeeding over the past three years. Descriptive statistics were performed.

Results: We reviewed charts of 21 adolescents, admitted from March, 2009 to May, 2012. Three adolescents (14%) had hypophosphatemia early in their hospital course (days one through three), but none received supplementation and phosphorus values self-corrected to normal the following day. One patient (5%) had hypokalemia for three consecutive days and was started on oral potassium supplement. No patients had clinically significant refeeding syndrome.

Conclusion: Patients experienced initial weight loss with modest weight gain despite relatively long hospital stays. A few patients experienced brief hypophosphatemia early in admission, which self-corrected within 12 to 24 hours, arguing against true refeeding syndrome. In our next study, we hope to implement more aggressive means of refeeding in the same setting and examine rates of weight gain, length of admission, tolerance, and safety with faster refeeding practices.

Abstract #: 62

Presented by: Neil Manimala, BS, Med II Student

Passing out from fatigue? Neurocardiogenic syncope as a presentation of chronic fatigue syndrome Neil J. Manimala, Jesal V. Popat MD, University of South Florida Morsani College of Medicine Internal Medicine

Keywords: chronic fatigue syndrome, case study

Objective: Chronic fatigue syndrome (CFS) is characterized by severe, disabling fatigue of at least 6 months that is neither exacerbated by exertion nor relieved by rest. Its pathophysiology is currently unknown. In this case, CFS is presented in the context of a patient with neurocardiogenic syncope (NCS) to better elucidate these debilitating conditions.

Methods: Patient history, physical exam, and study results were assessed to generate the diagnosis.

Results: A 46-year-old male presented in February 2013 complaining of months of weekly near-syncopal episodes, lightheadedness, severe fatigue, palpitations, dizziness, and post-exertional malaise. His fatigue became progressively worse since onset, requiring daily caffeine supplements and five-hour energy drinks to maintain an at-best poor energy level. History is remarkable for single post-urination vasovagal syncopal episode in 2011. Physical exam revealed no murmurs and intact cranial nerves with 5/5 strength throughout all extremities. Brain MRI/MRA, event monitoring, EKG, stress exercise testing and extensive laboratory work-up failed to reveal a cause of these findings. Patient had a positive tilt-table test, confirming NCS. He was diagnosed with CFS due to ongoing severe fatigue and other findings, which fulfill CDC diagnostic criteria.

Conclusion: There is some evidence of a "cross-cutting" process of dysautonomia-associated fatigue. Abnormal tilt-table results have been linked to CFS, suggesting an underlying neurally-mediated hypotension that may explain concurrent NCS in this patient. A model is proposed in which vagal nerve dysfunction that potentiates NCS may also permit development of CFS. Thus, the etiology of CFS, or at least a CFS subgroup, may be primarily ANS-dependent.

Presented by: Nerissa Moore, BS, Med IV Student

Cystic Soft-tissue Sarcoma Disguised as Chronic Hematoma: Complete Excision for Thorough Pathologic Examination is Crucial for Diagnosis

<u>Nerissa Moore¹, Jamie T. Caracciolo, MD², Jarret House, MD³, Omohodion Binitie, MD⁴, Marilyn M. Bui, MD, PhD^{1,4,5,6} ¹University of South Florida Morsani College of Medicine, ²Department of Radiology, Diagnostic Imaging, ³Moffitt Cancer Center Department of Pathology and Cell Biology, ⁴USF Morsani College of Medicine Department of Oncologic Sciences, ⁵Moffitt Cancer Center Department of Anatomic Pathology, ⁶University of South Florida Morsani College of Medicine Pathology and Cell Biology</u>

Keywords: Case Series, soft-tissue sarcoma, chronic hematoma, pathologic examination, immunostaining

Objective: To show the similarity in presentation of cystic soft-tissue sarcomas and chronic hematomas and the importance of thorough pathologic examination in lesions suspicious for malignancy.

Methods: We reviewed two cases of space-occupying masses previously diagnosed as chronic hematomas; both with recent changes concerning for malignancy. Magnetic resonance image results of both were inconclusive, leaving tissue biopsy the only remaining method of diagnosis. In one case, incisional and excisional biopsies confirmed the diagnosis of chronic hematoma. However, incisional biopsy in the other case revealed that over 90% of the lesion was hemorrhagic and necrotic, resulting in an indeterminate diagnosis. Given the patient's long history with the mass and recent changes suspicious for malignancy, an excisional biopsy was performed. A thorough specimen sampling technique was used to examine the excised mass.

Results: Using the thorough specimen sampling technique, the malignant area was identified by histologic examination and only comprised a fraction of the mass. Immunohistochemistry confirmed the previously diagnosed hematoma was a high-grade angiosarcoma.

Conclusion: Cystic soft-tissue sarcomas and chronic hematomas can both present similarly. Using a systematic approach to secen the two is crucial, as similar imaging findings may be present in both. Furthermore, the possibility of misdiagnosing a high-grade sarcoma must be considered if only a small portion of the mass in question is histologically examined. We propose physicians to have a high level of suspicion for cystic soft-tissue sarcomas mimicking chronic hematomas and suggest the best practice to rule out malignancy is thorough pathological examination of the completely excised mass.

Abstract #: 64

Presented by: Emily Ng, BS, Med I Student

Does Socioeconomic Status Matter With Perioperative Outcomes After Robotic-Assisted Pulmonary Lobectomy? <u>Emily Ng¹, Kathryn L. Rodriguez, BS¹, Frank O. Velez-Cubian, MD², Matthew R. Thau, BS, BA¹, Wei Wei Zhang, MD², Carla C. Moodie, PA-C³, Joseph R. Garrett, ARNP³, Jacques-Pierre Fontaine, MD^{2,3,4}, Lary A. Robinson, MD^{2,3,4}, and Eric M. Toloza, MD, <u>PhD^{2,3,4}</u>, ¹University of South Florida Morsani College of Medicine, ²Moffitt Cancer Center, Department of Surgery, ³Moffitt Cancer Center, Department of Thoracic Oncology, ⁴University of South Florida Morsani College of Medicine, Department of Oncologic Sciences</u>

Keywords: Chart review, Socio-economic, Robotic surgery

Objective: Lower socioeconomic status has been correlated with poor survival rate and surgical outcome in various cancers. This study sought to determine whether socioeconomic status affect surgical outcomes following robotic-assisted pulmonary lobectomy.

Methods: We retrospectively studied 189 consecutive patients who underwent robotic-assisted pulmonary lobectomy by one surgeon for known or suspected lung cancer. We used median income of residential ZIP codes as surrogate of socioeconomic status and grouped patients based on whether ZIP-based median income was less than (Group 1) or greater than (Group 2) 300% of the federal poverty line, which is the threshold for various federal benefits. Incidence of postoperative complications, chest tube duration, hospital length of stay (LOS), and in-hospital mortality were compared between the groups. Statistical significance (p<0.05) was determined by Fisher's exact test and Student's t-test.

Results: Group 1, with 8 of 20 (60%) patients who had post-op complications, tended to have a higher complication rate compared to Group 2, in which 63 of 169 (37%) patients had post-op complications (p=0.057). Median chest tube durations for Groups 1 and 2 (5 days vs. 4 days, respectively) did not differ significantly (p=0.09). Median hospital LOS for Groups 1 and 2 (5.5 days vs. 5 days, respectively) also did not differ significantly (p=0.33). Lastly, in-hospital mortality for Groups 1 and 2, which are 5.0% (1 of 20) and 1.8% (3 of 168) did not differ significantly (p=0.36).

Conclusion: Lower socio-economic status may result in higher likelihood of post-operative complications, but did not affect chest tube duration, hospital LOS, or in-hospital mortality after robotic-assisted pulmonary lobectomy.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

It's hard to see what's not there: A case of cryptorchidism that evolved into intra-abdominal metastatic seminoma Midhir J. Patel, MD, Kerry Thomas, MD, Joseph R. Grajo, MD, Nicholas Constantine, MD, University of South Florida Morsani College of Medicine, Department of Radiology

Keywords: case report, cryptorchidism, metastatic seminoma, testicular cancer

Objective: (1) Present a case of cryptorchidism that evolved into intra-abdominal metastatic seminoma (2) Review differential diagnosis of abdominal masses in young males and associated radiologic features (3) Review epidemiology, diagnostic work-up and clinical management of cryptorchidism and testicular cancer

Methods: Review a case of young man who developed acute abdominal pain and was found to have abdominal masses that represented metastatic seminoma. Differential diagnoses, epidemiology and clinical management of testicular tumors will be discussed. We emphasize radiology's role in diagnosis of testicular cancer.

Results: Abdominal computed tomography (CT) revealed multiple abdominal masses and testicles were not seen in the scrotum on ultrasound (US). Tumor markers were normal. Pathologic analysis of the CT guided biopsy samples confirmed the diagnosis of metastatic seminoma.

Conclusion: CT is the primary imaging modality for evaluation of acute abdominal pathology. Differential considerations in a young male with abdominal mass include lymphoma, testicular cancer, intestinal carcinoma, gastrointestinal stromal tumor (GIST) and desmoid tumor. Testicular cancer is the most common malignancy in young men. Risk increases in the setting of undescended testes (cryptorchidism), Klinefelter syndrome and family history. Diagnostic work-up includes scrotal US, CT of the chest, abdomen and pelvis, serum tumor markers and pathologic analysis of tissue sample. Treatment includes surgical resection, radiation and chemotherapy. Tumor type and stage dictate treatment and prognosis. Seminomas respond well to radiation and chemotherapy. This case highlights the integral role of imaging in diagnosis and management of testicular cancer.

Research supported by: USF Department of Radiology

Abstract #: 66

Presented by: Ronak Patel, DO, Resident

Hurdling obesity in the road to renal transplantation

Ronak Patel, DO, Michel Murr, MD, Ariel Rodriguez, MD, Werner Andrade, MD, Ovie Appresai, MD Tannous K. Fakhry, MD, Ian Mark, MSM University of South Florida Morsani College of Medicine, Department of Surgery

Keywords: Metabolic surgery, Renal transplantation, obesity, renal allograft, gastric bypass Case series **Objective:** Obesity is a contraindication to transplantation. We reviewed 17 patients who underwent metabolic surgery before or after renal transplantation (RT) to determine outcomes of metabolic surgery in this cohort of patients.

Methods: Data from patients with end-stage renal disease were abstracted from our database of 3,500 bariatric surgical patients (1998-2014). Demographics, comorbidities, weight loss, as well as early and late morbidity and mortality were reviewed retrospectively.

Results: 5 men and 12 women aged between 35 and 76 years underwent Laparoscopic Gastric banding [LAGB] (4 patients) or Roux N Y Gastric Bypass [RYGB] (13 patients). 3 patients were post-RT and 14 patients were receiving hemodialysis. Follow-up after metabolic surgery was 1-8 years. In patients with ESRD weight loss was 120±72 lb, %EBWL was 60±23 at 35±23 months of follow-up. Weight loss in patients who underwent metabolic surgery after RT was 114±46 lbs; %EBWL was 65±23 at 53±37 months of follow up. Of the 14 patients receiving hemodialysis, 4 were placed on the RT list subsequent to weight loss; subsequently 3 patients received renal allografts. 3 patients achieved the prerequisite weight loss for RT but have not been listed. 1 patient died while on RT waiting list. 2 patients were lost to follow up, 1 developed rectal cancer and was removed from RT list. 3 patients received LAGB, 11 received RYGB. 3 LAGB mean weight loss 70lbs±30, one placed on to RT list. Of 11 RYGB 7 were placed on transplant list/transplanted. 3 patients who underwent metabolic surgery after RT maintained adequate graft function.

Conclusion: Metabolic surgery in patients with ESRD as well as renal transplantation is effective in inducing weight loss and improves access to the transplant waiting list.

Presented by: Rupal Patel, MD, Resident

Chronic opioid users are more difficult to sedate than alcoholics and non-substance users

<u>Rupal Patel, MD; Steven Clayton, MD; Eduardo Quintero, MD; Jeffrey Gill, MD,</u> University of South Florida Morsani College of Medicine, Department of Internal Medicine

Keywords: Chart Review. Keywords: Sedation; Opioids; Alcohol; Colonoscopy

Objective: The aim of this study was to compare the medication dosages to achieve conscious sedation during colonoscopy among patient groups deemed difficult to sedate.

Methods: The James A. Haley Veterans Administration (VA) endoscopic database was searched for patients who underwent colonoscopy and received diphenhydramine during the procedure. At our institution, diphenhydramine is given to patients deemed difficult to sedate. A chart review was performed to determine if each patient was either an abuser/chronic user of opioids, benzodiazepines, marijuana, alcohol, or combinations of the above. The dosage of demerol, fentanyl, and versed were collected for enrolled patients. All opioids were converted to the equivalent fentanyl dosage for comparison. The mean dose of fentanyl and versed administered in each group were compared using an unpaired two tailed student t-test. A p-value <0.05 was considered statistically significant.

Results: There were 239 patients enrolled in the study. The patients were placed into one of the following groups according to their substance abuse history: the alcohol group, the marijuana group, the benzodiazepine group, the opioid group, the poly-substance group, or the non-substance users group. The groups' demographics were compared. The opioid group, as compared to both the alcohol group and the group with no substance use, used a statistically higher mean medication dosage to achieve sedation. On average, the opioid group used 124mcg of fentanyl and 4.1mg of versed. On average, both the alcohol and non-substance users group used 101mcg of fentanyl and 3.3mg of versed.

Conclusion: In patients using daily opioids, it is important to anticipate the need for higher doses of medication to achieve adequate sedation during colonoscopy.

Abstract #: 68 Withdrawn Presented by: Jonathan Pavlinec, BS, Med IV Student

Penile Artery Shunt Syndrome: A Novel Cause of Erectile Dysfunction after Penile Revascularization Surgery Jonathan G. Pavlinec, Tario S. Hakky, Christopher Yang, Kama Massis, Ricardo Munariz, Rafael E. Carrion, University of South Florida Morsani College of Medicine, Department of Urology, Department of Radiology, Boston University, Department of Urology

Keywords: Penile Artery Shunt Syndrome, Erectile Dysfunction, Revascularization, Case Report

Withdrawn

Results: Diagnostic workup of the patient confirmed severe insufficiency of the left cavernosal artery, with no evidence of venous leak. The patient underwent penile microvascular arterial bypass surgery with anastomosis of the left inferior epigastric artery (IEA) to the left dorsal penile artery. The patient had persistence of severe ED despite patent anastomosis by penile duplex ultrasound. Subsequent arteriography revealed an arterial shunt due to an aberrant obturator artery (AOA) arising from the donor IEA. The patient underwent embolization of the AOA, with resolution of the shunt and marked improvement in erectile function.

Conclusion: The presence of an AOA arising from the IEA may predispose to persistent ED after revascularization due to the creation of a shunt-phenomenon. Pelvic arteriography may be useful in identifying anomalous anatomic considerations prior to penile revascularization and to evaluate patients with persistent post-operative ED.

Presented by: Gene Peir, BS, Med IV Student

Safety and Efficacy of Bosentan in Infant Pulmonary Hypertension

<u>Gene Peir¹, Rohit Aswani, MD¹, Lisa Hayman¹, Gina Nichols¹, Jennifer Leshko, RN, BSN², and Gul H Dadlani, MD^{1,2}, ¹University of South Florida Morsani College of Medicine, Department of Pediatrics, Tampa, Florida, ²Johns Hopkins All Children's Heart Institute, St. Petersburg, Florida</u>

Keywords: pulmonary hypertension, bosentan, pediatric cardiology

Objective: Neonatal pulmonary hypertension (PH) causes significant mortality. No medications are FDA approved for the treatment of PH in children < 1 year old. At our institution, infants with PH are initiated on a phosphodiesterase inhibitor, then an endothelin receptor blocker, then a prostacyclin. Endothelin receptor blockers have been associated with liver dysfunction and anemia in adults. Premature infants are at risk for liver dysfunction due to the need for total parental nutrition, and may develop chronic anemia secondary to prematurity complications.

Methods: Retrospective single center review of infants with PH at < 1 year old treated with bosentan. The data points were time of diagnosis and one month intervals; ECHO data including tricuspid regurgitation, shortening fraction, ejection fraction; and laboratory values: aspartate aminotransferase (AST), alanine aminotransferase (ALT), and hematocrit (HCT). Diagnosis and etiology of PH were obtained from patient chart. 2-tailed T-test was used to establish p-values.

Results: Twelve infants (6 alive/6 deceased) with PH received bosentan from 2008-2012 and initiated on PH therapy at 2-4.5 months of age. Initiation of bosentan occurred at 6 months. The deceased patients had more significant clinical disease, requiring medical therapy at an earlier age (2months, p = 0.06), and had a higher hematocrit (p = 0.02). There was no difference in baseline liver function (p = 0.17) or change in AST/ALT after bosentan therapy in the survivors (p = 0.15) or deceased group (p = 0.18). The HCT was unchanged in survivors, but decreased in deceased patients (p.008).

Conclusion: The use of bosentan in infants with PH was not associated with any significant change in liver function.

Research supported by: All Children's Heart Institute

Abstract #: 70

Presented by: Lela Posey, MPH, Med IV Student

Negative Pressure on Silver Nylon Dressings: Does it Reduce Infection Rates?

Lela Posey, Michael Grieco, Elia Charbel Abboud, James Ryan Williams, Timothy Legare, Judson Settle, Jorge Marcet, Jaime Sanchez, University of South Florida Morsani College of Medicine and Dept. Surgery

Keywords: Chart Review Silver Negative pressure wound therapy Post-operative negative pressure

Objective: To examine the effect of adding negative pressure to silver-nylon dressings (SNDs) on the incidence of early surgical site infection (SSIs).

Methods: A chart review was done for patients who underwent elective colorectal surgery requiring an abdominal incision from March 1 to June 30, 2013. Two groups were identified: those who received a SND alone, and those who received it in conjunction with post-operative negative pressure (PONP). The primary outcome studied was the incidence of SSI. Confounding variables were also analyzed: obesity, gender, length of stay, intraoperative blood loss, smoking history, procedure length, immunosuppressant use, wound type, and wound closure type.

Results: The incidence rate of SSI was found to be increased in patients with certain co-morbidities such as: inflammatory bowel disease (p=0.277), smoking history (p=.205), immunosuppressant use (p=0.061), open (vs. closed) wounds (p=0.189), intraoperative blood loss (p=0.061) and longer length of stay (p<0.001). Initially, before controlling for confounding factors, the use of PONP appeared to indicate a higher rate of SSI. After adjusting the statistics for the listed confounding factors, PONP appears to decrease the rate of SSI (OR=0.214, 0.021-2.157).

Conclusion: Higher risk patients were more likely to receive PONP accounting for most of the confounders, thus the unadjusted odds ratio for PONP appeared to be associated with a higher incidence of SSI. Once the final model was adequately adjusted for confounding, PONP was shown to be associated with a decreased risk of SSI. Our results indicate that utilizing PONP in conjunction with SNDs reduces the risk of SSI in colorectal surgery. A prospective randomized controlled trial would be needed to confirm these findings.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Clinical Features and Outcome of Clonal Mastocytosis Secondary to Chronic Myelomonocytic Leukemia (SM-AHNMD/CMML) Given Diverse Therapies

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Keywords: Chart Review, Systemic Mastocytosis,

Objective: We attempt a thorough examination of systemic mastocytosis associated with chronic myelomonocytic leukemia (SM-CMML). This rare entity poses a diagnostic challenge and treatment dilemma.

Methods: Following IRB guidelines SM-CMML cases from 1996 to 2013 were retrieved. The diagnosis was confirmed by histomorphology, laboratory data, phenotypic and molecular findings using current WHO criteria. Both solitary SM and SM-AHNMD other than CMML were excluded from this study.

Results: Ten cases with SM-CMML were identified. They had a median age of 71.4 years (range 43 - 82) and male: female ratio of 7:3. Nine of 10 patients had no prior evidence of extramedullary mast cell involvement. The length of time from the original CMML presentation to the diagnosis of SM-AHNMD was widely variable ranging from concurrent to > 80 months. All cases fit the WHO major criterion of aggregates of atypical mast cells. They also stained positive for CD117, CD2 and/or CD25 and mast cell tryptase. Serum tryptase was also elevated (>20ng/ml). Standard treatment protocols with azacitidine were used for CMML. After the diagnosis of SM-AHNMD was rendered the treatment strategies were variable. The median overall survival was 14.75 months (range 1.0 to 88 months) after CMML was diagnosed and 7.25 months (range 1.0 to 28 months) following diagnosis of SM-CMML.

Conclusion: The subtle morphologic features of a developing SM-CMML warrants careful histopathologic evaluation, IHC stains and ancillary studies. WHO criteria are important in the identification of these cases. Currently, established treatment guidelines for SM-CMML are non-existent. A large scale study is warranted to enrich physician experience in treatment of this rare entity and reduce the associated adverse outcomes.

Abstract #: 72

Presented by: Kathryn Rodriguez, BS, Med II Student

Inter-Clavicular Stabilization with the Synthes Sternal Fixation System after Radical Manubriectomy Kathryn Rodriguez¹, <u>Eric M. Toloza MD, PhD^{2,5,6}, Joseph R. Garrett ARNP², Christy Y.Chai MD⁵, Carla C. Moodie PA-C², Rajendra S. Bhati MD⁵, <u>Gerard C. Mosiello MD^{3,4}, Jonathan Zager MD^{3,5,6}</u>, ¹University of South Florida Morsani College of Medicine; Moffitt Cancer Center Departments of ²Thoracic Oncology & ³Cutaneous Oncology & ⁴Plastic Surgery Service; University of South Florida Morsani College of Medicine Departments of ⁵Surgery & ⁶Oncologic Sciences</u>

Introduction: Radical manubriectomy for manubrial tumors often destabilizes one or both upper extremities, and current reconstructive techniques prevent lateral but not medial clavicular displacement.

Case Presentation: Pt #1 is a 44-year-old man with manubrial plasmacytoma. Pt #2 is a 41-year-old man with upper chest basal cell carcinoma involving the manubrium. Pt #3 is a 64-year-old woman who is 14 months status post radical manubriectomy for metastatic thyroid cancer and whose clavicles were initially stabilized with daisy-chained loops of sternal wires, which broke while closing a car door. The three patients had mean age 49.7+7.2 yr, mean BSA 2.2+0.18 m2, mean BMI 39.3+5.8 st kg/m2, and mean smoking history 15.0+7.6 pk-yr. After radical manubriectomy in the 1 two patients and removal of the broken sternal wires in the 3rd patient, each patient underwent interclavicular stabilization using angled titanium plates from the Synthes Sternal Fixation System. Pt#2 also had bilateral pectoralis muscle flaps. Mean operative (skin-to-skin) time was 153+23.3 min; mean intraoperative estimated blood loss was 273+153 mL. Pt#2 was returned to OR on postoperative day (POD)#3 for right chest hematoma, and Pt#3 was returned to OR on POD#4 for left clavicular titanium sternal plate refixation. Additional perioperative complications occurred in Pt#2 (hypoxia from pneumonia) and in Pt#3 (hemorrhoids from loose stools). Mean hospital length of stay was 5.7+1.3 days. Follow-up of the 3 patients at 3 yr, 3 mon, and 2 yr, respectively, (mean 668+292 days) revealed no sternal plate dehiscence, despite Pt#1's routinely unloading and reloading his airboat onto its trailer and he is learning to SCUBA.

Conclusions: Interclavicular titanium sternal plates effectively prevent both lateral and medial clavicular displacement after radical manubriectomy.

Presented by: Rania Shamekh, MD, Resident

Sublingual dermoid cyst: A case report

<u>Rania Šhamekh MD¹, Řobert Wong MD³, Tapan Padhya MD³, Marino E. Leon MD^{2,3},</u> ¹University of South Florida Morsani College of Medicine, Dept. of Pathology & Cell Biology; H. Lee Moffitt Cancer Center & Research Institute ²Dept. of Anatomic Pathology, and, ³Head & Neck Oncology Program

Keywords: Cyst mass Floor of the mouth

Objective: Dermoid cysts are benign, well circumscribed, cystic masses which most likely occur in infancy and childhood. These lesions occur due to entrapped midline epithelium in regions of embryonic fusion. Cysts are lined by squamous epithelium with the presence of endodermal or ectodermal elements such as hair, skin, sweat glands and sebaceous glands. Dermoid cysts commonly develop in the head and neck, cranial cavity, along the spine, or within the abdomen.

Methods: We present an unusual, interesting case of a 23-year-old female with an intermittent swelling in the floor of the mouth that extended into the right side of the neck. CT scan of the neck showed a large 6.5 x 6 X 5 cm mass in the anterior midline bulging with displacement of tongue musculature. An enlarged multinodular right thyroid lobe was also noted. The clinical impression was a plunging ranula

Results: The patient underwent a transoral resection of right floor of mouth mass and the right sublingual gland without complications. Intraoperative findings revealed a well circumscribed and encapsulated cystic mass distinct from the sublingual gland that dissected easily from surrounding structures. The gross examination showed a cystic mass with a smooth lining. The histopathological diagnosis revealed an 8.5 cm dermoid cyst with focal chronic inflammation.

Conclusion: Dermoid cyst should be included in the differential diagnosis of patients with oral cavity, midline cystic lesions.

Abstract #: 74

Presented by: Saurabh Sharma, MD, Resident

Orbital complications of acute sinusitis in neonates and infants: A systematic review of 50 years and a case presentation

Saurabh Sharma¹, Gary Josephson MD, MBA², ¹ University of South Florida Morsani College of Medicine, Department of Otolaryngology-Head and Neck Surgery, Tampa, Florida, ² Nemours Children's Clinic, Division of Pediatric Otolaryngology-Head and Neck Surgery, Jacksonville, Florida.

Keywords: Subperiosteal, orbital abscess, pediatrics

Objective: To perform a systematic review over the past 50 years on the diagnosis and treatment of orbital complications in neonates and infants, and report a case.

Methods: Pubmed search was performed to collect all the case reports in English language with SPOA or orbital abscess in this age group.

Results: 10 cases of SPOA in infants were identified, our case report describing the 11th. Age ranged from 10 to 60 days. There were 6 females and 5 males. The right eye was affected in 5 cases, the left in 5 and both in one case. One reported mortality out of the 11 cases in the literature. Staph Aureus was the most common organism, isolated in nine of 11 cases. 7 cases had open surgical drainage, 2 had endoscopic procedures including ours and one spontaneous rupture. One case that did not have drainage performed expired.

Conclusion: Orbital complications due to ethmoiditis, though common in pediatric population is very rare in infants. Drainage in this age group appears to be paramount as the only case without surgical or spontaneous drainage expired. With technological advances, endoscopic approach for drainage and removal of nidus of infection has become safe and effective. We believe this to be the first report dedicated to the evaluation, treatment and outcomes of orbital complications in this age group.

Presented by: Kiran Soni, MD, Med I Student

Primary Cutaneous Fungal Infections in Oncology Patients

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Keywords: Neutropenia, Fungal, Oncology, Case Study

Objective: This project investigates if neutropenia increases the risk of primary cutaneous fungal infections in oncology patients.

Methods: A review was conducted of the literature available on PubMed. The causes, treatments, and outcomes of primary cutaneous fungal infections in oncology patients were analyzed.

Results: Neutropenia places oncology patients at great risk for developing primary cutaneous fungal infections. Subtle, seemingly innocuous injuries to the skin initiate the infection process. Within the healthcare setting, such necessary and common activities as IV catheters, adhesive tape, surgical dressings, arterial lines, and venipuncture, injection, and biopsy sites can cause skin injury. In the home environment, insect, spider, and pet bites, as well as cuts and scrapes due to falls or automobile accidents, can damage the skin. Fungi from the following genuses have caused primary cutaneous fungal infections in oncology patients: Absidia, Mucor, Rhizomucor, Rhizopus, Cunninghamella, Aspergillus, Fusarium, Cylindrocarpon, Acremonium, Curvularia, Alternaria, and Macrophomina.

Conclusion: Oncology patients are at high risk for developing primary cutaneous fungal infections. Treatment consists of surgical debridement and antifungal therapy. The preferred antifungal therapy for Mucorales consists of amphotericin B with posaconazole and for Aspergillus and Fusarium, voriconazole. In general, the neutropenia must subside first before the infection resolves. If the primary cutaneous fungal infection disseminates into the blood or rapidly progress into the muscles, tendons, and bones as necrotizing fasciitis, the mortality rate approaches a nearly inevitable 100%.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 76

Presented by: Matthew Thau, MD, Med II Student

Effect of body mass index on operative complications after robotic-assisted ivor-lewis esophagogastrostomy: Retrospective analysis of 133 cases

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Keywords: Robotic Surgery, Safety, BMI

Objective: The impact of body weight on robotic-assisted surgical morbidity has not been studied in esophageal cancer. We examined operative outcomes in patients according to their BMI following robotic-assisted Ivor-Lewis Esophagogastrostomy (RAIL) at Moffitt to evaluate the safety of robotic surgery in patients with an elevated BMI.

Methods: We retrospectively studied patients who underwent RAIL for confirmed malignancy in the distal esophagus and assessed morbidity and operative outcomes relative to BMI. We evaluated complications from surgery to discharge, including average operating time, estimated blood loss (EBL), pneumonia, atrial fibrillation, pulmonary embolism, deep vein thrombosis, wound infection, and surgical leaks. Median ICU days after surgery and 30 day operative mortality was assessed. Wilcoxon Rank-Sum and Spearman Coefficient were used.

Results: Of 134 total patients, 3 patients were underweight, 35 were normal weight, 62 were overweight, and 34 were obese, according to BMI. All patients had R0 resection. Among evaluated surgical complications, anastomotic leak rate was significantly higher in patients with high BMI (p=0.01). Median operating time was 407 mins and EBL was 150cc. High BMI was significantly associated with increased operation time and EBL (p=0.01 & p=0.05, respectively).

Conclusion: Patients with distal esophageal cancer and an elevated BMI undergoing RAIL have increased operative times and EBL during the procedure. An elevated postoperative risk for anastomotic leak also exists and must be monitored. However, BMI does not affect the quality of oncological resection as determined by the number of harvested lymph nodes and rates of R0 resection, suggesting similar outcomes irrespective of BMI among all patients undergoing RAIL.

Presented by: Kristie Vu, BS, Med II Student

High utilization of liver transplantation for hepatocellular carcinoma: Is it concerning?

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Keywords: Utilization, liver transplantation, hepatocellular carcinoma

Objective: Data regarding the utilization of liver transplantation (LTx) for hepatocellular carcinoma (HCC) is limited to registry studies, and thus updated studies are needed from experienced LTx centers such as Tampa General Hospital (TGH). We aimed to investigate the utilization of LTx for HCC in the last 4 years at TGH. Obstacles to referral and listing were also studied. We hypothesized that the utilization at this center is high based on resources allocated, a dedicated HCC program, MELD scores, and other factors.

Methods: The study comprised 353 consecutive HCC patients referred and evaluated at our transplant and cancer program between Jan. 2009 and Dec. 2012. Demographics, tumor characteristics, and Barcelona Clinic staging were calculated. Stage A and B patients were considered potentially eligible for LTx.

Results: 23% of all HCC patients and 29% of eligible HCC patients received LTx. Median Wait List Time was 35 days. The main reasons for not referring were tumor characteristics (76%) and progression (9%). Reasons for not listing were comorbidities (27%), tumor characteristics (25%), and financial/insurance (12%).

Conclusion: Our center listed and transplanted nearly a third of potentially eligible patients, based on stage. 23% of all HCC patients were transplanted, which is the highest utilization reported. This high benchmark favors HCC patients; the rising incidence of HCC, MELD scores in our center, and a well-organized liver cancer program likely produced this high utilization. Our most immediate concern is the detrimental effect of this high utilization on patients with end stage liver disease awaiting LTx, which requires further study. However, the high utilization of LTx for HCC in upcoming eras of hepatitis C cure may not be undesirable.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 78 Presented by: Jeremy Yesudas, BS, Med III Student

Secondary Malignant Transformation of Giant Cell Tumor: Case Review of a Rare Occurrence

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Keywords: Radiology, Giant cell tumor, Atypical presentation

Objective: Giant cell tumors are categorized as benign tumors of the bone. We describe a clinical case of an exceedingly rare occurrence of secondary malignant transformation of a giant cell tumor of bone not caused by radiation.

Methods: We reviewed the imaging characteristics on magnetic resonance imaging (MRI) and computed tomography (CT) in the detection of giant cell tumors of bone. This case will discuss the patient's History and the malignant course of a giant cell tumor. We will also provide radiologic and pathologic correlation of a malignant giant cell tumor.

Results: An X-ray of the thoracic spine was performed and demonstrated focal destruction of the left pedicle and vertebral body of T1 and the spinous process, right, and left pedicle of T3, suspicious for metastatic lesions. The MRI of the thoracic spine demonstrated a focal destructive lesion and compression fracture of T1, with multiple small rounded areas of increased T2-weighted signal involving the left pedicle, vertebral body and spinous process.

Conclusion: CT and MRI are critical in the radiologic characterization of giant cell tumor. CT scans give a more accurate assessment of cortical thinning and penetration, and the presence or absence of bone mineralization. Our patient had expansile lesions of T1 and T3 as well as 4 mm hypodense lesions in the L3 and L5 vertebral bodies. The expansile property of the tumor combined with the hypodensity points toward the extensive cortical thinning suggestive of a typical radiological presentation of GCT. However based on the scans and pathology reports the spread of the tumor can be seen in a chronological fashion. This points towards the malignant nature of this particular giant cell tumor.

Presented by: Olga Zayko, BS, Med IV Student

The surgical treatment of breast cancer in female veterans compared to the civilian population.

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Keywords: Chart Review, Breast Cancer, Female Veterans, Mastectomy Rates

Objective: As the population of female veterans increases, breast cancer care at Veterans Health Administrations (VHA) hospitals will continue to increase. Surgery is the mainstay of treatment for breast cancer and studies have shown that civilian comprehensive breast cancer care centers (CBCCC) have lower rates of mastectomy compared to VHA centers. In an effort to assess the practices of the CBCCC at the James A Haley Veterans Hospital (JAHVH) in Tampa Florida, we evaluated the treatment of breast cancer patients.

Methods: After IRB approval for the JAHVH, a retrospective review of female veterans diagnosed with breast cancer was performed. Data about past medical history, diagnostic methods, breast cancer stage, and treatment were collected. Descriptive statistics were used to analyze findings.

Results: Between 1/2005 and 7/2010, 66 female veterans were surgically treated for breast cancer at JAHVH. 66% were diagnosed with early stage disease (stage 0 and I). Among those 88% had a mastectomy vs. 41% reported by SEER database in 2009; 64% had bilateral mastectomies. 79% of women under the age of 49 choose contralateral prophylactic mastectomy (CPM) vs. 11% reported by SEER database in 2003 for all ages. Patients who had BRCA testing (n=14) chose mastectomies 100% with only one patient positive for mutation. 42% of patients underwent breast reconstruction.

Conclusion: The rate of mastectomies and CPM performed at JAHVH is higher than in the civilian population despite similar staging. While these practices are different from civilian CBCCC, this data is limited by a single institution and a few surgeons. Further investigation of the physician and patient related factors contributing to these differences are needed.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 80

Presented by: Andrea Abbott, MD, Resident

Vaginal and Vulvar Melanoma is Associated with a High Rate of Regional Nodal Disease Andrea M Abbott MD, Ingrid Ramirez-Diaz MD, Joseph Clara MD, Ragini Kudchadkar MD, Geoffrey Gibney MD, Javier Torres-Roca MD, Nikhil Rao MD, Andy Trotti MD, Patricia Judson MD, Vernon Sondak MD, Robert Wenham MD, Sachin Apte MD, Jonathan Zager MD (all Moffitt affiliated), University of South Florida Morsani College of Medicine

Keywords: Chart Review Melanoma, sentinel lymph node disease, multi-disciplinary management, surgical outcomes, vaginal and vulvar melanoma

Objective: Patients (pts) with vaginal or vulvar melanoma have a poor 5-year survival. Due to the rarity of this disease, limited treatment and outcomes data is available. While surgical excision is standard of care for the primary tumor, the role of sentinel lymph node (SLNB) biopsy, complete lymph node dissection (CLND) and elective CLND (ELND) therapy needs to be defined.

Methods: A retrospective review of pts with vulvar or vaginal melanoma from 2000 to 2013 was conducted. Clinicopathologic factors and surgical treatment of the nodal basins were analyzed.

Results: 35 pts (22 vulvar/13 vaginal), average age of 62 years, were identified. Of the 22 pts with vulvar melanoma, the median Breslow depth was 2.8mm and 12/22 (54%) had metastatic regional nodal disease. 10 pts had SLNB of which 5 (50%) were positive, 4 of whom had a CLND. There were no regional recurrences in the 5 pts with a positive SLN. In those pts with negative SLNB (5/10) there were 2 regional recurrences (false negative rate 28%). 6 pts had an ELND, 4 (66%) of whom had positive nodes in the specimen, 3 went on to have regional recurrence. 6 pts had no surgical nodal evaluation, 1 who developed a regional recurrence. In the vagina cohort the median Breslow depth was 4mm and 5/13 (38%) had metastatic regional nodal disease. 4 pts had a SLNB and none (0%) were positive, 1 pt eventually failed in the regional nodal basin synchronously with local and distant disease. 5 pts had ELND and 2 (40%) had positive nodes. There were no regional recurrences in these pts. 4 pts did not have surgical nodal evaluation, 3 of whom developed regional recurrences.

Conclusion: SLNB identifies occult disease in a significant percentage of cases and may improve the chance for regional disease control.

Development of New Risk Models for Hospital-Acquired Venous Thromboembolism in Children: Findings from a Large Single-Institutional Case-Control Study

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Keywords: Key Words: thrombosis, venous thromboembolism, risk factor, risk score, case-control study

Objective: Venous Thromboembolism (VTE) remains a major public health concern. Historically believed to be a problem of adulthood, hospital-acquired VTE (HA-VTE) is on the rise, with a rate of 1 in 200 hospitalized children. Unlike in adults, no validated HA-VTE prevention models exist in children. We sought to develop such models via a large single-institutional case-control study.

Methods: HA-VTE cases were obtained at All Childrens Hospital from 2013 retrospectively through 2006. Inclusion criteria consisted of: 1) VTE diagnosis by ICD-9, 2) verification of VTE diagnosis by review of radiologic reports. Exclusions included signs/symptoms of VTE and VTE within 24 hours of admission. Two randomly-selected controls were matched to each case. For all subjects, clinical data on demographics and putative risk factors for VTE were extracted from the medical record. Risk models for each admission location were derived via univariate and multiple logistic regression modeling.

Results: Among 40,733 admission, 179 met eligibility criteria for HA-VTE, for an occurrence rate of 1 in 228. After matching with 358 randomly-selected controls, logistic regression analyses revealed the following significant, independent risk factors for HA-VTE by admission unit: CVL, infection, and LOS definitively in the Wards; CVL and LOS preliminarily in the PICU; CVL alone preliminarily in the NICU; and none for the CVICU.

Conclusion: These data indicate that CVL, infection, and LOS are independent HA-VTE risk factors in children, but preliminarily suggest that risk factor profiles differ importantly by patient subgroup. Sample sizes will next be enlarged, in order to facilitate development of admission unit-specific pediatric HA-VTE prevention models.

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Abstract #: 82

Presented by: Jason Colizzo, MD, Resident

Elevated intrabolus pressure on high resolution manometry distinguishes fibrostenotic and inflammatory esosinophilic phenotypes

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Keywords: eosinophilic esophagitis, dysphagia, high resolution manometry

Objective: Eosinophilic esophagitis (EoE) is a chronic inflammatory disease characterized by the presence of esophageal eosinophilia in the clinical context of dysphagia. Two major subtypes of EoE have been described: inflammatory and fibrostenotic. Currently, there have been no studies incorporating high-resolution manometry (HRM) to differentiate these two subtypes. The aim of this study was to evaluate the manometric differences within these groups. Such recognition may lead to earlier diagnosis and improved understanding EoE pathophysiology.

Methods: Patients with a confirmed diagnosis of EoE according to clinicopathologic criteria managed at the Joy McCann Culverhouse Center for Swallowing Disorders were enrolled into the study. Previous findings on upper endoscopy were used to separate patients into either fibrostenotic or inflammatory phenotypes. We retrospectively analyzed HRM using the Chicago classification guidelines to identify abnormal motility patterns for each subtype.

Results: A total of 15 patients with confirmed EoE underwent HRM. Out of the 15 patients, 8 were fibrostenotic and 7 were inflammatory phenotypes. The fibrostenotic group displayed an overall average IBP of 22.2 mmHg and the inflammatory group demonstrated an average IBP of 14.12 mmHg (normal intrabolus pressure (IBP) is 11+/- 5mmHg averaged over 10 liquid swallows). Unpaired students t-test found a statistical significance (p=0.0261) between the groups.

Conclusion: The fibrostenotic group demonstrated an IBP that was significantly higher than that of patients with the inflammatory type. An elevated IBP therefore helps to distinguish between these two phenotypes. An increased IBP likely has a causative role in dysphagia symptoms and food-bolus impactions in patients with EoE.

Presented by: Erin Doren, MD, Resident

Effects of Obesity on Satisfaction with Breast Cancer Operations: An Outcomes Study

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Keywords: breast cancer treatment; mastectomy; breast reconstruction; obesity

Objective: The incidence and prevalence of breast cancer and obesity continue to rise. Obesity is a major predictor of surgical complications. Body mass index(BMI)predicts patient satisfaction with reconstruction. Does BMI relate to procedure type or satisfaction with other breast cancer procedures?

Methods: Women with a history of breast cancer surgery were recruited for electronic surveys; including a demographic survey and modules of the BREAST-Q©. Patients were classified by BMI category. Data were summarized, and analyzed.

Results: 7,622 women completed surveys. The distribution of procedure type by BMI differed significantly. As BMI category increased, rate of Mastectomy(M) increased. Those with higher BMI categories, underwent lower rates of breast reconstruction(BR) and higher rates of breast conservation surgery(BCS). Overweight, obese, and morbidly obese women reported similar satisfaction with BR and BCS. These women had significantly increased satisfaction scores with BR compared to M. Regression analysis revealed that all BMI categories experienced significantly higher satisfaction with BR using abdominal flaps. Women with M experienced the lowest satisfaction when compared to BCS.

Conclusion: Women with larger BMI experience significantly higher rates of M alone without reconstruction despite having higher satisfaction with reconstruction. This supports the notion that all women being considered for M should have the opportunity to discuss their reconstructive options with a plastic surgeon. Additionally, surgeons should not shy away from performing reconstruction in larger women, especially since abdominal flap reconstruction resulted in higher satisfaction than BCS regardless of BMI category.

Abstract #: 84

Presented by: Arantzazu Garate, BS, Graduate Student

Follow-up Attendance among USF BRIDGE Physical Therapy Patients

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Keywords: Physical Therapy, Patient Attendance, University of South Florida B.R.I.D.G.E. Clinic

Objective: To determine the percentage of patients who have attended their follow-up appointments. To establish baseline attendance data to inform quality improvement in patient follow-up care at the BRIDGE Physical Therapy Clinic.

Methods: Patient Coordinators of the BRIDGE PT staff, who are HIPAA and CITI certified and have existing access to medical records, will access patient records through Practice Fusion, the electronic health record (EHR) system utilized by the BRIDGE Clinic. This data will be compiled and reported as statistics of follow-up attendance in an Excel document. Data was compiled by SPSS software and reported as de-identified statistics of patient follow-up attendance.

Results: There is a high rate of non-attendance for initial physical therapy visits (40%). More follow-up visits are scheduled if initial visits are attended. 7 patients did not attend their initial visit, but still attended a portion of the subsequent visits, therefore initial visit dissatisfaction is not a likely factor in patient non-attendance.

Conclusion: The high rate of non-attendance indicates the need for efforts targeting reasons and measures to improve initial visit attendance. Inconsistency of care and transportation are suspected to be reasons for non-attendance of follow-up visits at the BRIDGE PT Clinic. The data obtained from this study will inform subsequent quality assurance measures, namely patient satisfaction, based on possible relationships between patient satisfaction and participation in follow-up care. Clinic recommendations: standardized classification system for patient chief complaints, ensure that follow-up visits are scheduled, maintain clinic operation throughout year.

Research supported by: Advising: Dr. John Mayer, DC, PhD, Dr. William S. Quillen PT, DPT, PhD, FACSM

Presented by: Erin Greenberg, MS, Med III Student

Quantitative image analysis applied to the grading of vitreous haze

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Keywords: Ophthalmology, Uveitis, Vitreous haze, Fundoscopic imaging, Fundoscopic image analysis

Objective: To develop a quantitative method for grading the "blurriness" of ocular fundus images in order to permit automated grading of the severity of vitritis.

Methods: Several different image-processing algorithms were written on the Matlab platform to quantify blurriness. These included Fourier spatial-frequency analysis, wavelet transforms, and entropy filtering methods. The algorithms were refined and validated using a set of 8 reference images that were acquired by masking a single "standard" fundus image with a series of analog spatial filters. After reference-set validation, the algorithms were applied without modification to a dataset of clinical images. The dataset consisted of 12 TIFF digital fundus images of 12 eyes of 12 patients with uveitis. Computer-scored results were then compared in a masked fashion with the subjective readings of an expert clinician (BM).

Results: Spatial frequency, wavelet transform, and entropy filtering algorithms by themselves all performed well for the reference set, giving scores that scaled in proportion to the known blur factor. They worked less well for the clinical set owing to the large inherent variation among patients and image takers. Better overall performance was achieved with a "mixed-method" algorithm that combined spatial frequency and entropy filtering. The Pearson correlation coefficient between the mixed-method scores and physician grades of blurriness was 0.81 (R2 = 0.66) for the clinical dataset.

Conclusion: We have developed a computer algorithm for grading vitreous haze in an unbiased and quantitative manner that correlates strongly with subjective readings of an expert clinician. We aim to now expand these findings to larger sets of fundus images and larger pools of experts.

Abstract #: 86 Withdrawn 1 28 14

Presented by: Tina Ho, DO, Resident

The Effect Of Packed Red Blood Cell Transfusions On Intestinal Inflammation In Very Low Birth Weight Infants Theo (Tine) Ho. D.O.¹. Branko Miladinovic, PhD¹. Ming Ji. PhD². Angel Luciano, MD¹. Mauroon Groor, PhD² and Terri

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Keywords: Necrotizing enterocolitis (NEC) Packed red blood cell transfusion (PRBCT) Fecal calprotectin (FC) Very low birth weight infant (VLBW)

Objective: To demonstrate the relationship between PRBCT and FC levels in VLBW infants, and to identify clinical characteristrationssocial addition the changes in FC levels following PRBCTs

Withdrawn

Results: We have analyzed 240 stool samples from 26 infants who received a total of 42 PRBCTs. Comparing 0-48 hours pre vs 0-48 hours post-transfusion, and > 48 hours pre vs > 48 hours post-transfusion, we observed a statistically non-significant increase in FC levels post transfusion (p = 0.063 and p = 0.072 respectively) and a significant association between FC levels and the number (1 vs >1) of transfusions given (p = 0.007 and p = 0.005 respectively). FC levels increased over time (p = 0.0021) and the rate of increase was higher after PRBCTs (slope before transfusion = 74.78 vs slope after transfusion = 77.69, p = 0.0176).

Conclusion: Our data indicate there is an association between FC levels and PRBCTs in VLBW infants. The rate of increase in FC levels was significantly higher after a PRBCT and the FC levels were significantly higher with later versus first PRBCT. These findings help to explain the association between PRBCTs and intestinal inflammation at the cellular level.

Research supported by: The Gerber Foundation

Presented by: Timothy Hoggard, BS, Med II Student

Impaction Grafting for Repair of Proximal Humeral Fractures with Hemiarthroplasty: Thermal and Biomechanical Implications

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Keywords: hemiarthroplasty, impaction grafting, proximal humerus fracture

Objective: Greater tuberosity malunion subsequent to hemiarthroplasty is often met with poor clinical results, including decreased functionality and patient dissatisfaction. While tuberosity failure involves several factors, it is known that thermal injury to bone occurs with the curing of methylmethacrylate cement used for implant fixation. This may be avoided using an impaction grafting technique, consisting of cementing the stem distally and the use of impacted bone graft proximally. Neither the thermal consequence nor the biomechanical stability of the impaction graft construct has been validated in a laboratory setting.

Methods: A surgical neck fracture was created in matched pairs of cadaveric humeri (n=7). Each was instrumented with a hemiarthroplasty stem and randomized to: (1) a cement group receiving full cementation or (2) an impaction grafting group receiving only cement distally and bone graft proximally. Thermocouples measured cortical temperature at the stem tip (representing the cement mantle) and at the surgical neck (tuberosity interface). Incremental cyclic torsional loading was applied to evaluate relative micromotion between the implant stem and humeral shaft.

Results: Thermal data demonstrated significant decrease in the maximum-recorded temperature at the surgical neck in Group 2 (39.7 +/- 4.1°C) compared to Group 1 (55.7 +/- 9.1°C, p=0.005). However, Group 2 demonstrated increased average relative micromotion at baseline (2.5 N-m, 1.4 +/- 0.6°) and maximal torsion (10 N-m, 5.8 +/- 2.0°) compared to Group 1 (0.3 +/- 0.1° and 1.7 +/- 0.6° respectively, p=0.002 and p=0.002).

Conclusion: Results demonstrate impaction grafting of hemiarthroplasty stems may avoid tuberosity thermal damage, but at the expense of construct stability.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 88

Presented by: Jarret House, MD, Resident

Diagnostic Digital Cytopathology: Are We Ready Yet?

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Keywords: Digital diagnostic cytopathology, virtual microscopy.

Objective: We studied the diagnostic concordance between glass and digital slides among diagnosticians with different profiles to assess the readiness of adopting digital cytology in routine practice.

Methods: This cohort consisted of 22 de identified previously screened and diagnosed cases, including non gynecological and gynecological slides using standard preparations. Glass slides were digitalized using Aperio ScanScope XT (x20 and x40). Cytopathologists with (3) and without (3) digital experience, cytotechnologists (4) and senior pathology residents (2) diagnosed the digital slides independently first and recorded the results. Glass slides were read and recorded separately 1 3 days later. Accuracy of diagnosis, time to diagnosis and diagnostician's profile were analyzed.

Results: Among 22 case pairs and four study groups, correct diagnosis (93% vs. 86%) was established using glass versus digital slides. Cytopathologists with no digital experience were the most accurate in digital diagnosis. Cytotechnologists had the fastest diagnosis time (3 min/digital vs. 1.7 min/glass), but not the best accuracy. Digital time was 1.5 min longer than glass slide time/per case for cytopathologists and cytotechnologists. Senior pathology residents were slower and less accurate with both methods.

Conclusion: There was good overall diagnostic agreement between the digital whole slide images and glass slides. Although glass slide diagnosis was more accurate and faster, the results of technologists and pathologists with no digital cytology experience suggest that solid diagnostic ability is a strong indicator for readiness of digital adoption.

Research supported by: This project was partially funded by the Amandalee Weiss Sarcoma Fund.

Presented by: Amanda Keene, BA, Staff

Preliminary Results from a Study Examining Sleep-Related Problems among Anxious Youth with Autism Spectrum Disorders

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Keywords: sleep, autism, anxiety

Objective: Youth with ASD experience more sleep related problems (SRPs) than typically developing youth (Polimeni, Richdale, & Francis, 2005). Common SRPs include difficulty falling asleep, nightmares, and sleep talking and walking (Alfano, Ginsburg, & Kingery, 2007; Fallone, Owens, & Deane, 2002). Comorbid anxiety disorders are common in youth with ASD (Levfer et al., 2006). However, there is a dearth of information about SRPs among youth with ASD and comorbid anxiety. This study examines the prevalence and correlates of SRPs in a sample of youth with ASD and comorbid anxiety and examines the predictive abilities of ASD-related social deficits and anxiety symptoms with respect to SRPs.

Methods: 110 youth (ages 7-16) with ASD and comorbid anxiety disorders and their parents were administered the Pediatric Anxiety Rating Scale (PARS) to assess severity of physical symptoms of anxiety. Youth completed a questionnaire assessing ASD-related social deficits (Social Responsiveness Scale; SRS). Parents completed the Multidimensional Anxiety Scale for Children-Parent Version (MASC-P), and the Child Behavior Checklist (CBCL). A composite measure of SRPs was formed using six items from the CBCL and two items from the MASC-P.

Results: The majority of parents endorsed at least one SRP, with half reporting four or more. The most frequently reported SRPs included sleeping with a night light (66%) and inability to sleep alone (57%). Physical symptoms of anxiety significantly predicted SRPs, even after controlling for ASD-related social deficits.

Conclusion: Findings suggest SRPs are common among youth with ASD and comorbid anxiety. Physical symptoms of anxiety are an important predictor of SRPs above and beyond ASD-related social deficits.

Research supported by: Funding from ACH and USF sources.

Abstract #: 90

Presented by: Aimee Klein, DPT, DSc, Faculty

A Biomechanical Analysis of the Relationship Between Hip Anatomy and Lower Extremity Musculoskeletal Injuries in Ballet Dancers

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Keywords: Turnout, Ballet Dancer, Hip Pain

Objective: Ballet dancers rate of injury ranges from 0.77 to 1.29 injuries per 1000 dance hours. Incidence rises significantly as a result of increased training requirements and reduced recovery time. Sixty percent of turnout is generated through the hip joint. The iliofemoral ligament is an important static structure contributing to hip stability and decreased musculature demands. Dynamic hip muscular control allows for balancing the pelvis, while achieving the aesthetically appealing turnout. The number and severity of non-traumatic injuries is correlated with degree of turnout and compensatory strategies to achieve turnout. Injury may present anywhere in the lower extremity (LE). The purpose of this investigation was to hypothesize the biomechanical causes for LE musculoskeletal injuries in dancers.

Methods: A literature search was performed to obtain evidence related to the biomechanical requirements for turnout. Hypotheses were developed to describe relationships between turnout and musculoskeletal injury.

Results: Proper, non-compensated turnout can be stabilized using the taut iliofemoral ligaments, limiting additional extension and external rotation (ER) of the hip. The two most common compensatory movement patterns are pelvic anterior tilting or improper use of the superficial hip ER muscles. These movements may result in excessive stress on the lumbar spine or compressive forces on the hip joint, contributing to risk of low back pain or hip muscular and labral dysfunction.

Conclusion: The excessive anatomic demands placed on dancers to achieve turnout during their career places them at high risk for LE musculoskeletal injuries. The evidence demonstrates the use of compensatory movement furthers this risk of injury.

Impact of BMI on Surgical Outcomes of Partial Nephrectomy: Does Size Matter?

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Keywords: nephrectomy; BMI; Urinary Leak

Objective: This study investigates if obesity, defined as a body mass index (BMI) ≥ 30, is predictive of perioperative complications after PN.

Network is the median patient age was of years (ICR 51-70) and the median BMI was 25 st ICR 25 2-33 9). 155 (77.9%) had open PN 18 (9.0%) laparoscopic, and 26 (13.1%) had a robotic PN. Obesity was significantly associated with urine leaks (p = 0.01) across all surgical modalities. A multivariate analysis found that only obesity was an independent predictor of urine leaks (p = 0.03). Based on the odds ratio, an obese patient was 5.7 times more likely to have a urinary leak after PN. For minimally invasive cases, there was a significant difference in EBL (p=0.06) with obese patients having greater intra-operative blood losses. Robotic cases had longer clamp times in obese patients (p = 0.11). Integrin of hospital stay (p = 0.64), and RENAL nephrometry risk score (p = 0.89).

Conclusion: Although other studies concur that urinary leak is a unique post surgical complication of PN, we found that it is significantly more prevalent in obese patients undergoing PN.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 92

Presented by: Umbareen Mahmood, MD, Resident

How Does Procedure Type Affect the Impact of Breast Cancer on Women's Lives

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Keywords: Impact of cancer, mastectomy, breast reconstruction, breast conservation surgery, lumpectomy

Objective: With 2.6 million breast cancer survivors, effect of treatment on long term-health related quality of life (HRQOL) must be assessed. As all three surgical options: breast conservation surgery with radiation (BCS), mastectomy (M), or mastectomy with breast reconstruction (BR), have comparable oncologic and survival outcomes, evaluation of HRQOL is needed to facilitate surgical decision-making and optimize long-term health.

Methods: The Army of Women (AOW) comprises over 360,000 women participating in breast cancer research. After IRB and AOW Committee approval, eligible women were asked to take the Impact of Cancer Version 2 (IOCv2) survey. The IOCv2 is a psychometric assessment of HRQOL and long-term survivorship with a Positive and Negative Impact Scale, each with four subscales. Regression analysis was used to evaluate factors associated with the positive and negative impact of cancer.

Results: 7619 women completed the survey; 3507 underwent BCS, 2328 had BR, 1269 had M, and 515 had a complex surgical history. Abdominal flap and implant based breast reconstruction demonstrated a higher than average positive IOC score compared to BCS (p=0.0219 and p=0.0059). A complex surgical history or implant reconstruction significantly increased the negative IOC score (p=0.0002 and p<0.0001).

Conclusion: Studies show that women select the treatment that optimizes HRQOL and long-term outcome. In this study, breast reconstruction using abdominal flaps reflected the highest HRQOL and least negative impact of cancer. Implant reconstruction increased both the positive and negative impact of cancer. Mastectomy alone had the highest negative impact of cancer score compared to BCS. Data from this large cohort will facilitate treatment and reconstructive decision-making.

Presented by: John Mayer, PhD, Faculty

Low Back Pain in the US Military: Epidemiology, Prevention, and Current Research

John M. Mayer, DC, PhD, CCRP¹, William S. Quillen, PT, DPT, PhD, FACSM¹, John Childs, PT, PhD, MBA², Jennifer L. <u>Libous, MS¹</u>, ¹School of Physical Therapy & Rehabilitation Sciences, Morsani College of Medicine, University of South Florida, Tampa, FL, ²Doctoral Program in Physical Therapy, US Army-Baylor University, Fort Sam Houston, TX, and Dept of Physical Therapy, Keesler Air Force Base, Biloxi, MS.

Keywords: injury prevention, low back pain, physical fitness, military

Objective: The purpose of this presentation is to: 1) Review the epidemiology of low back pain in the military and the best available evidence on interventions for prevention of low back pain in the military; and 2) Discuss the current USF DOD-funded research initiative on reduction of risk for low back pain in the military.

Methods: 1) A literature review was conducted using a narrative strategy to describe the current understanding of epidemiology and prevention of low back pain in the military. 2) A cluster randomized clinical trial led by USF investigators is currently underway with active duty US Army Soldiers at Fort Sam Houston, TX. The purpose of this study is to assess the effectiveness of a targeted exercise intervention on development of lumbar extensor strength and endurance.

Results: 1) Literature review: Numerous recent peer-reviewed citations were uncovered on low back pain in the military, with many describing the epidemiology of low back pain of warfighters in Operation Iraqi Freedom / Operation Enduring Freedom. Low back pain is responsible for the largest percentage of non-battle injuries among deployed warfighters, and has resulted in costly disabilities, functional loss, and reduced quality of life for active duty military personnel and veterans. The best available evidence on which interventions are most effective for prevention of low back pain in the military is unclear. 2) Current USF study: Data collection for this study was completed in 2013 and results are pending.

Conclusion: Low back pain in the US military is a common and disabling disorder. Research efforts, such as the current USF study, are needed to identify the effect of various interventions on risk reduction for low back pain in the military.

Research supported by: US DOD: W81XWH-11-2-0170

Abstract #: 94	Presented by: Adnan Muhammad, MD,
	Resident

Outcome and Predictors of Survival after Transjugular Intrahepatic Portosystemic Shunt (TIPS) in patients with Cirrhosis and Portal hypertension

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Keywords: TIPS Cirrhosis Portal hypertension Outcome

Objective: Cirrhosis of liver is the 10th leading cause of death in US. Major complications include variceal bleeding (VB) and refractory ascites (RA). Long-term treatment of VB and RA involves liver transplantation (LT) or transjugular intrahepatic portosystemic shunt (TIPS) in patients who are not candidates for LT. Aim: To determine the clinical outcome and predictors of survival after TIPS insertion.

Methods: This was a retrospective study. Data was collected on all consecutive patients with cirrhosis of liver who underwent TIPS insertion between Jan 2004 and March 2012. The KM method was employed to calculate survival and comparisons were made by log rank test. A multivariate analysis was carried out using the Cox proportional hazards model.

Results: Two hundred forty nine patients met the inclusion criteria. Mean age was 55 years (21-85). Baseline characteristics of the patients, etiology of cirrhosis, Child-Turcotte-Pugh (CTP) score, model for end stage liver disease (MELD) score, indication for TIPS and hepatic venous pressure gradient (HVPG) difference post TIPS were tabulated. HVPG difference was calculated by subtracting the post TIPS pressure gradient to pre TIPS pressure gradient. MELD score (p=0.017), CTP score (p=0.042) and TIPS indication (VB vs. RA) (p=0.004) were the significant predictors of survival. No significant difference in survival was noted in terms of age, gender, ethnicity, etiology of cirrhosis and HVPG difference post TIPS.

Conclusion: TIPS is a safe and effective way to manage the complication of portal hypertension. Mean survival was significantly lower in patients with VB and those with higher MELD and CTP scores. No significant difference in survival was seen in older patients (age \geq 65) when compared to younger age group.

Presented by: Travis Murphy, BS, Med IV Student

Variable Calcium Changes in Response to Surgery

<u>Travis W Murphy, BSc¹, Peter J Fabri, MD, PhD, FACS^{1,2}, Philip Foulis, MD²</u> ¹University of South Florida Morsani College of Medicine, ²James A Haley VA Hospital, USF Morsani College of Medicine, Surgery

Keywords: post-operative hypocalcemia, data mining

Objective: This study was designed to evaluate changes in serum calcium after a larger variety of surgical procedures than has previously been assessed.

Methods: Three years of de-identified laboratory records we searched to compare changes in calcium within 24 hours following an operation. 6425 date-matched procedures and calcium measurements pre- and post-operatively for 4745 unique patients were included in the analysis. Paired t-test and ANOVA testing was used to evaluate the findings. Normality was assessed using the Kolmogorov-Smirnov test. Significance was accepted if p<0.05.

Results: Initial examination of all changes in calcium following a surgical procedure showed a median change of -0.9mg/dL with the average change being -0.95 mg/dL with a standard error of the mean 0.01. A Wilcoxon signed rank-test of the 6425 pre and postoperative paired calcium levels showed a significant decrease in calcium following all of the many types of surgery.

Conclusion: What has been accomplished here is the identification of a trend in data not previously included in other studies on the subject of hypocalcemia. Postoperative drop in calcium in elective, non-parathyroid surgery is common. This was determined by analyzing a large database with appropriate statistical tests. Based on these findings, a shift in perception is necessary so that treatment for is directed only towards those patients who develop hypocalcemia of symptomatic significance rather than out-of-range laboratory values.

Research supported by: USF Health Scholarly Concentrations Summer Research Fellowship

Abstract #: 96

Presented by: Johnny Nguyen, MD, Resident

Practical Application of Next-Generation DNA Sequencing in Detection of ASXL1, RUNX1, EZH2, ETV6, and TP53 Mutations in Patients with Myelodysplastic Syndrome

<u>Johnny Nguyen¹, Lynn Moscinski², Ling Zhang².</u> ¹Department of Pathology & Cell Biology, University of South Florida Morsani College of Medicine, ²Department of Hematopathology, Moffitt Cancer Center

Keywords: Myelodysplastic syndrome; next-generation sequencing; prognosis

Objective: Next generation DNA sequencing technology facilitates understanding molecular mechanisms, provide diagnostic and prognostic values for myelodysplastic syndrome (MDS) and acute myeloid leukemia. ASXL1 and EZH2 regulate chromatin compaction and silence genes in hematopoiesis. RUNX1 gene encodes the core binding factor critical to leukemogenesis. ETV6 gene codes for a ubiquitous, transcription factor, and ETS family is required for hematopoiesis. TP53, and its mutation is reported to be associated with MDS/AML (Sebaa A et al 2012). Mutations in these 5 genes are recurrent molecular abnormalities and associated with poor prognosis, regardless of IPSS score/age (Bejar R et al 2011).

Methods: MDS molecular assay of these five genes has not been widely adopted. Peripheral blood or bone marrows were sent for next-generation DNA sequencing at a reference laboratory. Patients who have a clinical cytopenia suspicious for MDS or a MDS recent diagnosis between April to August 2013 were included. MDS diagnosis is according to 2008 WHO classification, clinical history and other studies.

Results: Specimens from 61 patients were analyzed for mutations. 58 had a complete report. 15 of 58 patients had either normal findings (9 patients) or non-MDS diseases. Somatic mutations were detected in 22 patients (47.8%) of the remaining cases. 88% of the mutations detected were clinically relevant. Four patients with AML ex MDS had one mutation (ASXL1). No clinical outcome is correlated with mutation status because of recent diagnosis. Sensitivity was 60.9%, specificity 100%, PPV 100%, and NPV 45.5% (p< 0.00001).

Conclusion: The MDS mutation panel aids diagnosis with high specificity. Further clinical data and close follow-up will be required for determination of outcomes.

Presented by: Priyal Patel, BA, Staff

Antibiotic Treatment Trial for the PANDAS/PANS Phenotype

Priyal Patel B.A., Laura Ramirez, M.S., P. Jane Mutch Ph.D., Adam B. Lewin Ph.D., Eric Storch Ph.D., Tanya K. Murphy M.D. University of South Florida Morsani College of Medicine Pediatrics

Keywords: PANDAS, PANS, OCD, tics, Group A Streptococcus

Objective: Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) is a subtype of rapid childhood onset obsessive compulsive disorder (OCD) that appears to be directly connected to an infectious trigger and is marked by a sudden onset or exacerbation of neurological symptoms. Our objective is to identify unique characteristics that may exist in participants with elevated strep titers, Mycoplasma IgM antibody, and those with neither elevated at baseline.

Methods: 38 youth, ages 4-14 (19 males; mean age of 8.2 years), with an acute-onset of OCD symptoms were invited to participate in the study. The primary outcome measures were ASO, Anti-DNase B, and Mycoplasma IgM titers, OCD severity, duration of illness, and comorbidity.

Results: Out of the 38 participants, 28 had elevated strep titers, 9 had elevated Mycoplasma IgM, and 8 did not have either antibody elevation at baseline. Significant group differences were observed for gender (F (2, 35) = 4.3, p = 0.011), but not for age, tic comorbidity, OCD severity, or duration of presenting OCD. Within the group that had elevated strep titers, a significant difference was observed between male and female participants for duration of presenting OCD (F (1, 26) = 4.3, p = 0.049).

Conclusion: The high frequency of participants with elevated titers suggests that symptoms were caused or exacerbated by an infectious trigger. Comparison of group differences for elevated antibodies suggests that the trigger type may not be a predictor for specific PANS symptoms, though gender differences in titer elevations are interesting and warrant further exploration.

Research supported by: Massachusetts General Hospital

Abstract #: 98

Presented by: Reed Pavan, MD, Faculty

Postmortem Ultrasound and OCT Imaging of the Posterior Segment

Pavan, Peter R.¹, McCartney, Mitchell D.², Saunders, Timothy³, Gore, Patrick², Sprehe, Nicholas², Saxon, Wyatt¹, Margo, <u>Curtis E.¹</u>, ¹USF Eye Institute, ²Lions Eye Institute for Transplant & Research, Private Practice/USF, ³Lions Eye Institute for Transplant & Research University of South Florida Morsani College of Medicine Ophthalmology

Keywords: imaging methods, ultrasound, comparative anatomy

Objective: To correlate optical coherence tomography (OCT) imaging with high frequency ultrasound images of the posterior pole in postmortem non-preserved donor tissue eyes.

Methods: Postmortem eye bank globes were enucleated using standard techniques and transported to the laboratory in saline soaked gauze moist chamber on ice. The fresh eyes were treated within 12 hours post-mortem with topical drops of 10% phenylephrine and 1% tropicamide, given in two rounds, three minutes apart. The globes were oriented and secured to a Styrofoam head with the corneas facing forward; balanced salt solution was injected with a 32 gauge needle into the vitreous cavity approximately 4 mm posterior to the limbus to achieve physiologic pressure as measured by palpation. OCT raster line scanning (OCT) images of the macula were obtained. The eyes were then reoriented in the Styrofoam head so the posterior pole was facing forward. A high-frequency (40 mHz)ultrasound biomicroscopy probe covered with a water filled ultrasound transducer cover was placed over the back of the eye to obtain images of the macula and adjacent retina. The eyes were fixed using a solution of 10% neutral formalin.

Results: The pharmacologic agents increased the pupil diameter an average of 1.87 mm. OCT imaging of the macula identified much of the anatomy appreciated in an in vivo scan, although postmortem retinal changes imposed some limitations. The UBM showed recognizable retinal landmarks in the posterior pole and correlated well with pathology seen on the OCT images such as epiretinal membranes causing macular puckering.

Conclusion: UBM successfully imaged fine retinal structures in postmortem eyes. This additional technique can be used to screen postmortem eyes for disease-specific conditions.

Presented by: Whitney Rigaud, BS, Graduate Student

Evaluating the Recovery Curve for Clinically-Assessed Reaction Time Following Concussion Injury

Whitney Rigaud ATC, Gianluca Del Rossi PhD, ATC, Barbara Morris DHSc ATC CSCS ROT, The SMART Institute, Dept of Orthopaedics & Sports Medicine, University of South Florida Morsani College of Medicine

Keywords: Brain Injury Concussion Recovery Trauma

Objective: To determine the recovery curve for clinically assessed simple reaction time following concussion injury.

Methods: Baseline simple reaction time using the ruler-drop test was assessed in over 300 high school athletes prior to the start of their athletic season. Eight participants (all males; 16.4 ± 1.2 years of age; 1 left-hand dominant, 7 right-hand dominant) suffered a concussion and completed the study protocol. Participants were required to complete 8 individual trials of the ruler-drop test at 7 time intervals. Along with baseline testing, participants who suffered a concussion were required to complete testing sessions at Day 3, Day 7, Day 10, Day 14, Day 21 and Day 28 post-injury. The ruler drop test involves grasping a measuring stick that has been dropped and then using the length the ruler has travelled before being grasped to assess simple reaction time. Reaction time was calculated (in milliseconds) using the formula for a falling body (d = 1/2gt²), where d is distance, g is acceleration due to gravity, and t is time.

Results: Statistical tests revealed a significant effect for time interval (F6, 42 = 7.49, p =0.002) with an average reaction time of 237.2±13.8ms at baseline, and 253.7±15.8ms, 248.8±19.7ms, 245.0±10.4ms, 234.2±14.5ms, 231.8±13.1, and 231.9±11.0ms at Days 3, 7, 10, 14, 21, and 28, respectively.

Conclusion: The trend in the data suggests that following a concussion it takes a high-school-aged patient, on average, 14 days for clinical reaction time to return to baseline levels. More research is needed to ascertain the usefulness of clinically-assessed simple reaction time as a means of tracking recovery from concussion injury.

Research supported by: Gianluca Del Rossi PhD ATC, Barbara Morris DHSc ATC CSCS ROT

Abstract #: 100

Presented by: Jose Soto, BS, Med II Student

Awareness of ongoing clinical trial information: physicians' and clinical trial administrators' perspectives Jose M. Soto^{1*}, Dariam Cardentey Oliva^{1*}, Hesborn Wao, PhD², Clement K. Gwede, PhD, MPH, RN^{3,1}, Rahul Mhaskar MPH, PhD² *Both authors contributed equally to this work. ¹Morsani College of Medicine, University of South Florida, Tampa, FL, ²Center for Evidence-Based Medicine and Health Outcomes Research, Department of Internal Medicine, University of South Florida Morsani College of Medicine, Tampa, FL, ³Moffitt Cancer Center, Tampa, FL

Keywords: Information Dissemination Recruitment Research Physicians

Objective: This pilot study investigated information seeking behaviors of physicians and information dissemination strategies employed by clinical trial administrators (CTAs).

Methods: After face-to-face, semi-structured interviews, thematic content analysis yielded themes regarding physicians' knowledge, attitudes, behaviors and barriers to information seeking about ongoing clinical trials and their perceptions regarding reliability of information obtained.

Results_: Sixteen physicians from nine specialties and three CTAs at University of South Florida were interviewed. Almost half of the physicians do not actively search for information on ongoing trials and instead rely on direct contact from CTAs. Most of the physicians who actively search rely on Google search and clinicaltrials.gov, but few used the institution's research website. Half of physicians interviewed felt that current trial advertising strategies are ineffective and cited time constraints as a reason for not searching actively. Most physicians would prefer to have trial staff present trial information directly to them at staff meetings. Most CTAs used mass emails, the institution's research website and physical newsletter advertisements to advertise trials. Most do not seek feedback for their strategies from physicians.

Conclusion: There is a disconnect between the strategies desired by physicians and those employed by CTAs. There is no assessment of the effectiveness of the advertisement strategies except for enrollment numbers. These findings have implications, not only for overall accrual to clinical trials but also for disparities in access to trials for medically underserved patients who may not routinely seek out clinical trials on their own.

Research supported by: USF MCOM, SELECT and Bringing Science Home

Presented by: Andrew Taitano, MD, Resident

Bariatric Surgery Improves Histological Features of Nonalcoholic Fatty Liver Disease and Liver Fibrosis

<u>Andrew Taitano¹, Michael Markow², Ronak Patel¹, Donald Wheeler², John Paul Gonzalvo¹, Jon Finan², Michel M Murr¹, ¹University of South Florida Morsani College of Medicine, Department of Surgery, ²University of South Florida Morsani College of Medicine, Department of Pathology and Cell Biology</u>

Keywords: bariatric surgery, liver fibrosis, NASH, chart review

Objective: Nonalcoholic fatty liver disease (NAFLD) is prevalent in bariatric patients. We sought to determine the effects of surgically-induced weight loss on the histological features of NAFLD in patients undergoing bariatric surgery.

Methods: A blinded pathologist reviewed all liver biopsies done during the index bariatric procedure and any subsequent abdominal operations from 1998-2013. Biopsies were examined using H&E, trichrome and iron stains and graded using the Brunt classification. Data for analysis were collected prospectively.

Results: Paired biopsies for 152 patients were included. Mean interval between biopsies was 29±22 months. Mean age was 46±11 years. Mean excess body weight loss was 62±22% at subsequent biopsy. Findings on the initial biopsy were steatosis 78%, lobular inflammation 42%, chronic portal inflammation 68%. Steatohepatitis was present in 33%. Grade 2-3 fibrosis was present in 41%, and cirrhosis was present in 2%. On post-op biopsy, steatosis resolved in 70%; lobular inflammation resolved in 74%; chronic portal inflammation resolved in 32% and steatohepatitis resolved in 88%. Fibrosis of any grade resolved in 21% and improved in another 23% of patients. Grade 2 fibrosis was present in 52 patients pre-op; 31% resolved, 31% improved, and 29% did not worsen post-op. Of the 10 patients with bridging fibrosis, one resolved and seven improved.

Conclusion: Bariatric surgery improves liver histology in severely obese patients and is associated with resolution of steatosis or steatohepatitis in the majority of patients. More importantly, Grade 2 or 3 (bridging) fibrosis is resolved or improved in 65% of patients. Bariatric surgery should be considered as the treatment of choice of NAFLD in severely obese patients.

Abstract #: 102

Presented by: Jiangchuan Tao, MD, Resident

Correlation of c-MYC, EZH2, IKZF1 and p-STAT5 Expression to the Prognosis of Adult B Lymphoblastic Leukemia Jiangchuan Tao^{1,2}, Bijal Shah^{1,2}, Xiaohui Zhang^{1,2,3}, Jianguo Tao^{1,2,3}, Hui-Yi Lin^{1,2}, Lynn Moscinski^{1,2,3}, Ling Zhang^{1,2,3} ¹Moffitt Cancer Center, Tampa, FL, University of South Florida Morsani College of Medicine, Departments of Oncologic Sciences² and, Pathology and Cell Biology³

Keywords: B-ALL, c-MYC, EZH2, p-STAT5, Tyrosine kinase inhibitor

Objective: Adult B-lymphoblastic leukemia (B-ALL) is frequently associated with Philadelphia chromosome t(9;22)(q34;q11.2)/BCL-ABL1. A new high risk group driven by alternative kinase pathways, namely Ph-like ALL, has recently been recognized in the subset of Ph (-) ALL. Increased STAT5 phosphorylation may broadly characterize such patients. However, the role of c-MYC, EZH2 andIKZF1 in Ph+ and Ph- B ALL is still unclear.

Methods: Expression of c-MYC, EZH2, IKZF1 and pSTAT5 on bone marrow biopsy was assessed by immunohistochemical stains (IHC). Clinical outcomes were correlated using standard statistics analyses.

Results: 29 B-ALL patients (15 Ph+ and 14 Ph-) with median age 58 years (M: F of 2.1), median WBC 10.1 k/uL, were included in the study. Statistically no significant difference in age, WBC, time to progression (TTP), or overall survival (OS) was apparent between Ph+ to Ph- patients. The IHC staining results showed nuclear expression of pSTAT5 to be more frequently present in Ph+ B-ALL than in Ph- B-ALL (73% vs 33%, p = 0.0574), and three Ph+ patient and one Ph- patient show loss of nuclear expression of IKZF1. c-MYC and EZH2 expressions were identified in 34% and 55% of patients with B-ALL, respectively. Overexpression of c-MYC was associated with decrease in OS (HR 4.1, 95%CI 1.2-13.9, p=0.02), particularly in the group of Ph+ ALL (p=0.0005). There was also a trend for impaired OS in EZH2 + patients with Ph+ ALL. Further analysis demonstrated a trend towards impaired TTP in the Ph- ALL patients with high expression of pSTAT5 (p=0.46).

Conclusion: Overexpression of pSTAT5, c-MYC or EZH2 may be good negative predictors for prognosis and potential therapeutic targets in B-ALL, especially in Ph+ B-ALL.

Presented by: Christina Teefey, MD, Resident

Maternal serum galectin-3 is correlated with obesity

<u>Christina P. Teefey¹, Laura K. Vricella², Maja Okuka¹, John Tsibris¹, Judette Louis¹, ¹Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, University of South Florida Morsani College of Medicine, Tampa, FL. ²Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Case Western Reserve University-MetroHealth Medical Center, Cleveland, OH</u>

Keywords: Galectin-3, cardiovascular disease, body mass index, pregnancy, obesity. Nested case cohort study.

Objective: Galectin-3 is a biomarker that is indicative of inflammation, cardiac remodeling and heart failure. We evaluate the correlation between obesity and serum levels of galectin-3 among healthy pregnant women.

Methods: We performed a nested case cohort study of healthy women recruited at >34 weeks gestation into a protocol to study blood volume. Diagnoses of Chronic hypertension and gestational diabetes were excluded. Fasting serum was collected and analyzed in duplicate for galectin-3 levels. Chi square, Mann Whitney U test and Spearman's correlation were used for data analysis. P<0.05 was considered significant.

Results: The cohort consisted of 30 normal weight (BMI<30 kg/m2) and 30 obese (\geq 30 kg/m2) women. Obese gravidas when compared to normal weight were similar in age (26 ± 1.1 vs. 24 ± 1.07 years, p=0.24) but had a higher pregravid BMI (41 ± 4 vs. 22 ± 2 kg/m2, p = 0.001), study visit BMI (42 ± 4 vs. 27 ± 2 kg/m2, p = 0.001), and fat body mass (43.8±4.8 vs. 27.8±5.2%, p<0.001). The mean galectin-3 levels for the cohort was 6.03±1.7 ng/ml. Obese women had higher serum levels of galectin-3 (6.5±0.29 vs. 5.5±0.33 ng/ml, p=0.02). Galectin-3 levels were significantly correlated with prepregnancy BMI (r=.34, p=0.008) and study visit BMI (r=.35, p=0.009) but not with maternal fat body mass (r=.229, p=.108). In our cohort, 8% of the subjects had a galectin-3 level> 14 ng/ml, indicating higher risk for cardiovascular disease. These women were all African-American (compared to 53% African-American of the remaining subjects).

Conclusion: Galectin-3 is found in the serum of pregnant women and appears to be correlated with obesity. Further larger studies can help delineate the utility of galectin-3 in the assessment of cardiac function among pregnant women.

Abstract #: 104

Presented by: Radouil Tzekov, PhD, Faculty

Ocular changes in patients with Spinocerebellar ataxia type 7

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Keywords: ataxia, cone-rod dystrophy, vision

Objective: Spinocerebellar ataxia type 7 (SCA-7) is a is a progressive, degenerative, autosomal-dominant genetic disease characterized by progressive cerebellar ataxia and cone-rod dystrophy with progressive central visual loss in affected adults. The purpose of this work is to describe the ophthalmological findings in two patients with SCA-7.

Methods: Two female members of the same family were followed up by ophthalmological examinations for five at USF. At the most recent ophthalmic evaluations, best-corrected visional acuity, color vision (Roth 28 Hue test), full-field electroretinography (ERG) and spectral-domain optical coherence tomography (SD-OCT) were performed. DNA was analyzed with polymerase chain reaction for CAG trinucleotide expansion repeats in the SCA 7 gene.

Results: Molecular analysis demonstrated abnormally expanded CAG repeats in both patients (more repeats in the younger patient) confirming the diagnosis of SCA 7. Discreet pigmentary changes in the fovea were present in both siblings, with otherwise unremarkable ophthalmoscopic appearance. SD-OCT demonstrated widespread central retinal thinning. Visual acuity was mildly decreased, but stable in the past five years. Very mild color vision disturbance was noted in the older sibling, while moderate color vision disturbance was present in the younger sibling. Scotopic ERG was within the normal range, while photopic ERG showed signs of mild cone dysfunction more pronounced in the younger sibling.

Conclusion: SCA 7 causes pigmentary foveal changes and widespread central retinal thinning. Preliminary correlation between the genotypic expression of the expansion repeats of the SCA-7 gene and the visual function is noted.

Presented by: Tahseen Ismail, BS, Med III Student

Underlying Causes of the Low Level of Fully Immunized Children in Rural Aligarh, Uttar Pradesh, India

Tahseen Ismail¹, Afzal Sayeed², Lynette Menezes³ ¹University of South Florida, Morsani College of Medicine, Tampa, FL, ²Department of Sociology and Social Work, Aligarh Muslim University, Aligarh, Uttar Pradesh, India ³Division of Infectious Disease & International Medicine, Morsani College of Medicine, Tampa, FL, University of South Florida Morsani College of Medicine Pediatrics

Keywords: Immunization, Aligarh, Childhood Vaccination

Objective: At 22%, the city of Aligarh in Uttar Pradesh has one of the lowest rates of fully vaccinated children in India. To improve these rates, the government provides free vaccines and has set up extensive village education programs, however the issue persists. This study investigates the reasons for the low rate of fully and partially vaccinated children in Aligarh.

Methods: A semi-structured survey was administered to a convenience sample of 60 mothers of children under one year of age and 15 village healthcare workers from 10 villages surrounding Aligarh. 5 villages with the highest vaccination rates (HVR) and 5 with the lowest vaccination rates (LVR) were selected. To assess whether Auxiliary Nurse Midwives (ANMs) were administering vaccines as reported, the vaccination logbooks of 10 ANMs assigned to these villages were evaluated and verified.

Results: In HVR villages, 43% of mothers cited fear of post-vaccination fever or illness as the reason for the lack of receiving immunization. In LVR villages, 53% of mothers cited ANM absenteeism and 47% reported refusal of ANMs to open a new vaccine vial as the main barriers to having their children fully immunized. Of the ANM logbooks reviewed, the majority (4 of 5) in the LVR villages had discrepancies between the number of ANM documented vaccinations versus the number documented by the village health workers, compared to the logbooks in HVR villages (2 of 5).

Conclusion: Although cultural ideas about vaccinations are a barrier to immunization in rural Aligarh, issues with ANMs not administering vaccines may be a more critical barrier to increasing vaccination rates. Educating ANMs and parents is essential to increase these rates in all of rural Aligarh.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 106

Presented by: Brian Madow, MD, Faculty

Remote screening for Diabetic Retinopathy

Brian Madow, USF Eye Institute, University of South Florida Morsani College of Medicine Ophthalmology

Keywords: Diabetic retinopathy screening, telemedicine

Objective: To implement a telemedicine based retinal imaging screening program for early detection of diabetic retinopathy in patients with known Diabetes mellitus evaluated at the newly established USF Diabetes home facility and to report the initial results from the screenings.

Methods: We established remote fundus image reading center and evaluated and implemented secure image transfer and archiving protocol. Standardization of the viewing condition were tested and applied. Graders were selected and trained in recognizing retinal pathology from diabetic retinopathy. Thirty three (21 males and 12 females) patients with Diabetes mellitus were imaged in the clinic and the images were remotely transferred to USF Eye institute diabetic retinopathy Reading Center for evaluation. Total of 66 (33 left eye and 33 right eye)retinal images were evaluated so far and the results were reported to the USF medicine providers.

Results: The age of the patients varied from 19-69 and the known duration of the Diabetes was from 1 month to 30 years. Out of 33 patients 10 patients had a positive screen for diabetic retinopathy and referral for clinical retinal evaluation was generated. The retinal changes were observed bilaterally.

Conclusion: A telemedicine based screening program was designed and successfully implemented. One third of the screened patients were positive for diabetic retinopathy previously undiagnosed and referred for retinal evaluation. Early detection of the retinopathy and prompt referral are invaluable in preventing complications and severe vision loss.

Presented by: Eric Shamas, BS, Med II Student

Voces de Cedro Galan: Community Based Participatory Research in a Resource Poor Region of Nicaragua Eric Shamas¹, Eric Monaco¹, Abraham Salinas MD, PhD², Robert Nelson MD³ ¹University of South Florida Morsani College of Medicine, ²University of South Florida College of Public Health, ³University of South Florida, USF Health Office of Children's Health,

Keywords: Community-based Participatory Research, Photovoice, Nominal Group, needs assessment, Nicaragua.

Objective: Preliminary research in the underserved Cedro Galán community in Nicaragua found that 79% of participants chose healthcare as their primary need. This study was conducted to assess specific health needs and concerns of community residents and to create a prioritized needs list to direct future interventions.

Methods: The Voces study uses a community-based participatory approach, employing a mixed methodology consisting of Photovoice and nominal group techniques. Participants included 10 community stakeholders in Cedro Galán, Nicaragua. In the Photovoice method, these community members photographed their community over five days and presented their photos during guided discussion sessions in which key themes were recorded. Participants were then presented with these themes in nominal group sessions, where they identified and selected the most important issues by assigning a numeric value in order to create a prioritized list of health needs.

Results: An extensive list of themes emerged during the Photovoice session that included both social and economic concerns related to health, such as lack of access to primary care, lack of transportation to medical care, poor water sanitation and waste management, lack of public health education, and poverty. The nominal group results specifically indicated that access to primary care services and affordable treatments are the most highly prioritized concerns requiring intervention.

Conclusion: Health interventions in Cedro Galán should focus on access to basic health services. Secondary interventions may target the wide range of health and social issues that emerged in the study.

Research supported by: USF Scholarly Concentration Program Summer Stipend Award and the International Medicine Scholarly Concentration.

Abstract #: 108

Presented by: Jonathan Wischhusen, MD, Med II Student

Factors Associated with Health Literacy in a Community-based Sample of Older Blacks <u>Wischhusen J^{1,2}, Davis SN², Jackson B², Govindaraju S², Lin HY², Fulp W², Gwede CK²</u> ¹Moffitt Cancer Center, ²University of South Florida Morsani College of Medicine, Department of Oncologic Sciences

Keywords: Health Literacy, Colorectal Cancer Screening, Community Based Participatory Research

Objective: Colorectal cancer screening (CRCS) saves lives, but utilization rates are low, especially among ethnically diverse Blacks. Lower health literacy (HL) has been shown to be associated with decreased knowledge of CRCS modalities and more negative attitudes towards CRCS. This preliminary analysis examines factors associated with HL in a sample of ethnically diverse Blacks.

Methods: Participants were enrolled in a community based intervention trial designed to promote CRCS with immunochemical fecal occult blood test among average risk men and women aged 50 to 75 years. 158 participants completed baseline surveys assessing HL, CRCS awareness, cancer fatalism, Preventive Health Model (PHM) constructs and demographics. HL was measured using the eight item REALM-R measure; a score of 7 or greater is considered high health literacy.

Results: Majority of participants were female (55%), born in the US (93%), and made > \$10K per year (65%). The median age was 55.5 and 53% of participants had high HL. Bivariate analysis found high HL was significantly associated with CRCS awareness, PHM salience, PHM susceptibility, PHM social influence, PHM religious beliefs, cancer fatalism, gender, employment, education and income. Final multivariable logistic regression model found that high HL was significantly positively associated with awareness (OR=:1.6, p=<.001) and higher income (OR=:5.0, p=0.003) and negatively associated with PHM social influence (OR=:0.9,p=0.033) and cancer fatalism (OR=: 0.8, p=0.017).

Conclusion: Better understanding of HL will be beneficial in targeting appropriate media messages for CRCS screening education. Specifically, lower income medically underserved groups require low literacy materials addressing cancer fatalism and negative CRCS beliefs.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Skill Assessment of Neonatal Intubation Performance: A descriptive study by use of Video Laryngoscope

Rohit Aswani,MD, Shari Roberts, RN,MSN, Judy Zaritt, RN,BSN, Angel A Luciano, MD, Laura Haubner, MD University South Florida Morsani College of Medicine, Department of Pediatrics, Division of Neonatal-Perinatal Medicine

Keywords: Neonatal Intubation, Video Laryngoscope, Skill Assessment

Objective: To describe the multiple components of neonatal tracheal intubation (TI) attempts in novices, advanced learners, and experts using direct larynge copy (DL) through ideo laryngescope recording review

Withdrawn

Results: Preliminary results demonstrated possible differences between levels of expertise (novice, advance and expertise) and different variables measured via video laryngoscope (Tables 1- 4). Expertise and time of best view and successful rate also was obtained from the preliminary videos (Figure 1 and 2.

Conclusion: Multiple components of neonatal intubation technique can be accurately measured using video laryngoscopy. Understanding the specific causes of failure in trainees including pediatric house staff is necessary to develop effective training module and define measurable competencies of providers in the changing era of trainee duty hour limitation and increase in the use of non-invasive ventilation in the NICU.

Research supported by: University of South Florida GME Research Grant program.

Abstract #: 110

Presented by: Jack Burns, MD, Med IV Student

The Impact of Deliberate Practice in the Acquisition of Surgical Skills

Jack Burns¹, Jeffrey Cone², Jessica Ching², Paul Smith² ¹University of South Florida Morsani College of Medicine, ²USF Morsani College of Medicine, Department of Surgery, Division of Plastic Surgery

Keywords: Breast Reconstruction, Deliberate Practice, Resident Education

Objective: Deliberate practice is defined as a structured activity in which the explicit goal of the activity is to improve performance. In the field of medicine, deliberate practice is specifically described as an activity in which there is repetitive performance of cognitive or psychomotor skills, rigorous skills assessment, continual feedback, and improved skills performance. The purpose of this study was to assess the impact of K. Anders Ericsson's theory of deliberate practice on the operative times of breast reconstruction via transverse rectus abdominis myocutaneous (TRAM) flaps.

Methods: A retrospective review of TRAM flap breast reconstruction was performed of resident-associated cases at the Moffitt Cancer Center from 2009-2011. Residents trained according to the deliberate practice model over their four-month rotations and trained along a continuum of increasing resident independence. Operative times were categorized into the 1st, 2nd, 3rd, and 4th months of the rotation.

Results: There were 75 cases (n=75) that met inclusion criteria. Median duration of procedures for the 1st, 2nd, 3rd, and 4th months were 5.63 hours, 5.17 hours, 4.93 hours, and 4.80 hours, respectively. While the decline in procedure time was not statistically significant (p=0.2440), the correlation coefficient (r=-0.25) for operative times for these cases over the four months was significant (p=0.048).

Conclusion: This study marks the first application of the theory of deliberate practice to a complex skill set in the surgical literature. Further evaluation is warranted to determine whether this didactic model can be formalized to potentially accelerate the acquisition of the complex skill set required for breast reconstruction via TRAM flaps.

Research supported by: Moffitt Cancer Center Breast Program

Presented by: Kevin Cronin, BS, Med III Student

What Factors Influence a 4th Year Medical Student's Rank Order List?

Kevin Cronin, Pete Peterson, Frazier Stevenson University of South Florida Morsani College of Medicine

Keywords: Education, Residency, Students

Objective: Each year, fourth year medical students from across the country and abroad vie for the more than 26,000 firstyear residency program positions at U.S teaching hospitals. To be considered for one of these slots, students must construct a Rank Order List (ROL) – a list of each residency program where the student interviewed and is willing to attend, ranked from most to least desirable. Though this is one of the most stressful aspects of a student's journey, little to no recent data exist on how medical students prioritize their ROL.

Methods: To better understand these factors, we anonymously surveyed the University of South Florida Morsani College of Medicine Class of 2013 regarding what factors were most important when ranking residency programs. Data was collected regarding factors used to rank programs highly, factors used to rank programs lowly, information regarding post interview day contact, and information regarding inappropriate questioning during residency interviews.

Results: Factors leading to a higher ranking for an individual program were interactions with current residents, geographic location, and general reputation. Negative factors most commonly listed included interactions with current residents, geographic location, and interactions with the residency director.

Conclusion: Factors which positively impact a residency program's ranking are similar but not mutually exclusive with factors which negatively impact programs. Post interview day contact was found to be quite commonplace though the effect on a program's ranking is unclear. Inappropriate questioning of applicants was also found to be widespread.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine.

Abstract #: 112

Presented by: Anastasia Groshev, BS, Med I Student

Interprofessional - Interdisciplinary Education: Simulating the future of healthcare to prepare the Professionals of tomorrow

<u>Anastasia Groshev¹, Yashwant Pathak²</u> ¹University of South Florida Morsani College of Medicine, Tampa FL, ²USF Health College of Pharmacy, Tampa, FL

Keywords: interdisciplinary collaboration, interdisciplinary competence, interdisciplinary education methods, medical professional education, medical errors

Objective: Current healthcare networks consisting of increasing number of specialist and professionals such as doctors, pharmacists, physician aids, practical nurses, nurses, and technicians warrants increasing complexity and number or interactions within the healthcare team. Thus, interdisciplinary collaborations are of especial importance in tackling patient safety issues in healthcare.

Methods: A systematic literature survey was done with the questions considered about receptivity of the students, current methods, the degree of improvement in interdisciplinary literacy and patient safety.

Results: One of the key issues in healthcare is patient safety. Growing complexity of the healthcare team allows providing more holistic care, but also increases the number of potential errors. High of incidence of medical errors is the reality of today. Current literature demonstrates a great deal of receptivity of students to learn in interdisciplinary setting. Current methodology in specific to interdisciplinary education is limited; however, few classes where students from various disciplines have been attempted. Although assessment of the success of such interventions is difficult to measure, the results of surveys document increase in interdisciplinary literacy.

Conclusion: Incorporation of focus on interdisciplinary education is necessary to adequately prepare the students for their practice in the healthcare setting. Ideally simulation of healthcare issues is currently the best method of helping the students learn to collaborate to tackle the problems. Classes where students come together from various disciplines to learn and brainstorm together equip students for optimal performance in interdisciplinary healthcare teams.

Presented by: Gregory Horn, BA, Med IV Student

Fundamentals of Laparoscopic Surgery Skill Acquisition: A comparison of blocked versus interleaved practice <u>Horn GT¹, Schnaus MJ¹, Goldin S¹, Grichanik M², Ducey AJ², Nofsinger C¹, Hernandez D¹, Shames M¹, Singh R¹, Brannick <u>MT²</u> ¹University of South Florida Morsani College of Medicine, Department of Surgery, ²University of South Florida, Department of Psychology</u>

Keywords: FLS, surgical training, learning curve, surgical skill, education

Objective: FLS certification is required for general surgery. The recommended practice for learning FLS is to practice tasks one at a time until proficient (blocked practice). Learning theory suggests that interleaved practice, a method in which tasks are rotated rather than learned one at a time, may result in superior learning.

Methods: Residents were randomized into one of two groups: blocked practice or interleaved practice. We compared the performance of residents across groups over 20 trials of each of four FLS tasks (peg transfer, pattern cut, extracorporeal suture, intracorporeal suture). Four weeks later, participants returned to the lab and completed two additional trials of each of the four tasks.

Results: Performance on each of the tasks improved with increased practice. The interleaved group showed significantly better performance on the peg transfer task; trends favoring the interleaved group resulted for the other tasks. Standardized mean differences in favor of the interleaved group were substantial both at the end of practice and at follow-up with the sole exception of the pattern cut.

Conclusion: Interleaved practice appears superior to blocked practice in developing and retaining FLS skills within our limited study. We encourage others to experiment with the method to confirm our findings.

Research supported by: USF Morsani College of Medicine Department of Surgery

Abstract #: 114

Presented by: Aaron Lozano, BS, Med IV Student

Learning to be a First World Physician in a Third World Country <u>Aaron Lozano, BS; Orhan Arslan, DVM, PhD; Asef Mahmud, MD</u> University of South Florida Morsani College of Medicine

Keywords: anatomy, 3D, social media, physical diagnosis

Objective: To assess the efficacy of modern technology in enhancing the development of basic physical exam and diagnostic skills in a setting with limited resources.

Methods: A visually-driven case-based presentation was created using previously developed interactive anatomical models in order to educate students on basic human anatomy and common associated clinical pathologies. Modern known social media modalities were used to engage students during these presentations as well as to provide them with a long-term medical resource that can effectively be used to engage the designated material after the conclusion of the presentation. A digital assessment method was also created to measure students' level of knowledge in basic physical exam and mastery of diagnostic skills before and after their engagement with the designated material. Given their intended focus on learning clinical medicine and their background in natural sciences, first year medical students serve as an ideal demographic theme for these presentations.

Results: By the time the necessary presentations and assessments are developed, most first year medical students in U.S. medical schools will have advanced in their curriculum beyond the material covered in these presentations. Therefore, the intended sample size could not be obtained in order to deliver and completely assess the effectiveness of this model.

Conclusion: By having the necessary presentations and assessments already developed prior to the start of the 2014-2015 medical school class, implementation of these works and extraction of data that fulfills our objective should be feasible with next year's class of first year medical students early on in their curriculum.

Research supported by: 2011 Scholarly Concentrations Program Summer Award

How Many Ultrasound Examinations Are Necessary To Gain Proficiency In Accurately Identifying The Nerves Of The Brachial Plexus?

Raymond Merritt, DO, Charlotte Derr, MD, RDMS, Saundra Jackson MD, RDMS, Zuheily Closser MD, Tabitha Campbell MD, Leah Boyette MD, Branko Miladinovic, PhD. University of South Florida Morsani College of Medicine

Keywords: education ultrasound anatomy resident training nerve block

Objective: The purpose of this study is to establish the number of supervised examinations required for an Emergency Medicine physician to gain proficiency in accurately locating and identifying the nerves of the brachial plexus at the level of the interscalene space and supraclavicular fossa.

Methods: Proficiency was defined as the number of attempts a resident needed to locate and identify the nerves of the brachial plexus for 10 consecutive examinations. Didactic education was provided via a one hour lecture on brachial plexus, sonographic technique, identification of the interscalene space and supraclavicular fossa, 2 supervised hands-on exams for each region prior to testing. Count data are summarized using percents or medians and range. Random effects negative binomial regression was used for modeling panel count data where negative coefficients indicate increase in proficiency.

Results: Complete data for the number of attempts, confidence, gender, and years in practice was available for 24 residents. 14 male and 10 female residents were studied. years in training: 9 in year 1, 9 in year 2, and 6 in year 3. The median number of attempts and range for the interscalene space and supraclavicular fossa were 2 (1-3) and 2 (1-3) respectively. The median level of confidence and range for the interscalene space and supraclavicular fossa were 3 for both. Negative binomial regression identified a significant association between confidence and proficiency (P = 0.009).

Conclusion: proficiency can be quickly obtained in identifying the nerves of the brachial plexus after only a few proctored examinations. A significant association was found between confidence and proficiency, implying that confidence increases as the number of exams performed increases.

Abstract #: 116

Presented by: Shreya Narayanan, BS, Med II Student

Nutrition Education: a curriculum to increase nutrition competency among medical students <u>Shreya Narayanan, B.S.¹, Candace L. Haddox¹, William Johnson¹, Ellen Kent², Frazier Stevenson¹</u> ¹University of South Florida Morsani College of Medicine, ²USF College of Public Health

Keywords: nutrition, community outreach, medical education

Objective: Despite the rise in obesity and metabolic syndrome, medical school curricula have fallen short of training students to become proficient in nutrition counseling. This project aims to increase the nutrition proficiency of USF medical students via online modules and nutrition counseling.

Methods: The curriculum includes five online modules, a didactic session, a clinical skills session, and opportunities for practical application at local health fairs. The modules present a nutrition overview, dietary considerations for diabetes, hypertension, and hyperlipidemia, and a discussion on obesity and approaches to counseling patients with metabolic syndrome. The didactic session focuses on nutrition counseling and prepares students for a practice counseling session with a standardized patient. At the health fair, students interpret patients' results, review their diet, and set goals for diet modification. We collected preliminary data on the effectiveness of the diabetes module and the health fair experience. Students received a survey to assess their nutrition knowledge and counseling ability before and after the diabetes module.

Results: Ten students have completed the diabetes curriculum and participated in three health fairs. Overall, 75 patients have received counseling. 90% of students reported an increase in nutrition knowledge and counseling ability following the module. Importantly, 100% of the students felt they were more likely to counsel patients in the future.

Conclusion: The nutrition curriculum increased the number of nutrition contact hours, which resulted in students feeling more comfortable with counseling patients on nutrition. In the future, we plan to further assess the impact on students' nutrition proficiency.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Neonatal abstinence syndrome management: A quality improvement (QI) initiative to educate caregivers, and providers in the outpatient setting.

Nguyen J, MD*, Chau K, DO*, Lilly C, MD, Ashmeade T, MD, Balakrishnan M, MD * indicates first authors University of South Florida Morsani College of Medicine Pediatrics

Keywords: Neonatal abstinence syndrome outpatient management

Objective: Outpatient medical management for neonatal abstinence syndrome (NAS) can reduce medical costs. Our aim is to demonstrate that implementation of an outpatient guideline for NAS will result in: $1. \ge 75\%$ of caregivers and providers having improved knowledge and attitudes regarding care of a NAS infant, $2. \ge 75\%$ of providers complying with the outpatient management guideline, $3. \ge 75\%$ of providers using EMR outpatient templates, $4. \ge 40\%$ reduction in days of outpatient methadone therapy (goal ≤ 42 days).

Methods: The USF/ TGH Joint Neonatal Follow-up Program (JNFP) uses methadone for outpatient management of NAS. Infants in TGH'S NICU who are cleared for outpatient management can be discharged when NAS symptoms are controlled with ≤0.16 mg/kg/day of methadone. The JNFP implemented a discharge program including NAS caregiver education, NAS symptom diary, care plan awareness, occupational therapy and social work consult. We also implemented an outpatient NAS management guideline and EMR template. The guidelines have been implemented for two QI cycles. Pre and post-implementation surveys were sent to caregivers and providers.

Results: From pre- to post-implementation, the percent of caregivers with a good understanding of NAS increased from 60% to >75%. Outpatient NAS guideline use increased from 69% to 77%, and EMR template use remained > 73%. There was a 25% decrease in mean length of methadone treatment from 67 days to 50 days. Post-implementation provider survey responses are pending.

Conclusion: Outpatient NAS management is feasible and safe when discharge planning, caregiver education, and NAS guidelines are used. This comprehensive education program improves caregiver knowledge and attitudes and decreases length of methadone treatment.

Research supported by: Healthy Start

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Abstract #: 118
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Presented by: Soha Patel, MD, Resident

Diabetic Ketoacidosis (DKA) in Pregnancy: A Comprehensive Simulation to Improve Patient Safety and Quality of Care

Soha S. Patel, MD¹, James Palmer, MD¹, Shelly Holmstrom, MD¹, Nikki Campbell, MSN, RN², David Craig, MEd², Valerie Whiteman, MD¹ ¹University of South Florida Morsani College of Medicine, Department of Obstetrics & Gynecology, ²USF Health Center for Advanced Medical Learning and Simulation (CAMLS).

Keywords: diabetic ketoacidosis (DKA), simulation, education, patient safety, obstetrics

Objective: Provide real-life scenarios to OB/GYN residents, attending physicians, and nurses in order to more effectively manage DKA in pregnancy via a simulated, multi-hour hospital admission

Methods: Eighteen participants from the Department of Obstetrics and Gynecology completed small group, simulatedbased education, feedback session, and skills assessments. The participating individuals were divided into three groups who participated in a simulation including changes in hemodynamics, laboratory results, and fetal heart monitoring. Skills included: 1. Identifying clinical signs and symptoms of DKA 2. Describing the major metabolic changes and causative factors of DKA 3. Ordering appropriate laboratory and diagnostic studies 4. Outlining medical management of DKA 5. Discussing potential complications and prognosis to both patient and fetus Participants were given a pre-simulation knowledge test, followed by a didactic course on management of DKA. They then participated in the simulation and a postsimulation knowledge test. Participants' post-simulation scores were compared with baseline pre-simulation scores to assess the effectiveness of the intervention.

Results: The knowledge assessments, pre- and post-simulation, were evaluated using unpaired t-tests, and the participants' overall scores were found to be significantly higher after participating in the simulation (67.75 versus 77.68, p = 0.0027).

Conclusion: After the simulation, participants' knowledge in managing DKA in pregnancy substantially improved based on the pre- and post-simulation assessments. Therefore, simulation-based education demonstrates its strong utility and effectiveness in high-risk, low-incidence medical emergency events.

Research supported by: USF Department of OB/GYN, Graduate Medical Education, CAMLS

Presented by: Jacob Pierce, BS, Med II Student

Examination of the factors influencing research efficiency

Jacob Pierce, Carolyn Hanna, Neal Rajyaguru, Frazier Stevenson MD University of South Florida Morsani College of Medicine

Keywords: Research, Efficiency, Education

Objective: The goal of this study is to analyze why academic research facilities have varying degrees of productivity. We hypothesize that researchers whose mentors favorably influenced their research career will likely have higher productivity than those who report otherwise. Also, researchers who report a high degree of collaboration with other researchers will have a higher productivity than those that do not. Essential to the hypothesis is that researchers will report that their education and degree of collaboration are strong determinants of their success. Our main objective is to determine which factors researchers believe to be the main determinant of their success.

Methods: Recorded 15 minute interviews will be requested of participants that will take place at a convenient location. All information collected is confidential, and will not be disclosed with identifiable information. The only inclusion criterion is that the subject is a student or faculty researcher at the USF MCoM.

Results: Our preliminary results show that funding is one of the most important factors governing research productivity. Greater than 75% of researchers believe that USF MCoM can improve in terms of research efficiency. Collaboration was almost unanimously listed as a positive force in research, however many admitted they do not collaborate as often as they would like. Concerning education, the majority of faculty researchers stated the mentorship model was ideal for learning to become an effective researcher.

Conclusion: The domains of Finance, Collaboration, and Education are key determinants of research efficiency. Other domains that appeared in the interviews included University Infrastructure, and Administrative responsibilities significantly impacting research efficiency.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 120

Presented by: Rita Raturi, BS, Med IV Student

Improving Collaborative Global Communications

<u>Rita Raturi BS¹, Michelle Grunauer MD PhD², Goldny A. Mills Bradshaw MD MPH³, Ana J Santo BS¹, Robert M Nelson MD MS⁴ ¹University of South Florida Morsani College of Medicine, ²Decana Esuela De Medicina, ³Universidad Central del Este-Epidemiologia, ⁴USF Health Office of Children's Health</u>

Keywords: telecommunication, skype, global, public health

Objective: To develop recommendations that assist with the exchange of international healthcare information via video conferencing and to develop a method for evaluation of this form of communication.

Methods: A literature review was performed in Pubmed on existing fund of knowledge about international health and telecommunications. Data was collected in the form of surveys after Skype sessions with medical students from international medical schools.

Results: International healthcare would benefit in terms of cost effectiveness and patient outcomes by utilizing telecommunications. Further development of telemedicine is particularly relevant in developing countries. Participants believed that promoting professional relationships and adequate exchange of information were important factors in video teleconferencing. Skype videoconferencing attendees recommended consistent methods and structure to better facilitate education during sessions.

Conclusion: Institutions should consider strategies and how to implement global information exchange. More data should be collected, particularly surveys of physician-to-physician interactions, satisfaction of telecommunication, and how to utilize open access websites and telecommunication to better meet international millennium goals.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Anatomy and Physiology: A curriculum to increase medical competency of URM high school students and promote medicine as a possible career option.

Charles DeMello-Schutt MS. University of South Florida Morsani College of Medicine

Keywords: PCAP, Anatomy, Physiology, Curriculum, OSDE

Objective: Pre collegiate Anatomy and Physiology (PCAP) curriculum at USF MCOM was created in order to address the disproportionately small percentage of medical school applicants, matriculates, and physicians who are considered underrepresented in medicine (URM). The goal of the program was to provide opportunity for high school URMs to be successful at an early age and expose them to different aspect of medicine to promote interest.

Methods: Following IRB approved educational research protocol, PCAP offered lectures with clinical correlations in Nervous, Cardiovascular, Digestive, Skeletal, Respiratory, Immune, and Integumentary systems. Anatomy lab periods were provided at the COM Anatomy Laboratory. Two separate summer enrichment programs in the Tampa Bay area received the curriculum: both of which identify as summer enrichment programs for underrepresented minorities. Curriculum effectiveness was determined by analyzing pre-course and post-course exam scores and faculty evaluations of student CPS presentation.

Results: Students showed significant improvement in all the subject matter covered and also had an increase in their interest in pursuing medicine as a lifelong profession. Group A students had a pretest average of 24% and an initial interest rate of 6.3. Following completion of the course, final exam average was 94% and interest rate of 9.4. Similarly, Group B stats were 14%:4.5 and following completion 85% and 9.4.

Conclusion: Results support prior efforts that indicate that early intervention is important to develop students who have greater self-efficacy about their pre-health careers. PCAP's CPS based teaching strategy along with anatomy lab access helps students grasp key concepts in six major body systems and promotes interest in medicine.

Research supported by: This research was supported by a stipend from the Scholarly Concentrations Program (Education Scholarly Concentration) at USF Health Morsani College of Medicine

Abstract #: 122

Presented by: Mary Cain, MD, Faculty

Timing of delivery of a gastroschisis affected pregnancy and its impact on perinatal outcomes and hospital costs Mary Ashley Cain, MD¹, Jason L Salemi, MPH², Jean P Tanner, MPH³, Mulubrhan F Mogos, PhD², Russell S Kirby², PhD, <u>Valerie E Whiteman, MD¹, Hamisu M Salihu, MD, PhD, MPH²</u> ¹University of South Florida Morsani College of Medicine Obstetrics & Gynecology, ²USF College of Public Health, Department of Epidemiology & Biostatistics, and, ³Department of Community & Family Health

Keywords: Cost; epidemiology; gastroschisis; gestational age; perinatal outcomes

Objective: To investigate the association between timing of delivery and perinatal outcomes among gastroschisis-affected pregnancies that result in live birth.

Methods: We conducted a population-based, retrospective cohort study using a linked maternal- infant database for over 2.3 million live-born infants in Florida from 1998-2009. Cases were identified using a combination of International Classification of Diseases, Ninth Edition, Clinical Modification diagnosis and procedure codes indicative of gastroschisis. We restricted our analyses to singleton cases without another major birth defect and without medical conditions that would justify early elective delivery. We categorized cases based on gestational age in weeks and compared perinatal outcomes, including inpatient costs and length of stay, among these groups.

Results: Among 1,005 infants with gastroschisis, 325 (32.3%) were isolated, singleton cases without another reason for early delivery. We observed an inverse relationship between gestational age and the prevalence of adverse pregnancy outcomes, including jaundice (<34 weeks: 38.5%; ≥39 weeks: 9.4%), respiratory distress syndrome (<34 weeks: 23.1%; ≥39 weeks: 6.3%), and the need for additional operations of the large and small intestine (<34 weeks: 15.4%; ≥39 weeks: 3.1%). As the timing of delivery increased, we observed fewer mean number of days spent in the hospital (55.9, 51.6, 36.9, 32.7) and lower direct inpatient medical costs (79, 71, 51, 45, in thousands, \$US), per infant, in the first year of life.

Conclusion: In pregnancies complicated by gastroschisis, and with no other known major indications, delivery at or beyond 37 weeks is associated with improved perinatal outcomes and lower medical costs.

Research supported by: Internal department funded.

Presented by: Matt Doepker, BS, Resident

Predictors of improved survival in patients undergoing pulmonary metastasectomy for sarcoma

Matt Doepker, Nasreen Vohra, Christy Chai, Shawn Tejiram, Anthony Conley, Eric Toloza, Jacques Fontaine, Douglas Letson, Jongphil Kim, Eric Sommers, Jonathan Zager, Ricardo J. Gonzalez. University of South Florida Morsani College of Medicine

Keywords: Pulmonary metastasectomy for sarcoma

Objective: Pulmonary metastasectomy (PM) for sarcoma can result in significant long term survival in selected patients. The aim was to determine factors associated with improved survival.

Methods: 120 pts undergoing PM for sarcoma at Moffitt Cancer Center over 12 years were reviewed. Survival calculated with Kaplan-Meier method and Cox proportional hazard uni/multivariate(MV) regression models used to analyze relationships amongst clinicopathologic variables and overall survival (OS).

Results: 95(79%) patients had soft tissue sarcomas, median follow up was 48 months. 14(15%) had synchronous metastasis with median OS of 21 months. Of the 81(85%) patients with local disease, the median disease free interval (DFI) from primary resection was 13 months and median OS was 48 months. On MV analysis, presence of synchronous metastasis (p=.005), older age at diagnosis(p=.02) and increasing number of lung lesions (p=.003) were independent predictors of poor survival. 71(59%) had 1 PM, 32(27%) had 2 and 17(14%) had 3 or more PM with OS being 17, 37 and 34 months in each group following first metastasectomy with a higher number of PM associated with improved survival(p=.01). The median OS of patients with a DFI \ge 12 vs. < 12 months following primary resection was 93 months and 43 months (p=.004) and following metastasectomy was 30 months and 34 months (p=.26).

Conclusion: Synchronous metastasis, advanced age and greater metastatic disease burden result in worse OS in patients with soft tissue sarcoma. Patients undergoing multiple PM have a survival benefit likely resulting from favorable disease biology. In patients with DFI of > 12 months and minimal comorbidities PM should be considered.

Abstract #: 124

Presented by: Eleazar Gil-Herrera, PhD, Postdoctoral Fellow

An iOS-based Application for Pain Management

<u>Eleazar Gil-Herrera, Ph.D, Athanasios Tsalatsanis, Ph.D, Jasmin Lacevic, Benjamin Djulvegovic, M.D, Ph.D,</u> University of South Florida Morsani College of Medicine, Department of Internal Medicine, Center for Evidence-based Medicine and Outcomes Research

Keywords: Pain Management, Mobile medical applications, Decision-making

Objective: To developed an evidence-based pain management application designed to assist physicians in the care of adult cancer patients.

Methods: Our application is implemented using the iOS platform and runs on Apple iPad mobile devices to support bedside care.

Results: The application is following the latest NCCN guidelines for pain management and includes features such as pain assessment; medication recommendation; medication dosage conversion; and prescription generation.

Conclusion: We develop a mobile pain management application. We hypothesize that including health care guidelines in the development of our application will improve decision-making in pain management. We intent to test this hypothesis in a clinical trial.

Research supported by: This work was supported by the Department of Army under grant #W81 XWH-09-2-0175 (PI. Dr. Benjamin Djulvegovic, M.D, Ph.D.)

Presented by: Nicholas Govsyeyev, BS, Med **II Student**

A Multi-Institutional Series of Pure Myxoid Liposarcomas of the Extremities and Torso

Nicholas Govsyeyev, BS¹, Katherine J. Baxter, MD², Sarah B. Fisher, MD², Jukes P. Namm, MD⁴, Thomas Krausz, MD⁵, Sharon W. Weiss, MD⁶, David K. Monson, MD⁷, Ricardo J. Gonzalez, MD^{1,3}, David Cheong, MD³, G. Doug Letson, MD³, Marilyn M. Bui, MD,PhD³, Kevin K. Roggin, MD⁴, Keith A. Delman, MD², Kenneth Cardona, MD², Jonathan S. Zager, MD^{1,3}. Department of Cutaneous Oncology, Moffitt Cancer Center, Tampa FL, ²Dept of Surgery, Div of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta GA, ³Sarcoma Dept, Moffitt Cancer Center, Tampa FL, ⁴Div of Surgical Oncology, University of Chicago, Chicago IL, ⁵Dept of Pathology, University of Chicago, Chicago, IL, ⁶Dept of Pathology & Laboratory Medicine, and, ⁷Dept of Orthopedic Surgery, Emory University, Atlanta GA

Keywords: pure myxoid liposarcoma surgical outcomes

Objective: The natural history of patients with pure (<5% round cell component) myxoid liposarcomas (MLPS) has not been well characterized. We hypothesized that the tenets of aggressive multimodality therapy (neoadjuvant/adjuvant radiation (XRT) or chemotherapy) and widely negative margins broadly applied to soft tissue sarcomas may not apply to MLPS.

Methods: This multi-institutional study retrospectively examined the natural history of patients with pure MLPS of the extremities or torso undergoing definitive surgical resection from 1/2000-1/2010.

Results: Of 103 patients with localized primary MLPS, the median age was 48yrs and 59 (57%) were male. Tumors were located on the lower extremity in 83 (81%), upper extremity in 6 (6%), and torso in 14 (14%) pts. Positive margins occurred in 13% of pts. Systemic chemotherapy was administered to 8 pts (8%). Preoperative or post-operative XRT was administered to 52 (51%) and 31 (30%) pts, respectively; 24 (23%) pts did not receive XRT. With a median follow-up of 49 mos, 15% of pts had recurred (2 local, 13 distant) and 6% of pts had died of disease. On Kaplan-Meier survival analysis, median recurrence free (RFS) and disease specific survival (DSS) were not reached; mean RFS and DSS were 118 and 149 mos, respectively. Margin status and use of chemotherapy were not associated with RFS. On multivariate analysis increasing tumor size was the only predictor of decreased RFS; XRT, when adjusted for age, tumor size, and grade did not impact RFS.

Conclusion: The incidence of local and distant recurrence in patients with localized, primary MLPS of the extremities or torso is low with favorable prognosis. In light of these findings, the role of multimodality therapy in this histologic subtype should be evaluated prospectively.

Abstract #: 126

Presented by: Monique Konstantinovic, BS, Med II Student

Sentinel node biopsy is indicated for thick clinically node-negative melanoma

Monique Konstantinovic, Maki Yamamoto MD, Joyce Y Wong MD, Kate J Fisher MA, Jonathan Koscso, Nicholas Govsyeyev, Jane L Messina MD, Amod A Sarnaik MD, C Wayne Cruse MD, Christopher A. Puleo, Ricardo J Gonzalez MD, Vernon K Sondak MD, Jonathan S Zager MD University of South Florida Morsani College of Medicine, Department of Surgery

Keywords: Melanoma, Sentinel Lymph Node Biopsy

Objective: Sentinel lymph node biopsy (SLNB) is standard of care and a staging procedure for intermediate thickness melanoma. Since the ASCO guidelines do not definitively recommend SLNB for thick melanoma, we sought to determine if there is a prognostic survival benefit to SLNB in these pts.

Methods: From 1999 to 2012, 571 pts with melanoma whose primary tumors were ≥4mm in Breslow depth were evaluated from a single institution. Associations between survival and clinicopathologic characteristics were explored.

Results: Of 571 pts, 401(70.2%) were male and median age was 66. The median Breslow depth was 6.2 mm (range 4-25). 412 pts (72%) underwent SLNB and 46 (8%) underwent complete node dissection due to clinically positive nodal disease. An additional 113 pts (20%) did not have a SLNB. A positive SLN was seen in 161 of 412 pts (39.1%). Nineteen pts presented with nodal recurrence in the mapped basin despite a negative SLNB (false negative rate [FNR] 10.6%). The median overall (OS) and disease-specific survival (DSS) for the cohort was 42.5 and 62.1 months, respectively. The median DSS for pts with a negative SLN was 82.4 months, 41.2 for positive SLN and 26.8 for those with clinically positive nodal disease at presentation (p<0.0001). Recurrence-free survival (RFS) showed a similar survival benefit for SLN negative pts, with a median survival of 32.4 months versus 14.3 for SLN positive and 6.8 for those with clinical positive disease (p<0.0001).

Conclusion: With a low FNR, pts with thick melanoma and negative SLNB have prolonged DSS and RFS over those with a positive SLNB. Identifying nodal disease at an occult stage is associated with increased survival and, thus, we consider SLNB to be indicated for pts with thick clinically node negative melanoma.

Presented by: Jonathan Koscso, BS, Med II Student

Factors associated with sentinel node positivity in patients with thick cutaneous melanoma (≥ 4mm) Jonathan Koscso¹, Monique Konstantinovic¹, Nick Govsyeyev, Maki Yamamoto MD²), Joyce Y Wong MD², Kate J Fisher MA², Jane L Messina MD², Amod A Sarnaik MD², C Wayne Cruse MD², Christopher A. Puleo², Ricardo J Gonzalez MD², Vernon K. Sondak MD², Jonathan S Zager MD² ¹University of South Florida Morsani College of Medicine, ²Moffitt Cancer Center

Keywords: Melanoma Sentinel node cutaneous surgery

Objective: Although sentinel lymph node biopsy (SLNB) is the standard of care for patients (pts) with intermediate thickness melanoma, controversy remains on its utility and prognostic value in thick melanoma. We sought to identify pt and tumor related factors that are predictive of clinically occult nodal metastasis in patients (pts) with thick melanoma.

Methods: From 1999 to 2012, 419 pts with thick melanoma (≥4 mm) who underwent SLNB from a single institution were retrospectively reviewed. Demographic and clinicopathologic characteristics were correlated with nodal status based on SLNB. Univariate (UV) and multivariate (MV) logistic regression analyses were performed.

Results: Of 419 pts, 292 (69.7%) were male and the median age was 64. Median Breslow thickness was 6 mm (range 4-25 mm). Overall, 161 pts (38.4%) had a positive sentinel node (SLN), 251 (59.9%) had a negative SLN, and 7 (1.7%) failed to map on lymphoscintigraphy and no SLNB was performed. On UV analysis, ulceration, trunk and extremity location, and satellitosis were predictive of SLN status. Mitotic rate (MR), tumor regression, and Breslow thickness were not predictive of SLN status. On MV analysis, truncal (odds ratio [OR] 4.60, p=0.0003) and extremity (OR 3.17, p=0.008) location, and satellitosis (OR 10.31, p=0.006), were significant predictors of a positive SLN. Desmoplastic subtype had a decreased likelihood (OR 0.09, p=0.001) for a positive SLN.

Conclusion: In pts with thick melanoma, factors historically associated with SLN status (ulceration, increasing Breslow thickness, MR) were not predictive of positive SLN. However, truncal or extremity primary tumors and satellitosis were predictive factors for a positive SLNB and appear to indicate which pts are at high risk of regional disease.

Abstract #: 128

Presented by: Samson Lu, BS, Med II Student

Culture Change in Trauma Surgery: Implementing a Standardized Handoff Checklist

Samson Lu, MS¹, Tom Fowler, MS¹, David Ciesla, MD² ¹University of South Florida Morsani College of Medicine, ²Tampa General Hospital, Regional Trauma Program, University of South Florida Morsani College of Medicine, Department of Surgery

Keywords: checklist, handoff, trauma surgery, quality improvement

Objective: After gathering focused research on the benefits of structured verbal communication in handoffs and establishing the support of our site mentor, Dr. David Ciesla, we initiated a Plan-Do-Study-Act (PDSA) cycle to pilot the implementation of a standardized verbal checklist during handoffs.

Methods: A checklist draft, modeled after Christopher DeRienzo et al.'s recommendations from Duke University,6 was presented to the trauma team leaders. Care was taken to ensure that we had support from the department leaders before attempting to implement a checklist because we predicted that the trauma team would be more willing to listen to their leaders than to medical students. Dr. Ciesla helped revise the checklist to better reflect the needs of his trauma team. The hospital's printing services also demonstrated enthusiasm to help in the effort to improve patient safety by printing 50 laminated copies of the revised checklist (Fig 1). The plan for data collection was to count the number of points on the checklist that were verbally addressed before and after its implementation. We predicted more points post-implementation.

Results: The number of points verbally addressed dramatically improved upon implementation (71.4%). The sixth handoff after the implementation handoff also had fewer lost items.

Conclusion: Our observations support that the checklist was most likely to be followed when a supervising attending is present and actively correcting during the handoff, which was not a factor collected in our current data set. Other future considerations would be the inclusion of handoff durations and a longer timeframe of data collection to account for variability of patient volume, complexity of cases, and variety of residents and attendings conducting the handoff.

Presented by: Thomas Sutton, BS, Med II Student

Acute Appendicitis: Variation in Treatment and Outcomes by Insurance Status

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Keywords: Appendicitis, Insurance Status, Outcomes

Objective: The purpose of this study was to investigate the relationship between insurance status and outcomes in an inpatient population admitted with acute appendicitis (AA), and examine the implications for the Affordable Care Act.

Methods: Patients with AA were identified by ICD9 codes using the AHCA Florida Hospital Inpatient Discharge Datasets for 2002 to 2011. Four outcomes were examined: the probability of developing complicated versus uncomplicated appendicitis, the probability of receiving laparoscopic (LA) versus open appendectomy (OA), the probability of a post-operative complication, and the length of stay (LOS). Data were analyzed using logistic and negative binomial multivariate regression. A p-value less than 0.05 was considered significant. All equations controlled for patient demographics, comorbidities, and year and hospital fixed effects.

Results: The uninsured had a significantly greater risk of presenting with complicated appendicitis, were less likely to receive LA, were more likely to suffer from a surgical complication, and had longer LOS. However, the uninsured were less likely to suffer from a post-operative surgical complication after controlling for appendicitis and operation type. Statistical diagnostics suggests that this result is likely an artifact of collinearity or unobserved patient characteristics.

Conclusion: Patient insurance status is known to affect healthcare utilization. The uninsured may delay seeking medical assistance until later in the course of their disease, causing greater proportions of complicated, costlier to treat appendicitis. Decreasing the number of uninsured via the Affordable Care Act may improve patient outcomes and decrease hospital resource utilization related to acute appendicitis.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 130

Presented by: Patrick Teefey, MD, Faculty

Frozen-section reliability to identify endometrial cancer high-risk factors

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Keywords: Endometrial cancer Frozen section Pathology

Objective: The decision to perform lymphadenectomy in early stage endometrial cancer (EC) remains an ongoing area of debate. Identified clinico-pathologic factors are associated with increased risk of occult lymph node metastasis, and the ability to identify these high-risk factors may impact the decision to perform a lymphadenectomy. The objective of this study was to evaluate the detection of EC high-risk factors on frozen section compared to permanent pathologic analysis.

Methods: This is a retrospective clinico-pathologic study. High-risk endometrial cancer was defined by the presence of at least one of the following pathologic parameters: poor differentiation (or histological grade 3), myometrial invasion>50%, cervical extension, lympho-vascular involvement, and clear cell or serous histological subtype. Patients included in the study were 18 years or older, had a uterine intra-operative frozen section analysis performed, and had epithelial endometrial neoplasia. Kappa coefficient statistics were used as a measure of agreement between frozen and permanent assessment.

Results: We had 263/809 patients who met inclusion criterio from 2000-2010. There was an 85% agreement in high-risk factors between frozen and permanent sections. The strength of agreement was considered to be 'good', with a kappa=0.65.. The high-risk factor identified with most consistency between frozen and permanent sections was cervical involvement, with 94% (kappa=0.82).

Conclusion: Although frozen section is considered to have 'good' agreement with permanent analysis in detecting EC high-risk factors and may help to guide treatment during surgery, it should be used with caution and in combination with other clinical, pathologic and, potentially in future, molecular information.

Change in Providers' Knowledge Following ECHO, a Telehealth Training on HIV/AIDS Care: Meta-Analysis of Evaluation Data

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Keywords: Continuing education, telehealth, HIV/AIDS management, meta-analysis

objective: To determine the change in the providers' knowledge as a result of participating in a telehealth group of the second of the second second

Results: Thirty-three sessions were conducted over 1.5-year period in which 260 providers participated. Pooled results showed a significant increase in providers' knowledge in favor of the telehealth training (d = 0.347, 95% confidence intervals (CI): 0.254, 0.441) with no heterogeneity among the sessions (I2 = 0; P<0.00001). Change in knowledge varied by language whereby English sessions had significantly lower scores (d = 0.31, 95% CI: 0.11, 0.51) than Spanish sessions (d = 0.77, 95% CI: 0.39, 1.15) (test of interaction: P=0.03). However, change in knowledge did not vary by size of the session (number of participants) or didactic topic presented.

Conclusion: The telehealth training appears to be beneficial for physicians for management of patients with HIV/AIDS. Change in care providers' knowledge is associated with the language used but not the size of the training or topic presented. Agencies involved with telehealth education and training should consider adapting the language used in the training to the participants' preferences.

Research supported by: HRSA

Abstract #: 132

Presented by: Shaquria Adderley, PhD, Postdoctoral Fellow

Variable roles of the H1-H3 receptors and PKC in histamine-induced barrier dysfunction in cultured endothelial cells from different sources.

<u>Shaquria P. Adderley, Xun E. Zhang, Sandhya K. Sarangan and Jerome W. Breslin</u>. University of South Florida Morsani College of Medicine, Department of Molecular Pharmacology and Physiology

Keywords: histamine, protein kinases, endothelial cells

Objective: We tested the hypothesis that histamine-induced endothelial barrier dysfunction requires different receptors and signaling pathways depending upon endothelial cell (EC) source.

Methods: Changes in barrier function elicited by 10 µM histamine were compared between human umbilical vein EC (HUVEC) and human dermal microvascular EC (HMVEC-D) monolayers, using determination of transendothelial electrical resistance (TER). H1, H2, and H3 receptors were blocked with 10 µM mepyramine, 10 µM cimetidine, and 0.01-1 µM ciproxifan, respectively. Inhibitors of PKC (GFX109203X), PI3K (PI828) and phospholipase C (U73122) were used to evaluate downstream signals. Western blots and immunofluorescence microscopy analysis demonstrated H1, H2, and H3 expression in both EC types.

Results: Blockade of H1, H2, or H3 significantly inhibited the histamine-induced decrease in TER in HMVEC-D. In contrast, only blockade of H1 significantly attenuated the histamine-induced drop in TER in HUVEC. Inhibition of either PKC or PI3K significantly attenuated histamine-induced barrier dysfunction in HUVEC, but combined inhibition of both was required to attain significant attenuation in HMVEC-D. Inhibition of PLC also inhibited the histamine-induced decrease in TER in HMVEC-D, but interestingly, combined PLC and PKC inhibition did not.

Conclusion: This study suggests a common role for H1, but differential roles for H2 and H3 in histamine-induced endothelial barrier dysfunction among different endothelial cell types. In addition, PKC appears to have either a promoting or inhibitory role depending on the endothelial cell source.

Research supported by: Supported by NIH R01HL098215.

Presented by: Ruan Cox Jr, MS, Graduate Student

Hyperoxia Exposure Results in Decreased Expression of Pro-Resolution Receptor ALX/FPR2

Ruan Cox Jr., Oluwakemi Phillips, Jutaro Fukumoto, Itsuko Fukumoto, Richard Lockey, Narasaiah Kolliputi University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: Inflammation, Lung, Immunology, Resolution, Hyperoxia

Objective: Endogenously produced polyunsaturated fatty acids (PUFAs) are key mediators of the anti-inflammatory response following acute injury. PUFA's such as resolvins and lipoxins have demonstrated potent proresolutionary effects in acute lung injury. These molecules have been shown to bind and exert their effects through g-coupled protein receptor Lipoxin A4/formyl peptide receptor 2 (ALX/FPR2). Previous reports have shown that various septic or sterile insults lead to an increase in ALX/FPR2 expression; however, the response of ALX/FRP2 to oxidative stress has not been elucidated. In this study we investigated the role of ALX/FPR2 in a murine model of hyperoxic acute lung injury (HALI).

Methods: C57BL/6 Mice were exposed to hyperoxic (50, 75, or 95% O2) or normoxic (~ 21% O2) for 24, 48, or 72hrs. Following atmospheric treatment, mice were euthanized and bronchoalveolar lavage fluid as well as lung tissues were collected. Bronchoalveolar lavage fluid was used to assess alveolar protein leak. Lung tissue samples were used for histopathological analysis and to assess ALX/FPR2 protein and RNA expression following hyperoxia treatment.

Results: Results reveal that hyperoxia exposure results in a significant decrease in ALX/FRP2 expression in comparison to normoxia treated controls. This decrease was dose dependent and reduction in ALX/FRP2 was evident in as little as 24hrs following hyperoxia exposure.

Conclusion: Our results reveal, for the first time, a significant decrease in ALX/FRP2 expression which is not seen in other forms of acute lung injury. While the production of PUFAs in HALI may be normal, their proresolutionary effects may be blunted due to the decrease in receptor expression.

Research supported by: NIH RO1 AHA Joy McCann Culverhouse Endowment

Abstract #: 134

Presented by: Shelly DeForte, PhD, Graduate Student

Sequence-based classification of enzymes with an emphasis on the applicability of intrinsically disordered regions

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Keywords: Intrinsically disordered protein, enzymes, bioinformatics

Objective: Intrinsically disordered proteins pose no greater disruption to conventional wisdom than in the study of enzymes, where catalytic function is generally understood to follow from structural properties. This project seeks to determine the relationship between the amino acid sequence of an enzyme, the disorder propensity, and the function of that enzyme.

Methods: In order to identify large scale trends, we used a bioinformatic approach to analyze the amino acid sequence for every enzyme currently assigned an Enzyme Commission (EC) number, which describes the experimentally determined catalyzed reaction for a single protein. Using the intrinsic disorder predictors PONDR-FIT and PONDR-VLXT, we obtained predicted disorder propensities for over 200,000 enzymes, with the full human proteome as a control. We then compared disorder propensity both inside and outside of Pfam domains and explored the relationship between sequence conservation in a protein family and intrinsic disorder.

Results: Among our observations, we found that, while enzymes overall were largely predicted to be structured, the regions outside of conserved domains were much more likely to be disordered. We also found that patterns of disorder were often retained in a functional class and in some cases, disordered sequences were conserved through multiple taxonomic classifications.

Conclusion: Our research provides further evidence that enzyme function does not always depend on structural properties, and may in many cases depend on a pattern of flexibility. This research sheds new light on the role of intrinsic disorder in enzyme function and directly affects our understanding of protein mechanisms and interactions.

Research supported by: University of South Florida Department of Molecular Medicine

Presented by: John DeNigris, BS, Med II Student

Altered Dermal Fibroblast Behavior in a Collagen V Haploinsufficient Model of Classic Type Ehlers Danlos Syndrome.

<u>DeNigris J^{1,2}, Yao Q¹, and Birk DE³</u> ¹University of South Florida Morsani College of Medicine, ²(Research Scholarly Concentration), ³USF Morsani College of Medicine, Department of Molecular Pharmacology & Physiology

Keywords: Collagen V EDS Dermal Healing

Objective: Ehlers Danlos Syndrome Classic Type (EDS) is associated with mutations in collagen V. Clinical manifestations include joint hyperflexibility, hyperextensible skin, poor wound healing, and vascular problems. The hypothesis is that changes in collagen V expression are associated with altered dermal fibroblast behavior contributing to the poor wound healing response.

Methods: A Col5a1+/- mouse model was used with the EDS clinical features. Three independent dermal fibroblast strains were isolated from Col5a1+/+ and Col5a1+/- mice and utilized at passages 2-8. Cell proliferation rates were determined for each strain. Proliferation assays were conducted using Ki-67, a proliferation marker. Apoptosis was measured using immunofluorescence for DNA fragmentation. Cell attachment to collagens I, III, and fibronectin was analyzed.

Results: The Col5a1+/+ fibroblasts replicated 50-70% faster than Col5a1+/- fibroblasts. This difference was significant (p<0.001) with a mean growth slope of 886.6 \pm 85.7 for Col5a1+/+ and a mean growth slope of 310.2 \pm 82.3 for Col5a1+/-. A significant (p<0.001) increase in Ki-67 expression was observed with a mean of 43.3% \pm 5.2% for Col5a1+/+ and 14.5% \pm 2.3% for Col5a1+/- fibroblasts. No difference was observed in fibroblast apoptosis. For all three substrates, Col5a1+/+ cells attachment was significantly (p<0.001) increased compared to Col5a1+/- cells.

Conclusion: Markedly decreased fibroblast proliferation, and attachment ability were observed in EDS dermal fibroblasts. Our data indicate that the decreased fibroblast number is not due to cell death. These data suggest that decreased fibroblast proliferation and attachment contribute to the decreased wound healing response in EDS.

Research supported by: The AHA Medical 2013 Student Summer Research Award. rSC

Abstract #: 136	Presented by: Antwoine Flowers, PhD,
	Graduate Student

Impact of NT-020 treatment on gene expression in growth, survival, and senescence signaling pathways in an In-Vivo model of aging in the hippocampus.

Antwoine Flowers, Bethany Grimmig, Charles Hudson, P Bradshaw, V. Delic, Paula C Bickford University of South Florida Morsani College of Medicine Neurosurgery & Brain Repair

Keywords: Stem Cells, Anti-Aging, Neuroscience, dietary supplements, Cell signaling

Objective: The goal of our current work is to understand how compounds with high polyphenol content effect key growth, stress resistance, and senescence signaling pathways in the neurogeneic niche. Treatment with these compounds has been shown to have wide ranging positive effects. However the signaling mechanisms involved is still a topic of debate.

Methods: We performed a set of gene expression analyses on cellular pathways involved in cell aging, stress response, and proliferation. Male Fischer 344 rats were segregated into two groups young 3 months and old 18 months old. Between the young and aged cohorts two more groups were segregated, one being fed an NIH31 control diet and the experimental group was fed a modified diet which included the NT-020 formulation at 135mg/kg for 30 days. Upon Sacrifice the hippocampus was removed and used for RNA isolation. For RNA analysis we used QRT-PCR arrays from SaBiosciences. We examined 3 signaling pathways: PI 3k-AKT pathway, WNT pathway, and cellular senescence.

Results: Our results will detail the differential expression of genes and identify those that correlate with age and treatment. Initial findings suggest an activation of WNT pathways involved in proliferation and a reduction in activity of cellular senescence genes like CDKN2A.

Conclusion: High polyphenol diets may serve to enhance progenitor cells ability to maintain homeostasis in aged animals, and enhance the cells ability to cope with stress by down regulating senescence genes and enhancing DNA repair activity. These activities appear to be mediated by the cells canonical stress-response and self-renewal pathways. How these compounds specifically enhance these pathways activities is a focus of future work.

Research supported by: USPHS AG04419, VAMRS

Presented by: Jutaro Fukumoto, PhD, Postdoctoral Fellow

Deletion of ASK1 protects against hyperoxia-induced acute lung injury

<u>Jutaro Fukumoto, Itsuko Fukumoto, Ruan Cox, Richard F. Lockey and Narasaiah Kolliputi</u> Division of Allergy & Immunology, Dept of Internal Medicine, University of South Florida Morsani College of Medicine

Keywords: ASK1 hyperoxia ALI IL-1β

Objective: To determine whether ASK1 deletion ameliorates hyperoxia-induced acute lung injury.

Methods: C57BL/6 mice and age-matched ASK1 KO mice of the same genetic background were exposed to 100% oxygen. After 72 hours exposure to hyperoxia, mice were sacrificed to collect bronchoalveolar lavage fluid (BAL fluid) for absolute, differential cell counts and cytokine measurements.

Results: BAL fluid analysis revealed a significant decrease in IL-1β level in KO mice (83% decrease compared to WT mice). Differential cell count show that infiltration of macrophages and neutrophils into BAL fluid were suppressed in KO mice. ASK1 KO mice exhibited significant increase in protein concentration in BAL fluid (69% increase compared to WT mice).

Conclusion: ASK1 has a proinflammatory profile as revealed by dramatic decrease in IL-1 β level and neutrophil decrease in lung airspace. Meanwhile, the permeability increase observed in ASK1 KO mice indicates that ASK1 counteracts against hyperoxia-induced lung permeability increase, suggesting that ASK1 has both proinflammatory and anti-inflammatory roles.

Abstract #: 138

Presented by: Laura Hamel, MS, Graduate Student

Screening for Chemical Modulators of Protein Palmitoylation

Laura Hamel, Laura Pendleton, David Mitchell, Robert Deschenes University of South Florida Morsani College of Medicine Molecular Medicine

Keywords: Palmitoylation, Erf2, Ras, Chemical Modulators, Scaffold Library

Objective: Ras isoforms are implicated in ~30% of all cancers, but attempts to identify Ras inhibitors have met with limited success. We propose to examine the inhibition of Ras by targeting palmitoylation, a reversible post-translational modification that occurs on H-Ras, N-Ras, and other Ras family GTPases. Protein palmitoylation is a two-step reaction; autopalmitoylation of the enzyme using palmitoyl-CoA as a palmitoyl donor followed by transfer of the palmitoyl moiety from the intermediate to the substrate (i.e., Ras). We will screen a scaffold library of compounds as a first step in identifying chemical modulators of the Ras palmitoylation enzyme, Erf2.

Methods: A high throughput screen (HTS) that couples the production of NADH from α -KDH to the release of CoASH from palmitoyl-CoA during autopalmitoylation was used to monitor the reaction.

Results: Reproducibility of the HTS was evaluated over three days to determine day-to-day and plate-to-plate variability. Coefficient of Variance, Z'-value, and signal-to-noise ratio was determined for Erf2 as 6.2, 0.87 and greater than 20, respectively, compared to reactions using a transferase-dead point mutant derivative. We calculated an autopalmitoylation activity of 43.0 +/- 3.0 pmol/min/ug with a Km of 43 +/- 8 μ M. The initial HTS resulted in the identification of ~10 hits that were greater than or equal to 3 standard deviations from the mean of buffer alone.

Conclusion: Three potential inhibitors and 7 potential enhancers for the autopalmitoylation of Erf2 were identified implicating Erf2 as a novel potential drug target for the regulation of Ras, and supporting the capabilities of the HTS for identifying chemical modulators of protein palmitoylation.

Research supported by: NIH CA502-17 and a Fred Wright Jr. Cancer Research Endowment

Presented by: Shannon Ho, MD, Postdoctoral Fellow

From Proteomics to Personalized Medicine? The VEGFR-2 Protein Complexes in Human Placentas Near Term

<u>Shannon Ho, Christina Paidas-Teefey, Maja Okuka, Valerie Whiteman, William Spellacy, John Tsibris</u> University of South Florida Morsani College of Medicine Obstetrics & Gynecology

Keywords: Placenta, preeclampsia, VEGFR-2, P2Y2 receptor

Objective: Placental VEGF Receptor-2 (VEGFR-2 or KDR) controls key steps of vascularization and angiogenesis that are defective in preeclampsia. We analyzed proteins in the KDR complexes in the fetal compartment of placentas from 8 normotensive and 7 preeclamptic patients. Hypothesis: The composition of KDR complexes is different in the two patient groups.

Methods: KDR is confined to endothelial cells at term. Tissues were homogenized and membrane fractions extracted by ASB-14 and immunoprecipitated (IP) with KDR antibody. In collaboration with Dr. Stan Stevens we identified co-IP proteins by mass spectrometry. Western blots, immuno-histochem/–fluoresc confirmed KDR co-localization.

Results: We have reported the following proteins coIP with KDR: PDC-E2, a member of pyruvate dehydrogenase, adiponectin, cavin-1, vimentin, annexins, peroxiredoxin-2, heterogeneous nuclear ribonucleoproteins, tissue transglutaminase (TG) and certain IgG and IgM. As KDR catalyzes synthesis of dinucleoside polyphosphates, that activate purinergic receptors P2Y and regulate vasculogenesis and vascular tone, we tested IP-eluates for P2Y2/P2Y1/P2X4/P2X7; only P2Y2 coIP with KDR. Variable peptide coverage amid normotensive and preeclamptic placentas for each coIP protein may reflect different stoichiometries of the KDR network to optimize KDR signaling. Cytosolic P2Y2/P2X4/P2X7/TG/ oxytocin receptor levels did not correlate with preeclampsia but may be linked to labor.

Conclusion: We found associations not driven by known catalysis, as in KDR-P2Y2. Intra/ inter-group variations in protein expression were observed; some may be idiosyncratic. Study of coIP proteins will reveal KDR mechanisms to support fetal growth, immunology of pregnancy and possibly labor.

Research supported by: Dept. Ob-Gyn, College of Medicine

Abstract #: 140

Presented by: Mark Howell, MS, Graduate Student

In Vitro Anticancer Drug Screening Using a 3D Fibrous Scaffold

<u>Mark Howell¹*, Sriram Velamuri², Sameer Naik², Bill Baker⁴, Shyam Mohapatra^{1,3}, Subhra Mohapatra^{1,2} ¹University of South Florida Morsani College of Medicine Nanomedicine Research Center, ²USF Morsani College of Medicine, Department of Molecular Medicine, ³USF Morsani College of Medicine, Dept of Internal Medicine, Div of Translational Medicine, ⁴USF College of Arts and Sciences, Dept of Chemistry.</u>

Keywords: 3D Cell Culture, Drug Screening, Anti-Cancer Compounds, Tumoriods, Lung Cancer

Objective: Currently, >90% of potential anti-cancer drugs fail during clinical trials. The lack of success is in part due to the limitation of an appropriate system to mimic cancer cell behavior in vivo. Our lab has recently reported on the development and characterization of a 3D nanofibrous scaffold produced by electrospinning a mixture of certain polymers. We found that cancer cells cultured on the scaffold formed tight aggregates similar to in vivo tumors, referred to as tumoroids, which showed higher resistance to anticancer drugs than the same cells grown as monolayers.

Methods: Here we used this scaffold to grow tumoroids and screen a library of potential anti-cancer drugs. Lewis Lung Carcinoma (LLC) cells were grown on the scaffold for a period of four days after which tumoroids were treated with different concentrations of the drugs. Three days later cell viability was assessed using Cell Titer Glo assay. In addition, tumoroid number and average diameter were examined to estimate the effects of the drugs.

Results: Of a total of 30 drugs tested thus far, seven potent anti-cancer candidates have been found, of which four compounds appear novel. These compounds are currently being characterized.

Conclusion: Using our nanofibrous scaffold as a screening tool and LLC tumoriods as a lung cancer model, we have identified four drugs that warrant further study to determine their potential as therapeutics for lung cancer.

Research supported by: Research supported by grant CA152005 from the National Institutes of Health.

Presented by: Kevin Huang, BA, Med III Student

Vascular Maturation and Cellular Infiltration of Electrospun Scaffolds for Fibrous Tissue Repair via VEGF and PDGF Delivery from Sacrificial Fibers.

<u>Kevin Huang¹, Robert Mauck²</u> ¹University of South Florida Morsani College of Medicine, ²University of Pennsylvania, McKay Orthopedics Research Laboratory

Keywords: Tissue engineering, scaffolds, vascularization

Objective: Tissue repair relies on cellular infiltration and vascularization. Minimal vascular support and the physical stress placed on fibrous tissues make endogenous repair challenging. Aligned nano-fiber scaffolds provide a physical template to direct cell growth and differentiation. Our objective was to evaluate whether growth factor (GF) delivery via these scaffolds improves repair.

Methods: Scaffolds of poly-caprolactone and poly-ethylene glycol containing different concentrations of vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF): control (no GF); 1x and 2xPDGF; 1x and 2xVEGF; and dual (2x VEGF and PDGF). GF release was evaluated using ELISA. Scaffolds (n=6) were implanted subcutaneously in rats (n=3) and sacrificed at 1, 2, and 4 weeks. Immunohistochemical and fluorescent staining were used to analyze the scaffolds. Principle component analysis and ANOVA were applied for statistical analysis.

Results: Peak GF release occurred by the first 4 hrs in all groups. Cellular infiltration measured with DAPI was evident by week 1, but did not change significantly with respect to time (p=0.405) or group (p=0.429). Vascularization measured with phalloidin were apparent by week 2, and increased significantly week to week (p=0.00), but not by treatment group (p=0.707). Vessel formation was concentrated within the scaffold periphery in all groups.

Conclusion: Our model of GF delivery via sacrificial fibers was validated. While no significant differences between GF groups and control was observed, an analysis of the collagen and infiltrating cells may show changes in morphology and type across different treatments. Quantitative modalities such as micro CT will be helpful in modeling changes throughout the scaffold.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 142

Presented by: Tamina Johnson, MS, Graduate Student

Development of Recombinant Functional Biomaterials for Neuronal Regeneration

Tamina Johnson, Dr. Piyush Koria, University of South Florida College of Engineering, Department of Chemical & Biomedical Engineering

Keywords: Neurotrophin, Biomaterials, Neuronal Regeneration, Nanoparticles, Protein Purification

Objective: Nerve growth factor (NGF) and Brain-Derived Neurotrophic Factor (BDNF) are neurotrophins that will induce neural regeneration, however they quickly diffuse within the system. Our approach is to create a recombinant functional biomaterial that will ensure sustained delivery of a neurotrophin and provide a unique topographical scaffold surface at the injury site: specifically, a fusion protein comprising of a neurotrophin and elastin like peptide(ELP).

Methods: Protein fusion of NGF-ELP and BDNF-ELP were done using recombinant DNA technology using a bacterial expression system (E. coli). Assessment of the particle size was measured using dynamic light scattering (DLS). PC12 Cells were used as an in vitro model for the assessment of NGF-ELP bioactivity. HEK293 cells were transfected with a plasmid encoding TrkB receptor for evaluation of BDNF-ELP. BDNF-ELP was labeled by Cy3 using maleimide chemistry to visualize fusion protein internalization via confocal microscopy. Western blot analysis was done to confirm the specificity of NGF-ELP to TrkA antibody and the phosphorylation of the TrkB receptor upon internalization of BDNF-ELP.

Results: Novel bioactive fusion proteins that elicit neuronal regeneration have been developed. PC12 cells treated with NGF-ELP undergo neurite outgrowth, cell differentiation, and cell survival. Western blot analysis confirms that BDNF-ELP fusion phosphorylates the TrkB receptor upon internalization.

Conclusion: The fusion proteins self-assemble into nanoparticles varying between 130nm–350nm due to the physical phase transitioning property of ELPs. Thus, these nanoparticles can be delivered at the injury site with relative ease and will enhance the bioavailability of the neurotrophins by limiting its loss due to diffusion.

Presented by: Shannon Kesl, MS, Graduate Student

Methods of Sustaining Dietary Ketosis in Sprague-Dawley Rats

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Keywords: ketone, therapeutic ketosis, ketone supplement,

Objective: The ketogenic diet (KD) has been successfully used to treat pediatric refractory epilepsy since the 1920s and is currently being investigated for a broad range of disease states. Concerns regarding this treatment include low compliance and adverse effects on blood lipids. We hypothesized that dietary ketone supplementation would elevate blood ketone levels to therapeutic ranges (2-7mM) without dietary restriction. We tested the effects of the following ketone precursors on blood glucose, ketones, and lipids with a 28-day dose escalation study in male Sprague-Dawley rats: R,S-1,3-Butandiol (BD), a mineral (Na+/K+) salt of β -hydroxybutyrate (β HB) (BMS), medium chain triglyceride oil (MCT), BMS+MCT 1:1 mixture (BMS/MCT), acetoacetate ketone ester (KE), and control (H2O) (n ≥8).

Methods: Days 1-14, rats received a daily 5g/kg intragastric gavage, and days 15-28 rats received a 10g/kg dose of respective test substances. BD and KE rats were not increased to 10g/kg based on previous toxicology studies and were administered a 5g/kg dose for duration of study. Once weekly, whole blood samples (10 μ l) were acquired for analysis of glucose and β HB at 0, 0.5, 1, 4, 8, and 12 hours after test substance administration, or until β HB returned to baseline. At day 1 and 28, 10 μ L of whole blood were collected to measure triglycerides, total cholesterol, and HDL concentration.

Results: We showed significant elevation of blood ketones with a significant inverse relationship with blood glucose for the duration of the experiment. There were no significant changes in the lipid panel for any substance.

Conclusion: Inducing therapeutic ketosis without dietary restriction while not affecting the patient's lipid profile has a broad application to many pathological conditions.

Research supported by: Office of Naval Research

Abstract #: 144

Presented by: James Lee, BS, Med II Student

Nrf2, Sirt1, and PGC1α mediate improvements in oxidative stress after Roux-en-Y gastric bypass surgery <u>James Lee, Yanhua Peng, Steven Rakita, Michel Murr</u> University of South Florida Morsani College of Medicine and Department of Surgery, and J. A. Haley VA Medical Center, Surgery

Keywords: metabolic syndrome, Sirt1, Nrf2

Objective: Oxidative and inflammatory stress in the liver contributes to hepatic injury, insulin resistance, and cardiovascular disease risk. Using an obese rat model, we previously showed that Roux-en-Y gastric bypass (RYGB) reduces oxidative stress in the liver through Nrf2, a crucial protector against reactive oxygen species. RYGB also increased the levels of LKB1, AMPK, and Sirt1, which regulate energy metabolism. In this study, we now investigate whether Nrf2 and Sirt1 work synergistically to attenuate stress in the liver after RYGB.

Methods: Liver expression of TNFα, IL-6, glutathione-S-transferase (GST), Sirt1, PGC1α, Nrf1, and Nrf2 was measured in rats from RYGB and weight-matched sham cohorts. The nuclear to cytosolic ratios of Sirt1, Nrf2, and NF-κB were measured as well. A corresponding set of in vitro measurements were done in the Kupffer cell line RKC1. These cells were treated with glucose and /or fatty acids to mimic glucotoxicity and lipotoxicity. The cells were then treated with siRNA to deplete Sirt1. Afterwards, the expression levels and ratios of the above mentioned factors were measured.

Results: Compared to sham control, RYGB upregulated Sirt1, PGC-1 α , Nrf1, Nrf2, GST (p<0.001), and decreased NF- κ B, TNF α , and IL-6 (p<0.001) within the liver. In RKC1 cells, Sirt1 depletion down-regulated PGC1 α , Nrf1, Nrf2, and GST (p<0.001). In contrast, NF- κ B, TNF α , and IL-6 were increased significantly.

Conclusion: These results and previous studies suggest that Sirt1, PGC1α, and Nrf2 are important components for mitochondrial function, and regulation of this pathway in the liver may attenuate oxidative and inflammatory stress. Targeting the dysregulation of these molecules may benefit patients with metabolic syndrome and obesity-induced NASH.

Presented by: Wei Liu, PhD, Postdoctoral Fellow

HDAC6 Ubiquitinates RIP3 and Stimulates Programmed Necrosis

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Keywords: HDAC6, Programmed Necrosis, RIP3, Ubiquitination

Objective: Increasing evidence suggests that necrotic cell death often proceeds through a unique molecular program, but little is known how this program is regulated. Our study aims to identify histone deacetylase 6 (HDAC6) as a novel regulator in programmed necrosis and to elucidate the underlying mechanism.

Methods: Flow cytometry, electron microscope, MTT, Co-IP, western blotting, ubiquitin assay

Results: Here, we firstly identified HDAC6 as a regulator that stimulates tumor necrosis factor- α (TNF- α)- and oxidative stress-induced necrosis. Strikingly, we found that HDAC6 constitutively binds to receptor-interacting protein kinase 3 (RIP3), a crucial activator for TNF- α -induced necrosis. Moreover, HDAC6 ubiquitinates RIP3 In Vitro and In Vivo in response to necrotic stress. We further demonstrated that HDAC6 inhibition and HDAC6 ablation downstream undermine the production of reactive oxygen species and attenuate activation of MAPK-ERK1, 2 signaling.

Conclusion: Taken together, these results implicate HDAC6 as an positive regulator of programmed necrosis, and could provide a novel approach of HDAC6 inhibition to protect against necrotic injuries, including ischaemic stroke and myocardial infarction.

Research supported by: NCI R01CA164147 to X.Z.

Abstract #: 146

Presented by: Jashwanth Malipeddi, MS, Graduate Student

Feature extraction of the palmitoylproteome through sequence-based analysis

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Keywords: Intrinsically disordered, post-translational lipid modification regions, Palmitoylation, palmitoylproteome,

Objective: Palmitoylation is a reversible post-translational lipid modification that regulates a series of basic cellular processes such as membrane trafficking, protein stability and protein aggregation. Although proteomic approaches have been developed to accelerate analysis of palmitoylated substrates, experimental approaches alone cannot deal with the exponential increase in protein sequences. Instead it is highly desired to develop reliable, computational methods for predicting palmitoylated sites. However, present computational methods lack robustness, as the sites, features, and consensus patterns of palmitoylated sites are poorly understood. Incorporating predictions of intrinsically disordered regions (IDRs) could potentially remedy this, as IDRs are known for their high degree of flexibility and therefore solvent exposure and site accessibility for modification. We propose a model for predicting palmitoylation sites based on IDRs and sequence features.

Methods: Various computational methods including disorder predictions, sequence alignments, logo analysis and transmembrane predictors (TMP) were applied to the data set of experimentally verified validated palmitoylated proteins.

Results: Our preliminary analysis has shown that IDRs are constantly rich in binding sites, which have been found to be important locations for post-translational modifications. TMP and logo analysis suggest that motifs were composed of basic residues on the right side of the site, and hydrophobic residues on the left side of the site.

Conclusion: Incorporation of a disorder scoring parameter appears to contribute to building a robust stochastic model to identify palmitoylation sites in proteins.

Research supported by: NIH CA502-17 and the Fred Wright Jr Cancer Research Endowment

The basal oscillating secretory release of insulin from β cells is not driven by a feedback loop with either glucose or glucagon

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Keywords: insulin, oscillations, nonhuman primates

Withdrawn

Results: Significant sinusoidal patterns of insulin secretion with a frequency of 8-11 minutes occurred in 80% of baseline experiments. The remaining 20% of experiments had a power spectral density max <3.5%, indicating no detection of a significant periodicity. Mean insulin levels were strongly correlated with half amplitudes (r=0.476, p<0.001), with constant relative amplitudes. A similar, yet more irregular, oscillatory pattern was observed for glucose. Cross-correlation revealed that the lag between insulin and glucose was nearly zero, with neither insulin nor glucose leading the other. Glucagon was asynchronous with insulin and glucose oscillations and did not have a consistent frequency. In the OF monkeys, mean levels of insulin increased significantly at 140% OF and the oscillations of insulin were often disrupted at the highest percentages of OF (150-175%).

Conclusion: Neither glucose nor glucagon levels drive the basal oscillatory release of insulin from the pancreas.

Research supported by: NIH (HHSN263200800022C)

Abstract #: 148

Presented by: Yiru Qin, BS, Graduate Student

In vitro Immunotoxicity Evaluation of Graphene Quantum Dots

<u>Yiru Qin^{1, 2}, Zhi-Wei Zhou¹, Shu-Feng Zhou^{1, 2,*}</u> ¹Department of Pharmaceutical Science, College of Pharmacy, University of South Florida, Tampa, FL, ²Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL

Keywords: GQDs; immunotoxicity; THP-1 cells; cytokine

Objective: Graphene quantum dots (GQDs), a form of graphene-based carbon nano-material with all dimensions less than 10 nm, have exhibited great potential in biomedical applications, such as bioimaging, drug delivery and as antimycoplasma and antibacterial agents. With the growing attention and development of GQDs in biomedical applications, the potential health concerns have increased. This study aimed to evaluate the impact of GQDs on the immune system.

Methods: Transmission electron microscopy (TEM) and atomic force microscopy (AFM) were used to characterize GQDs. THP-1 derived macrophage cells were used to determine the immunotoxicity. The MTT assay was conducted to determine the cell viability after exposed to GQDs. Reactive oxygen species (ROS), lactate dehydrogenase (LDH), and proinflammatory cytokines were measured. Expression level of proteins involving in apoptotic and autophagic pathways was determined by Western blotting.

Results: The size range of GQDs was within 1 to 5 nm with a height of 1 nm. The MTT assay indicated that there was no significant decrease of the cellular viability or membrane integrity up to 100 μ g/ml of GQDs for 24 hour exposure. Increased ROS and pro-inflammatory cytokines (TNF-a, IL-1 β , & IL-8) levels were observed in a concentration-dependent manner. Also, autophagic and mitochondria-associate apoptotic proteins were activated.

Conclusion: Low dosage (less than 10 μ g/ml) of GQDs possess little immunotoxicity. While medium dosage (10-50 μ g/ml) of GQDs mainly causes inflammatory response of macrophages. High dosage (>100 μ g/ml) induces autophagy and apoptosis of macrophages.

Presented by: Krishna Reddy, BS, Graduate Student

A putative molecular recognition feature in zDHHC S-palmitoyltransferase C-termini is essential for zDHHC9 and ERF2 function in vivo

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Keywords: palmitoylation, X-Linked Intellectual Disability, intrinsic disorder, post-translational modification, zDHHC PAT

Objective: Defects in zDHHC genes are associated with diseases such as cancers and neurological disorders; for example, mutations in zDHHC9 are implicated in X-Linked Intellectual Disability (XLID), which affects 1-3% of the population. The 23 human zDHHC genes encode enzymes known as zDHHC protein acyltransferases (PATs), which catalyze the reversible post-translational lipidation known as palmitoylation, a process essential to normal cellular function through facilitation of membrane attachment, subcellular trafficking, and protein stability. While targeting of palmitoylation is tempting from a therapeutic standpoint, this is hindered by poor understanding of enzyme regulation. The aim of this study is to determine the role of intrinsically disordered C-termini on the functions of the Ras PATs zDHHC9 and Erf2.

Methods: A combination of computational sequence-based predictive tools and experimental techniques are used in this study. PONDR-FIT and PONDR VL-XT were used to determine level of intrinsic disorder. A RAS2 functional assay in S. cerevisiae was used to evaluate the function of zDHHC9 and ERF2 deletions and mutations.

Results: Intrinsic disorder prediction indicates that a conserved region known as a molecular recognition feature (MoRF) potentially exists in the C-termini of all PATs. In zDHHC9 and Erf2, this region is essential to in vivo RAS2 function. Suppression experiments suggest that the MoRF participates in a protein-protein interaction.

Conclusion: A putative MoRF observed in all zDHHC PAT C-termini is essential to zDHHC9 and Erf2 function. This MoRF potentially participates in a protein-protein interaction, representing a novel point of zDHHC PAT regulation for treatment of XLID.

Research supported by: NIH CA502-17 and the Fred Wright Jr Cancer Research Endowment

Abstract #: 150

Presented by: Bosko Stojanovski, BS, Graduate Student

Effect of pH and temperature on the structural integrity of 5-aminolevulinate synthase

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Keywords: ALAS, PLP, Heme, Circular Dichroism

Objective: 5-Aminolevulinate synthase (ALAS) is a pyridoxal 5'-phosphate (PLP) dependent enzyme that catalyzes the first, and regulatory step, of heme biosynthesis in non-plant eukaryotes. The objective of this study was to determine how changes in pH and temperature affect the structure of murine erythroid ALAS (mALAS2).

Methods: Circular dichroism was used to examine changes in the enzymatic secondary structure (190-260nm), tertiary structure (260-320nm), and PLP-binding site (320-500nm).

Results: In the alkaline pH range (pH 7.5-10.5) at either 20 or 37°C, mALAS2 retains ordered secondary structure. In the acidic pH range (pH 3-2), at either 20 or 37°C, the secondary structure becomes progressively unfolded; surprisingly, the secondary structure is regained at pH 1.2. Subtle changes in the tertiary structure of mALAS2 can be detected at 20°C as the pH is changed from 7.5 to 10.5; the same variations in the alkaline pH region at 37°C result in profound changes in the tertiary structure. The enzyme does not retain any tertiary structure in the acidic pH range (pH 3-1.2) at 20 or 37°C. Changes in the PLP-binding site proceed with the disappearance of the 420nm maxima as the pH changes from 7.5 to 9.5. At pH 10.5 and in the acidic pH range (pH 3-1.2), PLP is no longer bound to the active site. The changes in the PLP-binding site are independent of temperature. Finally, at either 20 or 37°C, mALAS2 undergoes subtle changes in the reorganization of its hydrophobic clusters in the alkaline pH range; on the other hand, maximal exposure of the hydrophobic clusters is achieved in the acidic pH range.

Conclusion: Overall, the data indicate that changes in pH and temperature affect the structural integrity of mALAS2.

Enhancing the Multilineage Differentiation of Bone Marrow Derived Mesenchymal Stem Cells in Three Dimensional PEG-Chitosan-Graphene Based Hydrogel

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Keywords: regenerative medicine, hydrogel, stem cells,

Objective: Bone marrow derived mesenchymal stem cells (BMSCs) are a valuable cell source for regenerative medicine due to their capacity to differentiate into multiple lineages. The low differentiation efficiency is a challenge for BMSCs therapy. To overcome this, we constructed a polyethylene glycol(PEG)-chitosan-graphene hydrogel(PCG) to promote the differentiation of BMSCs.

Methods: PCG was synthesized and its microstructure, swelling kinetics, absorption capacity, and biodegradation were examined. The cytotoxicity of PCG was tested by PrestBlue assay. The adipogenesis, chondrogenesis and osterogenesis of BMSCs in hydrogel was tested by Oil Red O, Alcian Blue and Alizarin Red staining, respectively. The immunofluorescent staining of Peroxisome Proliferator-Activated Receptor Gamma(PPAR_), chollagen II and osteopontin(OPN) that regulate differentiation were also performed.

Results: The PCG comprised of fibrillar network has high water content, high absorption capacity, and biodegradability. BMSCs in PCG hydrogel formed small round shape aggregates that increased in size over time. The adipogenesis of BMSCs in PCG was much higher than control as evidenced by Oil Red O staining. The PCG mediated adipogenesis enhancement was associated with up-regulation of PPAR Based on the results of Alizarin red staining, alkaline phosphatase activity, and OPN immunstaining, osteogenesis of BMSCs was strongly enhanced in PCG. Alician blue staining revealed a significant increase in glycosaminoglycan deposition on the PCG compared to control. The collagen II immunostaining showed enhanced chondrogensis on PCG.

Conclusion: PCG is biocompatible, biodegrable and can improve multipotent differentiation efficiency of stem cells.

Research supported by: National Institutes of Health

Abstract #: 152

Presented by: Miqi Wang, BA, Med II Student

Effects of local anesthetics on differentiation potential of human mesenchymal stem cells

<u>Miqi Wang^{1,2,3}, Robert Tamai², Justine Sun⁴, Alfred Kuo MD PhD^{3,4}</u> ¹University of South Florida Morsani College of Medicine, and ²Department of Orthopaedics and Sports Medicine, ³University of California San Francisco Orthopaedic Surgery and ⁴San Francisco Veterans Affairs Medical Center

Keywords: Local anesthetics, mesenchymal stem cells, differentiation.

Objective: We sought to elucidate the effects of three local anesthetics on the differentiation capabilities of mesenchymal stem cells (MSCs). We hypothesized that local anesthetics would adversely affect MSC differentiation.

Methods: Human MSCs were grown in tissue culture and treated for 1 hour with a saline control or one of the following anesthetics: (1) 2% lidocaine, (2) 0.5% bupivacaine, (3) 0.5% ropivacaine. After recovery in growth media for 24 hours, the cells were then grown under adipogenic, chondrogenic, and osteogenic conditions. Controls were grown in growth media. Differentiation was measured qualitatively using stains for differentiated cells. Differentiation was measured quantitatively using biochemical assays.

Results: Stains showed retention of adipogenic and osteogenic capabilities in cells treated with ropivacaine and bupivacaine. Lidocaine-treated samples did not reach the desired cell density to begin adipogenesis and therefore were not analyzed. Staining of these cells showed no evidence of osteogenesis. Quantitative assays showed baseline triglyceride content in all samples, including the saline control. Assays confirmed retention of osteogenic capabilities from cells treated with ropivacaine and bupivacaine, but also suggested osteogenesis of lidocaine treated cells. No sample underwent chondrogenesis.

Conclusion: Definitive conclusions have yet to be made, as experiments are ongoing. The next steps are to repeat the experiment using cells from the same donor and passage. The goals of these repetitions are to 1) ascertain that the data is reproducible and 2) to include pertinent controls, including cell count normalization for triglyceride and alkaline phosphatase assays and untreated-differentiated positive controls.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Presented by: Ryan Young, PhD, Postdoctoral Fellow

The Use of Human Sweat Metabolites as Bait for Monitoring Vectors of Onchocerciasis in West Africa and Latin America

Ryan Young¹, Nathan Burkett-Cadena², Jeremy Beau¹, TJ McGaha³, Mario A. Rodríguez-Pérez^{4,5}, Laurent Toé⁶, Raymond Noblet³, Eddie W. Cupp², Thomas Unnasch² and Bill J. Baker¹ ¹Department of Chemistry and Center for Drug Discovery and Innovation, University of South Florida; ²Department of Global Health, University of South Florida; ³Department of Entomology, University of Georgia; ⁴Centro de Biotecnología Genómica, Instituto Politécnico Nacional; ⁵ de Medicina, Universidad Autónoma de Nuevo León; ⁶ Multidisease Surveillance Centre, World Health Organization, University of South Florida Studies

Keywords: Onchocerciasis; Vector monitoring; Metabolomics

Objective: Onchocerciasis or river blindness disease is a parasitic disease caused by infection from the nematode Onchocerca volvulus. The parasite is transmitted to humans by black fly vectors of the genus Simulium. Most of the infections occur in central Africa, with significant incidence also in Central and South America. The World Health Organization (WHO) estimates 18 million people suffer from onchocerciasis. However, it is difficult to accurately access infection due to a prolonged period from infection to symptoms appearing in hosts. The current method for monitoring the spread employs human bait, which is neither optimal nor ethically sound. The need for a new monitoring method is crucial.

Methods: It was noticed that anthropophilic gravid flies are attracted to human scent. This study will describe our efforts to identify key primary metabolites in human sweat by the use of GC-MS. These compounds were taken onsite to breeding areas of S. occhraseum and S. damnosum in Southern Mexico and West Africa to identify which compounds attracted these vectors of onchocerciasis. This was achieved through the use of EAG and subsequently Y-Tube olefactometer.

Results: Several sweat components where identified as attractive in both species of black flies.

Conclusion: The identified compounds will be developed as bait for a field trap for monitoring vector pressure in both Latin America and Africa.

Research supported by: The Bill and Melinda Gates Foundation

Abstract #: 154	Presented by: Yuan Yuan, PhD, Graduate
	Student

Elastin like Peptides (ELPs) Modulate Cellular Behavior through interaction with Cell Surface Glycosaminoglycans <u>Yuan Yuan, Piyush Koria</u> University of South Florida College of Engineering Chemical & Biomedical Engineering

Keywords: Chronic wound, Elastin like Peptides, Fibroblasts

Objective: Chronic wounds affect 5.7 million patients and cost an estimated 20 billion dollars annually. Recently, we developed a growth factor delivery platform based on elastin like peptides (ELPs) for growth factor delivery to chronic wounds. Elastin like peptides are repeats of the pentapeptide (VPGXG, X=guest residue can be anything but Proline) derived from natural elastin. In this study, we aim to elucidate the effect of chain length and guest residues on the ELP induced modulation of fibroblasts and the mechanism of their interaction.

Methods: We created several ELPs with different chain lengths (number of VPGVG repeats) and having different amino acids in the guest residue position. These ELPs were recombinantly produced in bacteria using standard molecular biology and protein expression techniques.Normal human dermal fibroblasts were treated with different ELPs and proliferation was evaluated using BrdU assay.

Results: We observed that ELPs self-assembled into nanoparticles with different hydrodynamic diameters depending on their chain length and proportion of cysteines. We further found that ELPs increased fibroblast proliferation significantly in a dose dependent manner with saturation concentration of 1mg/ml

Conclusion: Our study suggests that ELPs induce fibroblast proliferation in a dose dependent manner. Furthermore, our data suggest that ELPs induce their biological effect on fibroblasts through interaction with the elastin receptor complex present on the fibroblast surface. We also have the data indicating that MAPK/Erk pathway is responsible for this ELP induced proliferation.

Research supported by: Dept. of Chemical and Biomedical Engineering, USF College of Engineering

Combination Therapy of Human Umbilical Cord Blood Cells and Granulocyte-Colony Stimulating Factor Exerts Neuroprotection in a Chronic TBI model

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Keywords: TBI, G-CSF, hUCBCs

Objective: Traumatic brain injury (TBI) is associated with neuro-inflammation, and cognitive impairments. Cell-based therapies are currently being investigated in treating neurotrauma to regulate the hostile brain milieu found in TBI. In tandem, the stimulation/mobilization of endogenous stem/progenitor cells from the bone marrow through granulocyte colony stimulating factor (G-CSF) poses as an attractive intervention for chronic TBI. In this study, we tested the potential of a combined therapy of human umbilical cord blood cells (hUCB) and G-CSF to counteract the progressive secondary effects of chronic TBI

Methods: Four groups of rats were treated with saline alone, G-CSF+saline, hUCB+saline or hUCB+G-CSF at 7-days post TBI. Eight weeks after TBI, hippocampal cell loss, neuroinflammatory response, and neurogenesis were analyzed using immunohistochemistry

Results: Results revealed that rats exposed to chronic TBI + saline exhibited widespread neuroinflammation, impaired endogenous neurogenesis in dentate gyrus and subventricular zone, and severe hippocampal cell loss. hUCB monotherapy suppressed neuroinflammation, nearly normalized the neurogenesis, and reduced hippocampal cell loss compared to saline alone. G-CSF monotherapy produced partial/short-lived benefits characterized by low levels of neuroinflammation, a modest neurogenesis, and a moderate reduction of hippocampal cells loss. On the other hand, combined therapy of hUCB+G-CSF displayed synergistic effects that robustly dampened neuroinflammation, while enhancing endogenous neurogenesis and reducing hippocampal cell loss

Conclusion: Combined treatment of hUCB+G-CSF rather than monotherapy appears optimal for abrogating chronic TBI associated impairments

Research supported by: Department of Defense W81XWH-11-1-0634

Abstract #: 156

Presented by: Jamileh Ahmed , MS, Graduate Student

Analysis of iPSC-Derived Dopaminergic Neuron Susceptibility to Influenza and Excitotoxicity in Non-Affective Psychosis

Jamileh Ahmed, Helena Hernandez-Cuervo, Juan Molina, G.A. De Erausquin University of South Florida Morsani College of Medicine, Department of Psychiatry and Behavioral Neurosciences

Keywords: iPSCs, Schizophrenia, Neuroscience

Objective: The susceptibility of iPSC-derived dopaminergic neurons from chronic non-affective psychosis patients and healthy individuals to the H1N1 virus will be compared in this study. Preliminary data was collected from C57/BL-6 mice.

Methods: Fibroblasts were reprogrammed into iPSCs using a sendai virus vector containing the oct-4, sox-2, klf-4, and the c-myc transcription factors (OSKC). The presence of iPSCs was verified using the alkaline phosphatase (AP) assay, immunostaining for the presence of ESC markers SSEA-1, nanog, oct-4 and sox-2. The presence of iPSCs was also verified by conducting RT- PCR for nanog, oct-4, sox-2, c-myc, and FGF-4.

Results: Positive staining for alkaline phosphatase indicated that pluripotent cells were present in the colonies. The verification of the presence of nanog, sox-2, oct-4, and ssea-1 with immunostaining also confirmed the presence of pluripotent cells. The iPSCs were differentiated into dopaminergic neurons after characterization tests were performed. The outcome of this experiment will be discussed in the Results section of this study.

Conclusion: After preliminary study completion, fibroblasts from four chronic non-affective psychosis patients, four healthy individuals, and four non-affected siblings from Argentina will be reprogrammed into iPSCs using a sendai-virus vector containing OSKC. The presence of iPSCs will be verified using the AP assay, immunostaining, and RT-PCR. The iPSCs will then be differentiated into dopaminergic neurons. The differences in H1N1 susceptibility in each cell group will be compared. The methylation/acetylation patterns of DNA will also be studied for all cell groups and differential gene expression patterns using custom designed microarrays.

Research supported by: Roskamp Laboratory, Department of Psychiatry and Behavioral Neuroscience

Presented by: Marina Bastawrous, BS, Graduate Student

Dopaminergic Cell Loss as a Pathological Link between Traumatic Brain Injury and Parkinson's Disease

<u>Marina Bastawrous¹, Alesia Antoine¹, Sandra A. Acosta¹, Mibel Pabon¹, Diana Hernandez-Ontiveros¹, Naoki Tajiri¹, Paul R. <u>Sanberg^{1,2}, Yuji Kaneko¹, Cesar V. Borlongan¹</u>* ¹Center of Excellence for Aging and Brain Repair, Department of Neurosurgery and Brain Repair, University of South Florida Morsani College of Medicine, Tampa, FL., ²USF Research and Innovation, University of South Florida, Tampa, FL</u>

Keywords: TBI, PD, alpha synuclein.

Objective: Long-term consequences of traumatic brain injury (TBI) are closely associated with the development of sensory-motor and cognitive problems. Notably, TBI may predispose long-term survivors to age-related neurodegenerative diseases such as Parkinson's disease (PD), yet preclinical studies on the pathophysiological changes in substantia nigra (SN) after chronic TBI are lacking. PD is characterized by a gradual degeneration of the nigrostriatal dopaminergic neurons. In the present in vivo study, we examined the pathological link between PD-associated dopaminergic neuronal loss and chronic TBI.

Methods: Sixty days post TBI, rats were euthanized and brain tissues harvested. Stereology was performed on brain sections immunostained with tyrosine hydroxylase (TH), an enzyme required for the synthesis of dopamine in neurons, and alpha synuclein, a presynaptic protein that plays a role in synaptic vesicle recycling, both key players in PD pathology.

Results: Stereology analyses revealed significant decrease of TH-positive expression in the surviving dopaminergic neurons of the (SN) pars compacta relative to sham control. In parallel, significant increments of expression of aggregated alpha synuclein were detected in the ipsilateral SN compared with the contralateral SN in TBI animals compared to the sham control.

Conclusion: Chronic TBI reduces the TH-positive cell survival in the SN pars compacta accompanied by alpha synuclein overexpression, thus resulting in a PD like pathology in chronic TBI. The decreased expression of TH positive dopaminergic neurons in the SN can be an indication of the long term damage seen in victims of TBI and their propensity to develop further into a neurodegenerative disease.

Research supported by: DOD W81XWH-11-1-0634.

Abstract #: 158

Presented by: Stephanie Blankenship, BS, Graduate Student

Novel Therapeutics Improve Motor Coordination and Seizure Activity in an Angelman Syndrome Mouse Model <u>Stephanie L. Blankenship, Joseph C. Grieco, and Edwin J. Weeber</u>, Department of Molecular Pharmacology and Physiology, University of South Florida Morsani College of Medicine, Tampa, FL

Keywords: Angelman syndrome, epilepsy, ataxia

Objective: Angelman Syndrome (AS) is a rare neurological disorder that presents with severe developmental delay, ataxia, absence of speech, bouts of laughter, and seizures. Treatment with anti-epileptic drugs is occasionally successful, but long-term use can cause toxic side effects, such as loss of coordination and memory problems. Recent research also suggests each successive seizure may critically affect cognition, especially in early development. Therefore, our objective is to evaluate novel, less-toxic seizure therapeutics in the AS mouse model. We will assess both ganaxolone and a ketone ester on their ability to decrease seizure frequency. We hypothesize that both will decrease seizure frequency and consequently enhance cognition.

Methods: 120dB white noise was used to induce audiogenic seizures in AS mice to determine if seizure activity was decreased. Behavioral testing was performed to determine effects on cognitive ability and learning (fear conditioning and Morris water maze tasks) and motor coordination and learning (rotarod).

Results: Results suggest both treatments significantly decreased the frequency of induced audiogenic seizures. Significant improvements were also seen in the motor impairment phenotype, with increased latency to fall off the rotarod observed in treated mice.

Conclusion: Both treatments decreased seizure frequency and ameliorated motor coordination deficits in the AS mouse model. These treatments may target a mechanism that enhances GABA-dependent control of excess neuronal activity, involving alterations in metabolism or GABA receptors, which causes marked improvements in the abnormal AS mouse model phenotype. Therefore, it is possible these treatments could be utilized in future clinical trials for AS.

Presented by: Leonid Breydo, PhD, Faculty

Solvent Interaction Analysis of Intrinsically Disordered Proteins in Aqueous Two-phase Systems

Leonid Breydo, Larissa M. Mikheeva, Pedro P. Madeira, Boris Y. Zaslavsky and Vladimir N. Uversky LB, VNU: Department of Molecular Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL 33612, USA LMM, BYZ: Analiza, Inc., 3516 Superior Ave., Suite 4407B, Cleveland, OH 44114, USA PPM: Laboratory of Separation and Reaction Engineering, Dpt. de Engenharia Qui´mica,Faculdade de Engenharia da Universidade do Porto, Rua Dr. Roberto Frias, s/n 4200-465, Porto, Portugal

Keywords: intrinsically disordered proteins, protein structure, partitioning in aqueous two-phase systems

Objective: Intrinsically disordered proteins (IDPs) are biologically active proteins without unique 3D-structures. More open structure of IDPs compared to folded proteins has been shown to result in more extensive hydration. In order to better characterize protein-solvent interaction of IDPs, we examined secondary structures and distributions of IDPs(alpha-synuclein and several of its variants) and several folded proteins in aqueous two-phase systems.

Methods: We have used the partition behavior of proteins in polymer-polymer aqueous two-phase systems to measure differences in protein-solvent interactions and circular dichroism to evaluate the secondary structure of proteins in these systems.

Results: We found that both partition coefficients and CD spectra indicate that point mutations in alpha-synuclein result in significant changes in folding of this protein in polymer solutions. These changes were much more significant than those observed for folded proteins. In fact, the difference in partition coefficients between alpha-synuclein and its mutants was larger than the differences between several unrelated folded proteins.

Conclusion: We found that a novel method of partitioning proteins in polymer-polymer aqueous two-phase systems can be used to measure differences in protein-solvent interactions between both IDPs and folded proteins. The results obtained by this method are consistent with the changes in the protein secondary structure. IDPs were shown to be much more sensitive to both mutations and changes in solvent composition than folded proteins. This increased sensitivity is likely due to both higher solvent exposure of IDPs and differences in amino acid composition between IDPs and folded proteins.

Abstract #: 160

Presented by: Lecia Brown, MS, Graduate Student

Evaluation of the Quantification of HIV Viral load & Chemistry Analytes in Cerebrospinal Fluid in Kisumu, Kenya. <u>Lecia Brown¹, Brian Giunta¹, Clement Zeh²</u> ¹Morsani College of Medicine, Dept. of Psychiatry and Behavioral Neurosciences, ²Centers for Disease Control and Prevention/Kenya Medical Research Institute

Keywords: Kenya, HIV, CSF, Viral load

Objective: As a pilot study for future validation, the experiments sought to 1) determine if the CSF sample type can be analyzed via the Roche Cobas Ampliprep/Taqman (CAP/CTM) platform for viral load and 2) determine if the CSF sample type can be analyzed by the Cobas Integra 400 platform in chemistry analyses on CSF samples.

Methods: CAP/CTM and Cobas Integra 400 platforms were evaluated for sensitivity, precision, and intra-assay accuracy for viral load and chemistry analytes, respectively.

Results: Using both systems, results showed there was no difference in either method when using CSF or PBS as a comparative diluent. In the CAP/CTM system, CSF sample dilutions averaged 6.28 log10 copies/ml in comparison with PBS dilutions of the same sample of 6.28 (Expected value: 6.57). In the Cobra Integra 400 system, 2 seropositive and 2 seronegative samples yielded no significant difference in expected values of analytes of known concentration dilutions.

Conclusion: From these results, it can be expected that CSF sample type can be analyzed on CAP/CTM and Cobas Integra 400 platforms. It is highly recommended to proceed to a full evaluation of both systems to aid in therapy monitoring and routine management of HIV-1 infection and neurocognition in Kisumu, Kenya.

Research supported by: University of South Florida, Centers for Disease Control and Prevention/Kenya Medical Research Institute, San Diego State University- The Minority Health and Health Disparities International Research Training

Presented by: Ming Chen, PhD, Faculty

High-energy compounds mobilize intracellular Ca2+ and activate calpain in SH-SY5Y neurons

<u>Huey T. Nguyen and Ming Chen,</u> Bay Pines VA Medical Center and Department of Molecular Pharmacology and Physiology, University of South Florida Morsani College of Medicine

Keywords: Alzheimer's disease, energy, calcium, calpain

Objective: Deficiency in energy metabolisms is perhaps the earliest modifiable defect in brain aging and Alzheimer's disease (AD). Several high-energy compounds (HECs) such as ATP, phosphoenol pyruvate, phosphocreatine and acetyl coenzyme A have been shown to exhibit neuroprotective effects. To understand their mechanism of actions, we tested the effects of these HECs on intracellular Ca2+, a central regulator in brain function.

Methods: Ca2+ imaging by confocal microscope; ATP measurement; intracellular calpain activity assay.

Results: The HECs robustly and dose-dependently mobilized intracellular Ca2+ in cultured SH-SY5Y cells, and the actions were sensitive to intracellular Ca2+ chelator BAPTA-AM or energy metabolism blocker rotenone. The Ca2+ influx triggered by the HECs was from both extracellular medium and intracellular stores and the HECs also induced repetitive Ca2+ oscillations, similar to those of classical Ca2+ agonists. The HECs may be viewed as a new group of physiological Ca2+ agonists. We also found that the HECs promoted the intracellular activity of calpain, a Ca2+-dependent protease, and the enzyme activity fluctuated in concert with cellular energy levels, suggesting that calpain activity may also be energy-driven or energy-dependent.

Conclusion: The findings add to current knowledge for the regulatory mechanisms of Ca2+ and calpain. Since Ca2+ and calpain undergo critical dysfunction in brain aging but the underlying mechanisms remain elusive, our work may provide a new perspective for understanding some of the key issues. More importantly, the HECs, as key intermediates in glucose catabolism, the primary source of energy supply in the brain, may be used as potential drugs for rational prevention of AD.

Research supported by: Supported by DVA and CWS Foundation.

Abstract #: 162

Presented by: Bruce Citron, PhD, Faculty

Treatment of Mild Traumatic Brain Injury in Mice With a Nrf2 Activator Affects Dendritic Complexity Jessica N. Chang^{1,2}, Ronald F. Mervis^{3,6}, Stephanie K. Foley^{5,6}, Peter Hanna⁵, Noah Peeri⁵, Nikhil Bhatia⁵, Sonya Bhaskar⁵, Gurtej Walha⁴, Lital Rachmany⁷, Anat Shaer⁷, Vardit Rubovitch⁷, Chaim G. Pick⁷, Bruce A. Citron^{1,2} ¹Lab. of Mol. Biol., R&D 151, Bay Pines VA; ²USF Morsani College of Medicine, Dept. of Molecular Medicine, and ³Ctr. for Aging & Brain Repair, Department of Neurosurgery; ⁴USF Morsani College of Medicine; ⁵Honors College, USF; ⁶NeuroStructural Research Labs., Tampa; ⁷Department of Anatomy &

Anthropology, Sackler School of Med., Tel Aviv U.

Keywords: Traumatic brain injury, Transcription factor, tBHQ, Inflammatory responses, Connectivity

Objective: Worldwide, the incidence of TBI is approximately 0.5% of individuals per year and the vast majority of TBIs are mild yet they frequently do result in significant negative effects on brain function. Unfortunately, TBI is much more frequent, with about 15% prevalence, among deployed military personnel. Our lab has uncovered molecular mechanisms, in particular certain inflammatory responsive regulatory factors involved in the health of neurons. We have previously presented cognitive improvements produced by treatment activating the transcription factor, Nrf2, by administration of tBHQ after injury and have identified pathway changes involved in the neuroprotection.

Methods: Here we describe the changes seen in dendritic complexity after tBHQ treatment and TBI in mice. We employed a closed head system involving a weight drop induced impact and rotational injury and have measured behavioral, mRNA, and protein changes. To determine alterations in connectivity, brain samples were stained with the Golgi method to quantitatively assess dendritic branching and spine morphologies and densities.

Results: Dendritic complexity, determined by several different measures including branch point analysis, was higher in the untreated TBI brains compared to sham injured or to brains from mice exposed to TBI plus treatment.

Conclusion: Our findings may indicate a preferential loss of the least connected neurons in the injured, untreated mice. Through these experiments we seek to develop effective treatment strategies to combat the secondary effects of traumatic brain injury.

Research supported by: Dept. of Veterans Affairs (Veterans Health Administration, Office of Research and Development, Biomedical Laboratory R&D), The Bay Pines Foundation, and Florida DOH James and Esther King Program.

Granulocyte Colony Stimulating Factor (GCSF) Attenuates Hemorrhagic Transformation after Delayed tPA treatment in a Rat Experimental Stroke Model

Ike dela Pena, Sandra Acosta, Mibel Pabon, Arum Yoo, Diana Hernandez, Meaghan Staples, Paolina Pantcheva, Cyrus Tamboli, Sharosh Tamboli, Kelsey Duncan, Diego Lozano, Marina Bastawrous, Alesia Antoine, Naoki Tajiri, Yuji Kaneko and Cesar Borlongan, Center of Excellence for Aging and Brain Repair, Department of Neurosurgery and Brain Repair, University of South Florida, Tampa, FL

Keywords: G-CSF, tPA, hemorrhagic transformation

Objective: Tissue plasminogen activator (tPA) is the only FDA-approved treatment for acute stroke. However, due to its short therapeutic time window, delayed tPA treatment has been associated with serious side effects including hemorrhagic transformation (HT). A number of studies have demonstrated neuroprotective activities of G-CSF in ischemia. None so far, has examined effects of G-CSF in the setting of tPA-induced HT in stroke. The objective of this study is to demonstrate that administration of G-CSF reduces HT after a delayed tPA treatment in experimental models of stroke.

Methods: Sprague-Dawley rats subjected to middle cerebral artery occlusion (MCAO) were given saline (control) or tPA (10 mg/kg, intraveous [i.v.]) at 5 hours after reperfusion (delayed tPA treatment group). Effects of G-CSF (300 ug/kg, i.v.) alone or G-CSF after delayed tPA on infarct volume and extent of intracerebral hemorrhage as well as neurological and behavioral outcomes were observed 24 hours and 3 days in rats subjected to MCAO.

Results: Administration of G-CSF reduced HT after a delayed tPA treatment in experimental models of stroke. As well, neurological outcomes were improved in G-CSF treated MCAO rats subjected to delayed tPA treatment.

Conclusion: These results indicate potential therapeutic value of G-CSF in attenuating HT during delayed tPA therapy. Studies are underway to examine the mechanism(s) involved in G-CSF-induced reduction of HT due to delayed treatment of tPA.

Research supported by: This study was supported by NIH NINDS 5R01NS071956-02.

Abstract #: 164

Presented by: Trish Dinh, BS, Med III Student

Effects of Genetic and Environmental Modulator in Schizophrenia Etiology.

<u>Trish Dinh, B.S.¹ Joshua Gamsby, PhD.², Danielle Gulick, PhD.²</u> ¹University of South Florida Morsani College of Medicine, ²Dept of Molecular Medicine, University of South Florida Morsani College of Medicine

Keywords: schizophrenia, mice models, poly I:C

Objective: We have developed a mouse line with multiple schizophrenia (SCZ)-linked gene mutations and prenatal immune activation via poly I:C or stress. We hypothesize that these mice will display greater severity of SCZ symptoms than other mouse models.

Methods: We use single mutation (disrupted-in-schizophrenia 1(DISC1) and Reelin (RELN)) as well as double transgenic DISC1-RELN crosses. After genotyping, behavioral testing is done to assess the severity of SCZ phenotypes. Novel objection recognition (NOR) measures learning and memory, while prepulse inhibition (PPI) measures sensory gating. Subjects: Male and female mice, between 8-14 weeks old. In NOR, the mice are placed in an open field for 10 minutes with two identical Lego's. 24 hours later, mice are placed in the open field again, with a novel Lego replacing an old one for 5 minutes. An hour later, the novel Lego is placed against a different wall and recording is done for another 5 minutes. In PPI, a low threshold initial stimulus, called a pre-pulse, suppresses subsequent responding to a startling stimulus. The mice are placed in a Plexiglas tube for 20 minutes, during which they are exposed to bried startle tones (120dB) alone or preceded by a prepulse (74-90 dB).

Results: Both male and female wild-types spent more time with the novel object in both phases of testing; these difference was attenuated by poly I:C treatment and in the RELN mutant mice. For PPI, DISC1 mice and wild-types that were exposed to poly I:C all demonstrated reduce startle, although PPI was only impaired in the wild-types exposed to both stress and Poly I:C.

Conclusion: These results will serve as a foundation for breeding more ideal animal models used in developing schizophrenia drug treatments.

Research supported by: USF Health Molecular Medicine

Presented by: Sarah Eisel, BA, Graduate Student

COMT, BDNF, CLSTN2, and Cognitive Function

Sarah L. Eisel¹, Colleen A. Pappas¹, Christina M. Martin¹, Shuai Huang², and Brent J. Small¹ ¹School of Aging Studies, College of Behavioral & Community Sciences, University of South Florida; ²Department of Industrial and Management Systems Engineering, College of Engineering, University of South Florida

Keywords: Genes, Cognition, Older Adults

Objective: Age-related changes in cognition have been described, however little is known about the impact of genes on normal cognitive functioning or mild cognitive impairment (MCI) in older adults. We investigated the relationship between multiple domains of cognitive performance and genetic polymorphisms of 3 genes Catechol-O-Methyltransferase (COMT), brain-derived neurotrophic factor (BDNF), and Calsyntenin 2 (CLSTN2) in older adults with normal cognitive functioning and persons with MCI.

Methods: Baseline and screening data from participants (n = 555) in the Alzheimer's Disease Neuroimaging Initiative (ADNI) study was examined. To observe the influence of different polymorphisms on cognitive functioning analyses of covariance were conducted. To evaluate differences in cognition by allelic classification for the genes encoding COMT, BDNF, and CLSTN2, Tukey post-hoc tests were utilized.

Results: On average, persons with MCI performed more poorly on cognitive tasks than those with normal cognition. Among the genetic predictors of cognitive performance, COMT genotype was related to functioning on two tests of episodic memory. BDNF genotype influenced a test of short-term memory. Finally, CLSTN2 genotype influenced a measure of executive functioning. Cognitive status did not interact with genotype to influence cognitive test scores.

Conclusion: Memory may be affected more by genetics than other cognitive domains. However, divergent findings suggest that the role of genetics on cognition is complex and warrants further research.

Abstract #: 166

Presented by: Darren Ferrell, MS, Graduate Student

Mechanistic Evaluation of Efavirenz Neurotoxicity: Implications for Cognitive Impairment

Darren Ferrell, M.S.^{1,2} Lecia A.M. Brown, M.S.^{1,2} Jingji Jin, Ph.D¹M.S.^{1,2}Adam J. Smith, Ph.D.³, Demian Obregon, M.D.⁴, <u>Edin Sadic, B.S.¹, Jun Tan, M.D., Ph.D^{2, 3,4,5}, Brian Giunta, M.D., Ph.D^{1,2,3,5}</u> ¹Dept. of Psychiatry and Behavioral Neurosciences, Neuroimmunology Laboratory, USF Morsani College of Medicine, Tampa, FL.²Dept. of Pharmacology and Physiology, USF Morsani College of Medicine, Tampa, FL ³Center of Excellence for Aging and Brain Repair, Dept. of Neurosciences, Rashid Developmental Neurobiology Laboratory, Silver Child Development Center, USF Morsani College of Medicine, Tampa, FL, ⁵James A. Haley Veterans Administration Hospital, Tampa, FL

Keywords: HIV, HAND, efavirenz, oxidative stress, amyloid-beta

Objective: To determine the neurotoxicity associated with the non-nucleoside reverse transcriptase inhibitor Evavirenz, a component of HIV-1 highly active anti-retroviral therapy regimen.

Methods: Neuronal Abeta production assay, Western immunoblotting, Mitochondrial Stress Analysis: ATP, MMP and ROS, Microglial Phagocytosis Assay, Statistical Analysis

Results: Abeta generation was found to be promoted by Efavirenz (EFV) or EFV/3TC/AZT treament in culured SweAPP N2a cells via BACE-1 activation.

Conclusion: Expanding on previous work, we show that antiretroviral compounds have neurotoxic effect, including the promotion of Amyloid beta production, a common marker for Alzheimer's disease as well as other neurodegenerative diseases. We conclude that components of the HAART regimen contribute to the formation of premature cognitive deficits associated with HIV-1 associated neurocognitive dementia (HAND).

Research supported by: BG is supported by NIMH/NIH grant (1R01MH098737-01) (PI). JT is supported by NIH grants (1R41AG031586-01), (1R43AG033417-01), and 1R43AT004871-01 as well as a Veterans Administration grant (MH080168).

Presented by: Joseph Grieco, MS, Graduate Student

The Effect of Minocycline in the Treatment of Children with Angelman Syndrome: A Pilot Study

¹Joseph C. Grieco, MS, ¹Stephanie L. Blankenship, BS, ²Maria Gieron-Korthals, MD, ³Mike R. Schoenberg, PhD, ⁴Amanda G. Smith, MD, ³Rex M. Philpot, PhD, ⁴Helen S. Heussler, MD and ¹Edwin J. Weeber, PhD University of South Florida Morsani College of Medicine, Departments of ¹Molecular Pharmacology and Physiology; ²Pediatrics; ³Psychiatry and Behavioral Neurosciences, ⁴USF Health Byrd Alzheimer's Institute

Keywords: Angelman, Cognitive Impairment, Ataxia, Epilepsy, Seizure

Objective: Minocycline, a member of the tetracycline family, has a low risk of adverse effects and an ability to improve behavioral performance in humans with cognitive disruption. Here, we performed a single-arm pilot trial in which children, diagnosed with Angelman syndrome (AS), were administered minocycline to determine the drug's effect on the cognitive and behavioral manifestations of the disorder.

Methods: 14 male and 11 female children, mean age 8 years and 4 months, were assessed during 3 study visits: baseline, after 8-weeks of minocycline treatment and after an 8-week wash out period. Each visit consisted of identical testing that included a history and physical examination, laboratory testing, EEG recording and neuropsychological testing.

Results: We observed a significant improvement in mean raw scores of the BSID-III subdomains communication and fine motor ability when baseline scores were compared to scores after the washout period. Further, mean scores of the BSID-III self-direction subdomain and CGI-S scale score were significantly improved both after minocycline treatment and the wash out period.

Conclusion: The improvements in clinical and neuropsychological measures warrant further investigation into the effect minocycline has on patients with Angelman Syndrome. The data presented here justify a larger scale, controlled clinical trial.

Research supported by: The Foundation for Angelman Syndrome Therapeutics

Abstract #: 168	Presented by: Beth Grimmig, BA, Graduate
	Student

Fractalkine Signaling Mediates Cognitive Decline During Aging Across Cognitive Domains. <u>Grimmig,B.,¹ DesFosses, L.,¹ X. Wang, ² Hudson, C.,¹ Weeber, E.,¹ Bickford, P.^{1,3}</u> ¹ Dept of Neurosurgery and Brain repair, University of South Florida, Morsani College of Medicine, Tampa FL²Dept of Molecular Pharmacology and Physiology, Byrd Alzheimer's Institute, University of South Florida, Tampa FL ³James A Haley Veteran's Hospital, Tampa FL

Keywords: Aging, Cognition, Fractalkine, Microglia, Neurogenesis

Objective: Mice lacking the fractalkine receptor (CX3CR1 -/-) are subject to compromised cognitive function due to the loss of receptor-ligand regulation. This strain of mice exhibits reduced hippocampal neurogenesis and deficits in hippocampal dependent tasks by 6 months of age. The objective of the current study was to characterize the behavior of mice missing the fractalkine ligand and to establish a how the varying domains of cognitive function change with age.

Methods: CX3CL1 -/- mice and age matched controls were evaluated at different ages in battery behavioral tests. Motor Coordination was evaluated by accelerated rotarod (4 trails a day for 2 days) and hippocampal function was assessed using a standard 2 shock protocol of contextual and cued fear conditioning.

Results: Young CX3CL1 deficient mice display reduced freezing behavior in contextual fear conditioning 24 hours after training compared to wild type controls. However, this deficit improves with age, and the effect is blunted at later time points. In contrast, fractalkine null mice exhibit better motor coordination at younger ages than wild type mice, indicated by longer latency to fall off the rotarod. Performance on the rotarod is dramatically reduced in the aged CX3CL1 -/- mice and at this age show deficits compared with WT mice.

Conclusion: These data suggest that interruption of normal fractalkine-receptor signaling does impact cognitive function but the precise role on the cognitive domains is variable across time. Future work will strive to determine a timeline of cognitive decline across the various domains.

Research supported by: USPHS Grant, AG04419, VAMRS

Presented by: Ahsan Habib, PhD, Graduate Student

Mycoplasma Hyorhinis Markedly Degrades β-amyloid Peptides in vitro and ex vivo: a Novel Biological Approach for Treating Alzheimer's Disease?

<u>A Habib¹, J Deng^{1,3}, HY Hou¹, B Giunta², D Obregon¹, D Sawmiller¹, S Li^{1,4}, J Tan¹ ¹ Rashid Laboratory for Developmental Neurobiology, Silver Child Development Center, Morsani College of Medicine, University of South Florida; ² Neuroimmunology Laboratory, Morsani College of Medicine, University of South Florida; ³ Department of Neurology, Daping Hospital, The Third Military Medical University, China; ⁴ School of Physics and Optoelectronic Technology, Dalian University of Technology, China</u>

Keywords: Mycoplasma, Alzheimer's disease, amyloid-β peptide, amyloid precursor protein

Objective: Accumulation of amyloid- β (A β) peptides (predominantly A β 40, 42) and their aggregation into plaques in the brain are thought to be the one of the major causes of Alzheimer's disease (AD).

Methods: We fully characterized the Mycoplasma species as Mycoplasma hyorhinis(M. hyorhinis) by genetic and colony morphological analyses by light microscopy. We further evaluated its Aβ degradation effect both in vivo and in vitro.

Results: Most interestingly, we attenuated the pathogenicity of M. hyorhinis by γ irradiation (3.5 Gy), and found that its ability to degrade A β was retained. On the other hand, heated and sonicated M. hyorhinis failed to retain this ability to degrade A β , suggesting that this degradation requires viable cells and likely a biologically active signaling pathway. In addition, we found that M. hyorhinis can degrade A β produced in AD model mice (PSAPP mice) ex vivo. Finally, we found that irradiated (non-pathogenic) M. hyorhinis also can degrade A β produced in PSAPP mice in vivo.

Conclusion: These studies suggest that irradiated (non-pathogenic) M. hyorhinis can be a novel and alternative biological strategy for AD treatment.

Research supported by: This work was supported by the NIH/NIA (R01AG032432) and the Silver Endowment. Ahsan Habib and Juan Deng equally contribute to this work.

Abstract #: 170

Presented by: Diana G Hernandez-Ontiveros, MS, Graduate Student

CD-36 a Novel Inflammatory Marker in a Rat Model of Traumatic Brain Injury

Diana G Hernandez-Ontiveros¹, Naoki Tajiri^{1,2}, Sandra Acosta^{1,2}, Mibel M Pabon^{1,2}, Kazutaka, Shinozuka,¹ Hiroto, Ishikawa,¹ Yuji Kaneko^{1,2}, Paula C. Bickford^{1,2}, Cesario V Borlongan^{1,2}, ¹Center of Excellence for Aging and Brain Repair, ²Department of Neurosurgery and Brain Repair, University of South Florida, Morsani College of Medicine, Tampa, FL

Keywords: Fatty acid translocase(FAT,CD-36), traumatic brain injury (TBI), modified low density lipoprotein (mLDL), monocyte chemo attractant protein 1 (MCP1), ionized calcium-binding adapter molecule 1 (lba1)

Objective: Intense military conflict worldwide urges for valuable clinical treatment to wounded soldiers whose impacted brains suffer multiple head injuries, if left untreated they may lead to progressive neurodegeneration, chronic neuroinflammation, and cell death. FAT/CD-36, a scavenger receptor of mLDLs found in splenocytes, and monocytes has been implicated in lipid metabolism, atherosclerosis, oxidative stress, the inflammatory response after stroke, and some neurodegenerative diseases. CD-36 may play a key pathological role in mediating the neuroinflammatory response in a rat model of TBI.

Methods: Preliminary data implicating splenic CD-36 expression after TBI and data suggesting the inhibitory action of soluble receptor of advanced glycation end products blocking CD36-mediated uptake of mLDL in various cell types we have characterized pathological alterations in the acute and chronic TBI stages. Adult Sprague-Dawley rats underwent TBI using controlled cortical impact injury model (CCI). Controls were age-matched rats receiving sham surgery. Both groups were euthanized at 1, 2, 7 and 60 days post-surgery, their brains removed, processed for protein analysis and immunohistochemistry against CD-36, MCP1, and Iba1 for microglia.

Results: We observed brain co-localization of CD-36, MCP1 and Iba1 on impact cortical area, significant increases of CD-36 and MCP1 positive cells in the ipsi vs. contra hemispheres of TBI vs. sham groups, but no significant increases of Iba-1 expressing cells over time. Immunoblotting support overexpression of CD-36 in brain and spleen at acute post-TBI time points vs. sham.

Conclusion: Based on these data, CD-36 serves a key role as a pathological link between inflammation and TBI.

Research supported by: Dept. of Defense, USF-VA Reintegration Funds

Presented by: Danielle Kamis, BS, Med III Student

Parkinsonism and Transcranial Ultrasound in Schizophrenics and Healthy Relatives: Sex and Laterality

<u>Kamis, Danielle¹; Stratton, Lee²; Calvó, Maria³; Padilla, Eduardo3; Florenzano, Néstor⁴; Guerrero, Gonzalo³; Molina-Rangeon, <u>Beatriz³; Molina, Juan²; de Erausquin, Gabriel²</u> ¹University of South Florida Morsani College of Medicine, and ²Department of Psychiatry and Behavioral Neurosciences, Roskamp Laboratory of Brain Development, Modulation and Repair; ³Hospital Neuropsiquiátrico Néstor Sequeiros; ⁴Universidad de Buenos Aires</u>

Keywords: parkinsonism, trancranial ultrasound, schizophrenia, laterality, sex

Objective: We tested the hypothesis that loss of substantia nigra neurons in subjects at risk of schizophrenia (1), as reflected by midbrain hyperechogenicity (2) and parkinsonian motor impairment (3), is asymmetric and influenced by sex.

Methods: We evaluated 62 subjects with never-treated chronic schizophrenia, 80 of their adult, unaffected first degree relatives and 62 healthy controls (matched by sex and age to the cases), part of an Andean population of Northern Argentina. Parkinsonism was scored blindly using UPDRS-3 on videotaped exams by 2 independent raters. Trancranial ultrasound was performed by an expert sonographist blind to subject condition with a 2.5 MHz transducer through a temporal bone window. Quantification of echogenic area was carried out on saved images by a different evaluator.

Results: We found a significant difference in parkinsonian motor impairment between patients, their relatives as well as controls. All three groups showed worse parkinsonism on the left side than the right, corresponding with increased echogenicity on the right substantia nigra compared with the left. Females had less asymmetry, and overall less echogenicity than males. Male patients had the most right hyperechogenicity and the most severe left parkinsonism. Male unaffected relatives were significantly more echogenic than controls on that side. On the left, only female patients had significant echogenicity.

Conclusion: Our data supports the notion that unaffected relatives of schizophrenic subjects have increased parkinsonism and concomitant brainstem abnormalities which may represent a vulnerability to the disease. Both motor and brainstem abnormalities are asymmetric and influenced by sex.

Research supported by: This research was supported by the Scholarly Concentrations Program at USF Health, Morsani College of Medicine and the Roskamp Laboratory for Brain Development.

Abstract #: 172

Presented by: Seol-Hee Kim, MS, Graduate Student

Effect of Methylsulfonylmethane (MSM) Against HIV-1 Tat Induced Oxidative Stress

<u>Seol-Hee Kim¹, Adam J. Smith¹, Brian Giunta², R. Douglas Shytle¹</u> ¹Center of Excellence for Aging and Brain Repair, Department of Neurosurgery and Brain Repair, Morsani College of Medicine, University of South Florida, Tampa, FL ²Neuroimmunology Laboratory, Department of Psychiatry and Behavioral Neurosciences, Morsani College of Medicine, University of South Florida, Tampa, FL

Keywords: Oxidative stress, Glutathione (GSH), HIV-1 Tat, Methylsulfonylmethane, HIV-associated neurocognitive disorder (HAND)

Objective: HAND caused by neuronal loss is common among HIV infected patients. Tat protein, transactivator of transcription, is released from HIV-1 infected cells and is the key factor causes neuronal dysregulation. GSH is the major antioxidant in the brain. It acts as a substrate to neutralize hydroxyl radicals via glutathione peroxidase (GPx) and detoxifies xenobiotics by acting a substrate for glutathione-S-trasnferase (GST). In this study, Tat induced oxidative stress was measured and therapeutic effect of MSM, naturally occurring organic sulfur compound, was assessed in murine neuroblastoma(N2a) cells.

Methods: Tat protein and MSM were co-administered to N2a neuronal cells. Cell viability (MTT), reactive oxygen species (ROS) and nitric oxide (NO) release were measured to assess Tat induced oxidative stress. GSH, GPx and GST were measured to determine antioxidant effect of MSM.

Results: Tat administration leads to elevated ROS and NO levels, but did not show significant differences in cell survival rate. Also, Tat decreased GSH levels, GPx and GST activities. MSM treatment decreased ROS and NO production, but did not change cell survival rate. MSM treatment also replenished GSH levels, GPx and GST activities.

Conclusion: These results suggest that Tat disturbs redox homeostasis in N2a cells by inducing ROS and NO production, but did not lead to cell death. In addition, MSM showed neuroprotective effect by boosting antioxidant capacity in neuronal cells by replenishing glutathione levels and related enzyme activities. Further studies will be needed to characterize the functional consequences of this redox stabilization with MSM.

Research supported by: BG is supported by NIMH/NIH grant (1R01MH098737-02). Recombinant HIV-1 Tat protein was obtained from NIH reagent aid program.

Presented by: Lisa Kirouac, MS, Graduate Student

A Functional Relevance of Proliferation-Associated Proteins in Alzheimer 's Disease

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Keywords: γ-synuclein (SNCG) amyloid precursor protein (APP) Alzheimer's disease (AD) amyloid-beta (Aβ) Stable Isotope Labeling by Amino Acids in Culture (SILAC)

Objective: APP is a key player in AD and its altered processing can be regulated in a cell cycle-dependent manner. To define a functional role for APP in vitro, we used comparative studies in B103 cells that are null for or express APP. Using SILAC and mass spectrometry, we recently showed a 60-fold increase in SNCG expression and a significant induction in proliferation-associated proteins, such as Ras and P-ERK, in APP expressing cells. Here we examine APP-dependent signaling mechanisms that we believe underlie neurodegeneration.

Methods: To see if Aβ, a pathogenic derivative of APP, induces expression of proliferation-associated proteins, primary neurons were treated with Aβ for 24 hours and were analyzed by western blot and immunofluorescence for changes in Ras or ERK expression and distribution. Western blot was used to analyze brain lysates from late AD (LAD), mild cognitive impaired (MCI) and non-AD patients for changes in Ras and SNCG expression. Brain sections from nontransgenic (NTG), APP and Presenilin/APP (PS/APP) mice were analyzed by immunohistochemistry for tissue distribution of SNCG and Ras.

Results: Aβ treated neurons show increased expression of Ras and P-ERK. Expression of Ras and SNCG are increased in MCI and LAD patients. Brain sections from APP and PS/APP transgenic mice show enhanced staining of Ras and SNCG proximal to amyloid plaques, with no staining in NTG controls.

Conclusion: Increased expression of pro-proliferative proteins by APP and Aβ suggests that APP and its metabolites can induce the Ras/ERK signaling and this is further underscored with expression localized to amyloid plaque pathology. Increased Ras and SNCG expression in MCI patients suggest that these changes correlate with disease progression.

Research supported by: NIA and Alz. Association

Abstract #: 174

Presented by: Chase Lambert, MS, Graduate Student

Varenicline Ameliorates Spatial and Temporal Gait Deficits Following 3-Acetylpyridine-Induced Ataxia in Rats <u>C.S. Lambert¹, R.M. Philpot², M.E. Engberg², and L. Wecker^{1,2}</u> University of South Florida Morsani College of Medicine, Depts of ¹Molecular Pharmacology & Physiology, and ²Psychiatry & Behavioral Neurosciences

Keywords: nicotinic agonist, ataxia, varenicline, treadmill, gait

Objective: A recent study from our laboratory has provided proof-of-concept supporting the use of nAChR agonists for the treatment of olivocerebellar ataxias (Wecker et al., 2013). This study further investigated the potential use of the nicotinic agonist varenicline to alleviate gait abnormalities in rats with olivocerebellar lesions. Dose-response effects of varenicline upon temporospatial gait parameters were assessed using the DigiGait[™] system, an automated digital imaging treadmill.

Methods: Rats received injections of 3-acetylpyridine followed by nicotinamide 3.5 hours later to selectively lesion the olivocerebellar pathway. Gait was assessed prior to and 1 week following impairment. Following the establishment of the ataxic phenotype, animals were assigned to one of four groups, and received injections of saline or varenicline (0.3, 1, or 3 mg free base/kg, s.c.) daily for 2 weeks, and gait was reassessed.

Results: Numerous gait alterations were apparent in both spatial (shorter stride length, wider stance width) and temporal (shorter stride and stance durations and increased stride frequency) parameters. Gait parameters were unaffected by saline administration, as well as by the two lower doses of varenicline. In contrast, administration of 3 mg/kg varenicline led to significant improvements in selective temporospatial gait parameters, including longer stride length, increased stride and stance durations, and decreased stride frequency.

Conclusion: Several gait parameters of animals who received 3 mg/kg varenicline did not differ significantly from agematched control animals, indicating that this dose of varenicline normalized several gait parameters to control values.

Research supported by: NINDS of the National Institutes of Health, Award Number R01NS072114.

Presented by: Jea-Young Lee, PhD, Postdoctoral Fellow

Treatment of Young and Aged Rats Increases Nuclear Expression of Nrf2 and Beta-catenin

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Keywords: Aging, neurogenesis, microglia, astrocytes, neurons

Objective: Aging is associated with a decline in stem cell proliferation. In this study we examined the neurogenic niche of young and aged rats to determine if treatment with NT-020 regulated oxidative stress response pathways in neurons, astrocytes and microglia in the dentate gyrus subgranluar zone (SGZ) and in the subventricular zone (SVZ), two neurogenic rich areas of the brain.

Methods: Immunohistochemistry was used to identify co-labeling of Nrf2, HO-1 or Beta-catenin in either neurons (NeuN), microglia (IBA-1), astrocytes (GFAP) or neuronal progenitors (dourblecortin, DCX) observed in adult and aged F344 rat brain. The primary antiserum (1:500) were polyclonal antibody raised in rabbit against Neun, IBA-1, GFAP, DCX and monoclonal antibody raised in mouse against Beta-catenin, HO-1, Nrf2. The secondary antiserum (1:500) were Alexa488 anti-mouse, Alexa555 anti-rabbit IgG. Then examined and photographed using Zeiss confocal microscope to verify double labeling of immunostains.

Results: We observed an increase in immunopositive labeling of Beta-catenin, HO-1 and Nrf2 in all subsets of cell types in both young and aged rats in the SGZ following NT-020 treatment. In NeuN positive cells there was a basal increase in nuclear Beta-catenin in the aged rats, that was not observed in DCX labeled cells, microglia or astrocytes.

Conclusion: The results suggest that NT-020 activates oxidative stress response pathways showing that Nrf2 and Betacatenin translocate to the nucleus. One downstream effector of Nrf2, HO-1 was also increased. This indicates that antioxidant response pathways and stem cell pluripotency pathways are activated by NT-020, which may be involved in the mechanism by which they increase neurogenesis in aged rats.

Research supported by: USPHS grant AG-044919, VAMRS

Abstract #: 176

Presented by: Song Li, Postdoctoral Fellow

Aβ₁₋₁₇ Antibody 6E10 Blocks APP α-cleavage and Promotes Membrane Accumulation of β-CTF

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Objective

Previous research reports have indicated an anti-amyloidogenic effect of Aβ antibodies in TgAPP mutant mouse model. However, the potential influences of A^β antibodies to normal un-mutated APP processing are still rarely investigated. Methods

Here, using human wild-type APP stably transfected CHO (CHO/APPwt) cells and primary cultured TgAPPwt mice cortical neuron cells, the effect of 6E10, a selective anti-N-terminal A β_{1-17} antibody, on APP metabolism was evaluated.

Results

Our data suggests that 6E10 dose-dependently inhibits APP α-cleavage as evidenced by reduced levels of α-CTF and sAPP α but with the absence of significant changes of A β production. WB analysis also revealed that 6E10 antibody notably increases cell surface APP levels and markedly increases cell surface β-CTF compared to IgG1 isotype control. In addition, 6E10 treatment does not increase cytosolic β-CTF and full-length APP levels, predicting an inhibition of APP endocytosis.

Conclusion

All these findings suggest that APP₆₇₁₋₆₈₈ region (corresponding to $A\beta_{1-17}$) is critical for normal APP processing. Modifications or blocking of this region may provide evidences for different AD pathological mechanisms and novel treatment strategies.

Research supported by: This work was supported by the NIH/NIA (JT) and a Veterans Affairs Merit Grant (JT). The authors declare no other financial conflicts of interest.

Presented by: Demian Obregon, MD, Resident

GFAP expression and social deficits in transgenic mice overexpressing human sAPPalpha

Demian F. Obregon, Antoinette R. Bailey, Huayan Hou, Min Song, Samantha Portis, Steven Barger, Doug Shytle, Saundra Stock, Takashi Mori, Paul G. Sanberg, Tanya Murphy and Jun Tan. Department of Psychiatry and Behavioral Neurosciences, Rashid Laboratory for Developmental Neurobiology, Morsani College of Medicine, University of South Florida, Tampa, FL

Keywords: Astrogliosis, autism, behavior, IL-6, Notch.

Objective: Autistic individuals display impaired social interactions and language, and restricted, stereotyped behaviors. Elevated levels of secreted amyloid precursor protein-alpha (sAPPalpha), the product of alpha-secretase cleavage of APP, are found in the plasma of some individuals with autism. The sAPPalpha protein is neurotrophic and neuroprotective and recently showed a correlation to glial differentiation in human neural stem cells (NSCs) via the IL-6 pathway.

Methods: Considering evidence of gliosis in postmortem autistic brains, we hypothesized that subsets of patients with autism would exhibit elevations in CNS sAPPalpha and mice generated to mimic this observation would display markers suggestive of gliosis and autism-like behavior.

Results: Elevations in sAPPalpha levels were observed in brains of autistic patients compared to controls. Transgenic mice engineered to overexpress human sAPPalpha (TgsAPPalpha mice) displayed hypoactivity, impaired sociability, increased brain glial fibrillary acidic protein (GFAP) expression, and altered Notch1 and IL-6 levels. NSCs isolated from TgsAPPa mice, and those derived from wild-type mice treated with sAPPalpha, displayed suppressed beta-tubulin III and elevated GFAP expression.

Conclusion: These results suggest that elevations in brain sAPPalpha levels are observed in subsets of individuals with autism and TgsAPPalpha mice display signs suggestive of gliosis and behavioral impairment.

Research supported by: Silver Endowment and NIH/NIMH; Grant number: R21MH087849.

Abstract #: 178

Presented by: Mibel Pabón, PhD, Postdoctoral Fellow

Gender-linked Differences of Stem Cell Alterations in Stroke

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Keywords: Gender, Stroke, EPCs

Objective: Stroke is a major health problem that affects both male and female, yet many preclinical studies have only tested experimental therapeutics in male stroke animals. Current statistics reveal that more women in the U.S. suffer from stroke than men and the morbidity and mortality is higher in women. Stroke affects women at a later age as compared to males, which is likely due to a decrease in hormonal levels since the incidence in female stroke victims increases at the menopausal stages. A major component of stroke pathology that has been recently recognized is the reduced capacity of stem cell regeneration, which may be subject to gender-mediated alterations. The objective of the study is to determine if there are gender disparities in endothelial progenitor cells (EPCs) after stroke.

Methods: In the in vitro analysis, cultured male and female derived EPCs were compared to each other when exposed to ambient and oxygen glucose deprivation (OGD) conditions as a model of stroke.

Results: In vitro preliminary data, demonstrated that under ambient conditions both male- and female-derived EPCs did not differ in viability, stemness, proliferation, and migration. Interestingly, when EPCs were exposed to OGD, the cultured female-derived cells showed an increased resistance to OGD, but male-derived cells displayed better proliferation and migration levels.

Conclusion: Understanding the genotypic and phenotypic differences of dimorphisms, likely to be reflected in the gender of stem cell donors, will further optimize the safety and efficacy of stem cell use for stroke.

Research supported by: USF Women's Health Collaborative Grant

Presented by: Paolina Pantcheva, MS, Med I Student

G-CSF Reduces Endothelial Progenitor Cell Injury after Delayed tPA Treatment in an in vitro Model of Oxygen-Glucose Deprivation

Paolina Pantcheva, Ike dela Peña, Sandra Acosta, Mibel Pabon, Arum Yoo, Diana Hernandez, Meaghan Staples, Cyrus Tamboli, Sharosh Tamboli, Kelsey Duncan, Diego Lozano, Marina Bastawrous, Alesia Antoine, Naoki Tajiri, Yuji Kaneko and Cesar V Borlongan University of South Florida Morsani College of Medicine, and Center of Excellence for Aging and Brain Repair, Department of Psychiatry & Behavioral Neurosciences, Tampa, FL

Keywords: GCSF, tPA, endothelial progenitor cell

Objective: Granulocyte colony-stimulating factor (G-CSF) promotes brain neurogenesis and improves functional outcome in animal models following stroke through mechanisms which influence apoptotic pathways and suppress edema formation. Tissue plasminogen activator (tPA) is currently the most effective treatment for acute ischemic stroke, but leads to edema formation and hemorrhagic transformation when given to patients beyond its therapeutic time window. Based on these observations, we hypothesized that combination of G-CSF with tPA will attenuate the risk of hemorrhagic transformation of tPA and improve the safety and impact of tPA.

Methods: An in vitro study was performed to investigate the tPA toxicity in cultured endothelial progenitor cells and to examine the effects of G-CSF on tPA-induced BBB breakdown and endothelial progenitor cell death.

Results: In vitro, G-CSF decreased oxygen-glucose deprivation-induced BBB permeability and endothelial progenitor cell injury.

Conclusion: In vitro results support the protective action of G-CSF under ischemic conditions and suggest a reduced risk of hemorrhagic transformation in vivo. Administration of G-CSF in delayed tPA treatment holds potential therapeutic value.

Research supported by: This study was supported by NIH NINDS 5R01NS071956-02 and the Scholarly Concentrations Program at USF Health, Morsani College of Medicine

Abstract #: 180

Presented by: Tam-Anh Phan, BS, Graduate Student

The Effects of Caloric Restriction on Isolated Brain Mitochondrial Function in a Transgenic P301L tau Mouse Model of Alzheimer's Disease

Tam-Anh Phan, Christian Reynes, Sandra Zivkovic, Kenyaria Noble, Milene Brownlow, Aurelie Joly Amado, Vedad Delic, David Morgan, Patrick C. Bradshaw Department of Cell Biology, Microbiology, and Molecular biology, University of South Florida College of Arts and Sciences and Byrd Alzheimer's Institute, Department of Molecular Pharmacology & Physiology, University of South Florida Morsani College of Medicine

Keywords: Alzheimer's, Tau, mitochondria, DR, CR

Objective: To determine the effects of dietary restriction on Alzheimer's model mice cortical mitochondria.

Methods: Tg4510 transgenic P301L tau Alzheimer's mice on a CR diet, sacrificed the mice at 8 months of age, and measured many facets of cerebral cortical mitochondrial function to determine if mutant tau causes mitochondrial dysfunction in this model and if CR mutes any of the effects of tau expression on mitochondrial function.

Results: Mitochondria isolated from P301L tau mice cannot achieve maximum oxidative phosphorylation. P301L tau mice have a higher membrane potential than the WT mitochondria. Additionally (data not shown)CR results in significantly decreased F0F1-ATP synthase activity. This decrease is not due to decreased amounts of ATP synthase.

Conclusion: P301L tau mitochondria were unable to obtain optimal respiratory rates in the presence of ADP. P301L tau mitochondria were able to generate and maintain a high MMP but were unable to use it effectively for ATP synthesis. Caloric restriction does not improve P301L tau-induced mitochondrial dysfunction, but does have a small positive effect on wt mitochondria. Dietary restriction decreases brain mitochondrial F0F1-ATP synthase activity but does not improve mitochondrial respiratory function in aged tau mice

Research supported by: Dr. David Morgan and the Byrd Alzheimer's Institute and Principal Investigator startup funds for Dr. Patrick Bradshaw from the University of South Florida College of Arts & Sciences, Dept of CMM Biology.

Presented by: Samantha Portis, MS, Graduate Student

The Use of the Bioflavonoid Luteolin as Therapy for Fragile X Syndrome

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Keywords: Fragile X Syndrome, bioflavonoid, glycogen synthase kinase-3, luteolin, lithium

Objective: Fragile X Syndrome (FXS) is the most common form of genetic intellectual disability and is an autism spectrum disorder (ASD). Glycogen-synthase kinase-3 (GSK-3) is a ubiquitous kinase that has been found to be over-active in murine models of FXS (fmr1 knockout mice). Recent studies have utilized lithium as a GSK-3 inhibitor in these animal models. Though lithium is an effective GSK3 inhibitor, the drug is known to have a deleterious effect on hepatic function and the endocrine system. Thus, long-term lithium administration could be highly toxic and risky therapeutic option, particularly for small children. The current study found that the bioflavonoid luteolin decreases GSK3 activity by facilitating inhibitory phosphorylation of GSK3- α at serine-21 and GSK3 β at serine-9 in mouse embryonic fibroblast cells (MEF) derived from fmr1 KO mice. In addition, luteolin treatment increased inhibitory serine-phosphorylation of both isoforms in neuroblastoma (N2a) cells. Behavior tests that assess anxiety, sociability, and learning and memory were also performed on four-month-old fmr1 knockout mice.

Methods: Mouse embryonic fibroblast cells derived from fmr1 knockout mice and wild-type mice and cultured with DMEM with 10% fetal bovine serum. Cells were plated on a coated 24-well plate and treated at various time points (0, 5, 15, 30 and 60 minutes) with 10uM luteolin. Cell lysate was collected and used for Western blot analysis. The same methods were utilized for N2a cells. The behavior tests used were open field, elevated plus maze, social interaction,Morris water maze, and fear conditioning.

Results: Results indicate that use of a bioflavonoid as a GSK3 inhibitor may prove a safer therapy for FXS.

Conclusion: Luteolin is a viable GSK-3 inhibitor.

Abstract #: 182

Presented by: Md Shahaduzzaman, MD, Faculty

Anti-α-Synuclein Antibodies Provide Neuroprotection and Reduce Behavioral Deficit In an AAV-α-Synuclein Rat Parkinson's Disease Model

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Keywords: α-Synuclein, immunotherapeutic, Parkinson 's disease

Objective: Abnormal accumulation of α -synuclein (α -Syn) plays a central role in the pathogenesis of Parkinson's disease (PD) and thus is a valuable target for developing novel therapeutics. Immunotherapies have been investigated to inhibit aggregation and enhance clearance of α -Syn; however, few approaches tested have achieved clinical endpoints for PD. Here, we have determined the effectiveness of a novel antibody from human α -Syn peptides on α -Syn-induced cell death and behavioral deficits in an AAV9- α -Syn rat model of PD.

Methods: Fisher 344 rats were randomly assigned to AAV- α -Syn-IgG (antibody control), AAV- α -Syn-AB1 (treatment1), AAV- α -Syn-AB2 (treatment2) or AAV-GFP (control) group. We injected rats with 1.5ul of either GFP 1 x 1013 vg/ml or AAV9- α -Syn 1.7 x1013 vg/ml to the right substantia nigra (SN). Beginning 1 week after AAV9- α -Syn injection, rats were treated i.p. either with IgG, AB1, or AB2 at 1mg/rat in 200 µl 1XPBS and then boosted every two weeks for three months. The blood antibody titer was monitored and cylinder test was performed monthly.

Results: An unbiased Stereological estimation of TH +, NeuN+, and OX-6 + cell revealed both antibodies prevent α -Syninduced dopaminergic cell (DA) loss (one-way ANOVA (F (3, 30) = 5.8, p= 0.002) and decrease the number of activated microglia in the ipsilateral SN (one-way ANOVA F=14.09; p = 0.0003). Antibody treated animals had lower levels of α -Syn at ipsilateral SN (one-way ANOVA F (7, 37) = 9.786; p=0.0001) and showed an intermediate improvement of behavioral deficits.

Conclusion: Taken together, our data suggested that α -Syn is a valid therapeutic target for PD, and α -Syn peptide based immunotherapy will be a potential approach to protect the DA neuron loss in PD.

Research supported by: VA MRS

Presented by: Adam Smith, PhD, Postdoctoral Fellow

Improving Lithium Therapeutics by Crystal Engineering of Novel Ionic Cocrystals

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Keywords: lithium, cocrystals, bipolar disorder, gsk-3, pharmacokinetics

Objective: Current FDA-approved lithium salts are plagued with a narrow therapeutic window. Recent attempts to find alternative drugs have identified new chemical entities but lithium's polypharmacological mechanisms for treating neuropsychiatric disorders are highly debated and are not yet matched. Thus, re-engineering current lithium solid forms in order to optimize performance represents a low cost and low risk approach to the desired therapeutic outcome.

Methods: In this contribution, we employed a crystal engineering strategy to synthesize the first ionic cocrystals (ICCs) of lithium salts with organic anions. We evaluated the efficacy of the new ICCs versus conventional lithium salts in various in vitro models. Next, we evaluated the preclinical plasma and brain pharmacokinetics of a new ICC of lithium versus lithium carbonate in rats following a single oral dose of 4meq/kg.

Results: We are unaware of any previous studies that have assessed the biological efficacy of any ICCs and encouragingly we found that the new speciation did not negatively affect established bioactivities of lithium. We also observed that lithium ICCs exhibit modulated pharmacokinetics compared to lithium carbonate.

Conclusion: Since we have attained a more attractive in vivo pharmacokinetic profile and equivalent in vitro bioactivity at key therapeutic points, it would be quite significant if we could alleviate side effects in vivo or exploit synergistic activities with these or other lithium ICCs. Indeed these findings represent an important initial step in the crystal engineering enabled development of the next generation of lithium therapeutics.

Research supported by: This work was supported by royalty research funds awarded to DS for the sublicense of a CNS drug.

Abstract #: 184

Presented by: Robert Sullivan, BS, Med II Student

Trophic Factor-Mediated Stem Cell Neuroprotection Against Kainic Acid Models of Epilepsy

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Keywords: Epilepsy, stem cell, neurotrophic factor

Objective: Epilepsy is a debilitating neurological disorder affecting more than 2 million Americans and 50 million people worldwide. 30% of epilepsy patients will have seizures refractory to standard therapeutics, highlighting the need for new, more effective treatments.

Methods: In a previous study, we found that administration of stem cell conditioned media provided significant reduction in KA-induced cell death in vitro. Similarly, in vivo transplantation of stem cells demonstrated significant reduction of KA-induced hippocampal cell loss despite low graft cell survival, suggesting a stem cell trophic factor-mediated response. In the current study we expanded upon these preliminary results by quantifying expression of neurotrophic factors BDNF, NGF, FGF-2, and GDNF in tissue harvested from several regions of the adult epileptic brain in order to evaluate their role in the neuroprotective effects of human neural stem cells (hNSCs) against KA models of epilepsy.

Results: Results revealed that BDNF, GDNF, and NGF were upregulated in human epileptic neocortex when compared to hippocampus and amygdala, while FGF-2 was downregulted in the neocortex compared to the hippocampus and amygdala.

Conclusion: Neurotrophic factors BDNF, GDNF, NGF, and FGF-2 are expressed in distinct patterns in the adult epileptic brain. These factors may contribute to the observed neuroprotective effects of hNSCs against KA models of epilepsy. Further studies in which these factors are over expressed or knocked down in KA models of epilepsy will be needed to better elucidate their contributions to neuroprotection and assess their therapeutic value.

Research supported by: Department of Neurosurgery and Brain Repair, NIH NINDS, DOD, James and Esther King Research Program, and Morsani College of Medicine Research Scholarly Concentration

Hyperbaric Oxygen Treatment and Exercise Attenuate Behavioral and Histological Deficits in Adult Rats Exposed to Experimental Traumatic Brain Injury

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Keywords: traumatic brain injury (TBI); hyperbaric oxygen therapy (HBOT); Rehabilitation exercise; neuroprotection; motor and cognitive function

Objective: The primary injury induced by traumatic brain injury (TBI) is largely unavoidable, but triggers secondary brain cell death that may be readily treatable. This proposal examined an urgent health-related issue of high military significance, which will have direct impact on treating soldiers at risk of presenting with TBI or have succumbed to TBI. Here, we evaluated their therapeutic effects in TBI either as stand-alone treatments or combination therapy.

Methods: Adult, male Sprague-Dawley rats were exposed to the TBI model of controlled cortical impact (CCI). Rats were then randomly assigned to hyperbaric oxygen therapy (HBOT) of 1.5 atmospheres absolute (ATA) for 90-minutes either as a single treatment (day 3 post-TBI) or multiple treatments (days 3, 4, and 5 post-TBI). In addition, randomly selected animals were subsequently exposed to rehabilitation therapy (RT) either as single (90-minute running wheel exercise) or multiple exposure (days 3, 4, and 5 post-TBI).

Results: Results revealed that TBI-induced histological deficits in the frontal cortex were significantly reduced in TBI animals exposed to a single HBOT and/or RT. Quantitative analyses revealed that the single exposure to HBOT with or without RT resulted in reduction of the impacted cortical damage. RT alone did not significantly reduce cortical damage. There was also a trend in protection of the peri-impact cortical area with HBOT with or without RT, but did not reach statistical significance. These histological benefits corresponded with significant amelioration of TBI-induced motor and neurological deficits in animals exposed to HBOT with or without RT.

Conclusion: These results demonstrated the efficacy of combination therapy of HBOT and RT in TBI.

Research supported by: USF Neurosurgery & Brain Repair Funds.

Abstract #: 186

Presented by: Jung A Woo, MS, Graduate Student

Coordinated Roles of Cofilin, SSH1, and b1-Integrin Engagement in Abeta Oligomer-Induced Neurotoxicity and APP processing

Jung A A. Woo¹, Hirah Khan¹, Courtney Uhlnar¹, Taylor Boggess¹, Xinmin Wang², Aurelie Jolie², George Cappos¹, Vinishaa Ankala¹, Xingyu Zhao¹, Edwin Weeber², David Morgan², and David E. Kang¹ University of South Florida Morsani College of Medicine Departments of ¹Molecular Medicine, and ²Molecular Pharmacology & Physiology, and USF Health Byrd Alzheimer's Institute

Keywords: Amyloid beta, Cofilin, b1-integrin, focal adhesion

Objective: The accumulation of Abeta is an early event associated with synaptic damage in Alzheimer's disease(AD).

Methods: Transfections Cell Surface Biotinylation Assay Immunoblotting AnnexinV/PI Apoptosis Assay Immunocytochoemistry primary culture Immunohistochemistry Stereotaxic Surgery Electrophysiology in Mouse Brain Slices Behavioral Analysis

Results: Abeta oligomers Induce the Loss of Cell Surface b1-integrin. Abeta oligomers Rapidly Disrupt Integrin-Associated Focal Complexes and Activate Cofilin. Endogenous SSH1 and Cofilin Mediate Abeta oligomer-Induced Disruption of Integrin-Associated Focal Complexes and Apoptosis. Genetic Reduction in Cofilin Mitigates Astrogliosis and Synaptic Degeneration in APP/PS1 Mice. Abeta oligomer-Induced Loss of Postsynaptic Proteins in Primary Neurons Genetic Reduction in Cofilin Rescues Deficits in Synaptic Plasticity and Contextual Fear Conditioning Associated with APP/PS1 Mice.

Conclusion: We found that Abeta oligomers rapidly induced the loss of surface b1-integrin and reorganization of Integrinassociated focal complexes, Talin and Vinculin. Allosteric b1-integrin inhibition rescued Abeta-induced disruption of focal complexes Abeta oligomer-induced disruption of Talin/Vinculin focal complexes and apoptosis required Cofilin and its activator SSH1, and genetic reduction in Cofilin rescued synaptic damage in APP/PS1 mice as well as Abeta oligomer-induced loss of dendritic spine proteins Drebrin, PSD95, and F-Actin in primary neurons. Endogenous Cofilin and SSH1 were also required for beta-secretase processing of APP and Abeta secretion and genetic reduction in Cofilin suppressed Abeta burden and rescued deficits in LTP and contextual fear conditioning in APP/PS1 mice.

Research supported by: NIH R01, AHAF, Alzheimer's Association

Neurological and Histopathological Deficits in Adult Rats Exposed to a Middle Cerebral Artery Occlusion with an Incomplete Reperfusion

<u>ARum Yoo, Sandra Acosta, Mibel Pabon, Diana Hernandez-Ontiveros, Ike dela Pena, Naoki Tajiri, Cesario V. Borlongan</u> Department of Neurosurgery & Brain Repair, University of South Florida Morsani College of Medicine, Tampa FL

Keywords: Ischemic stroke, Incomplete reperfusion, Animals, Neurological outcomes, Histopathology

Objective: Stroke is a major cause of death and even non-fatal strokes lead to significantly reduced quality of life. To date, only tissue plasminogen activator (tPA) is effective drug in stroke but with very limited therapeutic window. Exploring novel treatments for stroke is an unmet clinical need. Testing such therapeutic agents requires a clinically relevant stroke model. The middle cerebral artery (MCA) is a key vasculature supplying the brain thus a major candidate artery to induce ischemic stroke. Here, we produce an MCA occlusion (MCAo) with incomplete reperfusion to mimic stroke patients who do not benefit from the thrombolytic effects of tPA.

Methods: Adult Sprague-Dawley rats underwent MCAo surgery by inserting a nylon filament from bifurcation of the common carotid artery (CCA) and external carotid artery towards the internal carotid artery. Laser Doppler was used to reveal cerebral blood flow prior to, during the 1h occlusion, and after the filament removal. Following filament retrieval, the CCA was ligated thereby allowing only an incomplete reperfusion from the contralateral CCA. Later assessed the neurological deficits and subsequently euthanized the animals for histological evaluations of cerebral infarcts.

Results: TTC staining at 3 days after MCAo surgery revealed infarction confirmed by cerebral blood flow reduction via laser Doppler. Consequently, these brain infarcted animals displayed significant neurological deficits.

Conclusion: Our team establishes a model of focal stroke with incomplete reperfusion resembling the histopathological symptoms seen in stroke patients who do not benefit from thrombolytic therapy, which should allow testing of novel therapeutics for this specific stroke population.

Research supported by: Department of Neurosurgery and Brain Repair

Abstract #: 188 Presented by: Sandra Zivkovic, MS, Graduate Student

A Citric Acid Cycle Ester Restores Mitochondrial Function in a Cellular Model of Parkinson's Disease Sandra Zivkovic and Yumeng Zhang, Vedad Delic, Daniel Lee, Patrick Bradshaw University of South Florida, College of Arts and Sciences, Dept. of Cell Biology, Microbiology & Molecular Biology

Keywords: Parkinson's, mitochondria, alpha-synuclein, ATP, Iron

Objective: To determine the effects of citric acid cycle esters on cell models of Parkinson's disease

Methods: M17 neuroblastoma cells that over-express wild type α -synuclein (WT21), were used as a model of PD. Furthermore, the cells were subjected to high Iron environment. The initial screen was performed using Paraquat insult.

Results: citric acid cycle ester forms are able to rescue SYP levels following both paraquat insult, and Iron insult in cells over expressing alpha synuclein.

Conclusion: combination of an iron-rich environment (amplification of oxidative stress via the Fenton reaction), older age (increased oxidative stress) and genetic and environmental factors leading to increased α-synuclein levels lead to mitochondrial deficits in dopaminergic neurons, eventually leading to neuronal cell death in the substantia nigra. Our data also suggest that CACE supplementation may enhance mitochondrial function and rescues neural cells from PD phenotypes, likely by entering through passive diffusion, being hydrolyzed by cellular esterases, and subsequently being shunted into the TCA cycle to enhance mitochondrial function and cellular metabolism deficient in PD.

Research supported by: This study was supported by the University of South Florida (College of Arts & Sciences, CMM Biology Department) principal investigator startup funds awarded to Dr. Patrick Bradshaw.

Presented by: Jerrica Farias, BS, Graduate Student

Analysis of Alert Programs for Missing Persons with Dementia

<u>Jerrica Farias¹, Glenna Brewster¹, Meredeth Rowe¹, Eric Reinhardt², Lisa Brown³, Lawrence Schonfeld⁴, Claire Duval⁵, Stephen Arnold¹ ¹University of South Florida College of Nursing; ²Carolinas Healthcare System; ³USF College of Behavioral and Community Sciences, School of Aging Studies; ⁴USF College of Behavioral and Community Sciences; ⁵USF Health Memory Disorders Clinic</u>

Keywords: dementia, missing incidents, Silver Alert

Objective: To analyze state missing persons alerts (MPA) used for missing persons with dementia (MPWD) while comparing dementia-specific alerts (DSA) to non-dementia specific alerts (NDSA).

Methods: Data was collected regarding alert eligibility requirements, activation protocols, and responses from government websites, state legislation, and alert representatives.

Results: Forty-four MPA have been implemented or approved by legislation; 17 are DSA (38.6%) and only two (4.5%) are model Silver Alert (SA) programs without additional age or endangerment requirements. Consistent with expert recommendations, no MPA requires a waiting period. Active LE notifications are used in more NDSA (51.8%; n=14) than DSA (41.1%; n=7). Although immediate statewide LE notification occurs in 41.1% of DSA (n=7), alerts should be regional for driving MPWD, local for MPWD on foot, and disseminated to progressively distant LE agencies as duration of the missing incident increases. This strategy is used in seven NDSA (25.9%) and seven DSA (41.1%). Public notifications include use of media broadcast (NDSA 96.3%, n=26; 88.2%, n=15 DSA), electronic highway signs (NSDA 37.0%, n=10; DSA 64.7%, n=11), and local citizen telephone alerts (NDSA 14.8%, n=4; 41.1%, n=7 DSA).

Conclusion: Alert eligibility and response is highly variable, even in SA states. As few states maintain data for analysis of alert efficacy, an expert committee should design a national SA protocol with uniform eligibility and response requirements to specifically improve outcomes for MPWD.

Research supported by: SAFEROAD Project Department of Justice Award #2012-SJ-BX-K001.

Abstract #: 190	Presented by: Ellen Marcolongo, MS,
	Graduate Student

The Relationships Between Sleep Disturbances, Depression, and Inflammatory Markers in Female Veterans <u>Ellen Marcolongo, PhD</u>, University of South Florida, College of Nursing

Keywords: Sexual assault, Sexual harassment, Pittsburgh Sleep Quality Index, Center for Epidemiologic Studies Depression Scale, Inflammatory Markers

Objective: The purpose of this poster presentation will be to display the results of a secondary data analysis examining data collected for a study conducted by the College of Nursing Women's Health Research group entitled Empowering Female Veterans. The purpose of the parent study was to conduct an investigation of bio-behavioral health in female veterans. The purpose of the secondary data analysis was to explored relationships among sleep disturbances, depressive symptoms, inflammatory markers, and sexual trauma frequency in female veterans.

Methods: Spearman Rho correlational analyses were conducted to assess the strength of relationships among sleep disturbances, depressive symptoms, inflammatory markers, and sexual trauma frequency in female veterans.

Results: Reports of more frequent sexual harassment was correlated with longer sleep latency, poorer daytime functioning, and poorer overall total sleep quality. These reports were also correlated with a depressed affect and more anhedonia episodes. Frequent reports of more sexual assault (rape or attempted rape) were correlated with increased anhedonia, an increased likelihood of a depressed affect and with an increased overall total depression score. Frequent episodes of sexual harassment and/or frequent sexual assault were not correlated with C-reactive protein and/or interleukin-6 levels.

Conclusion: In conclusion, female veterans who were victims of frequent sexual trauma episodes had more sleep disturbances and had increased depressive symptoms. Disturbed sleep and increased depressive symptoms may contribute to future costly health problems.

Presented by: Sammy Alnajm, MS, Graduate Student

Pathway Analysis of Smoking Effects on Human Lung Gene Expression

Sammy S. Alnajm^{1,} Yan Xu², Diane Allen Gibson², Feng Cheng^{2,3},* University of South Florida College of Pharmacy, Department of Pharmaceutical Sciences

Keywords: Lung, COPD, Smoking, Microarray, Pathway.

Objective: Precise detection of changes in gene pathways between smokers and non-smokers is crucial to the understanding of the molecular and cellular mechanisms of tobacco smoke induced COPD and lung cancer and in finding effective drug targets against these diseases.

Methods: Four published microarray sets from the NCBI Gene Expression Omnibus (GEO) repository were integrated in the study to compare gene expression in alveolar macrophage, small airways epithelial cells, large airways epithelial cells, and trachea epithelial cells of smokers and non-smokers. Differentially expressed (DEX) genes were identified by SAM package in R (http://www.r-project.org/). The DEX genes identified by SAM were submitted to the NIH DAVID database to find smoking-related pathways in each cell type.

Results: Gap junction is one of cell junction's pathways that are regulated in smoking at the trachea epithelium. Tight junction is one of the cell junction's pathways that is regulated by smoking at the alveolar macrophage, trachea epithelium, and large airway epithelium. Macrophages can release cytokines and chemokines to call for a highly developed network of defensive cells. Alveolar macrophage are also involved in the phagocytosis of apoptotic and necrotic cells that have undergone cell-death.

Conclusion: Integration of this information will provide the basis for understanding the molecular mechanisms involved in the observed difference susceptibility to develop lung disease.

Research supported by: University of South Florida College of Pharmacy research start-up grant.

Abstract #: 192

Presented by: Chuanhai Cao, PhD, Graduate Student

TCR clonality in T Cell Subpopulation as Biomarker to Differentiate AD and PD

<u>Chuanhai Cao¹, Xiaoyang Lin¹, Ge Bai², Guixin Zhang³, Juan Sanchez-Ramos⁴, Jianfeng Cai², ¹University of South Florida College of Pharmacy, Dept. of Pharmaceutical Sciences, ²USF College of Arts and Sciences, Dept. of Chemistry, ³Dalian Medical University, China ⁴USF Morsani College of Medicine</u>

Keywords: T cell receptor, Alzheimer's disease, Parkinson's disease, alpha synuclein, amyloid beta, biomarker

Objective: This research is to study the role of immune system in neurodegenerative diseases and find the novel biomarker in PD and AD, and a method can differentiate AD/PD patient.

Methods: This report is the first comprehensive investigation into T-cell receptor (TCR) changes in PD and AD patients using RT-PCR assay for the TCR V β chain CDR3 region that covers the entire TCR V β family. Clonning and sequencing assay are used for clonality confirmation.

Results: The results from clinical patients show that there is significant loss of TCR V β diversity in CD4+ T cells and CD8+ T cells of PD patients and a specific clonality change in CD8+ T cell in AD. Additionally, the pattern of V β clonality in CD8+ cells of PD patients was found to be quite different from those of AD patients. Cloning and sequencing of single bands of the CD4+ V β chain of PD patient resulted in identical sequences and proved to be true monoclonal of TCR, but different sequences in CD8+ (oligoclonality). However, we discovered true clonality in CD8+ T instead of CD4+ T cell cells of AD with a disease dependent manner from AD subjects. Our result implies that T cell epitope in A β peptide may involve in AD development and alpha synuclein is related to PD. It also implies that TCR clonality may be an early and reliable biomarker candidate for PD and AD.

Conclusion: Since CD4 clonality only occurred in PD and CD8 TCR clonality happened in AD. The clonality is accordingly response to the protein stimulation when the peptides are used in vitro test. Our result indicated that TCR clonality can differentiate PD from and may be an important marker to identify AD/PD patient clinically.

Research supported by: MJFF and FADRC

Sex Difference in the Brain of Patients with Down's Syndrome

Feng Cheng and Shu-Feng Zhou Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: Sex difference brain Down's syndrome

Objective: Down's syndrome (DS) is caused by the presence of an extra copy of chromosome 21. It was estimated by the Centers for Disease Control and Prevention (CDC) that the prevalence of DS was around 12 per 10,000 live births in the United States in 2003. Many DS patients develop dementia in their late 40s or early 50s. Sex differences in DS patients in intellectual disability were revealed by some previous studies. Lai et al. found that women with DS were about twice as likely to develop dementia as men with DS. Female DS patients also had an earlier onset of dementia than males. However, the mechanism for this sex effect is unclear.

Methods: In this paper, we analyzed expression microarray data of human adult brain dorsolateral prefrontal cortex tissue from female and male DS patients (NCBI GEO data set: GSE5390).

Results: Differentially expressed (DEX) genes between female and male DS groups were identified. Gene ontology enrichment analysis of these DEX genes shows that myelination (including KLK6, CD9, C11ORF9, PLLP, MAL, & MBP), AXON (NCAM1, SEMA6A, PSEN1, SYNJ2, CA2, AQP1, NEFL, NEFM, & MBP) and neuron projection (NCAM1, SYT1, SEMA6A, PSEN1, SYNJ2, CA2, TTLL7, AQP1, KCNJ2, NEFL, NEFM, & MBP) pathways are highly expressed in male DS brain tissue. Myelin is a fatty sheath that coats and protects nerve axons, and the loss or downgrade of myelin will cause dementia and other cognitive disabilities.

Conclusion: We have identified the sex difference in the transcriptome of DS patients' brains. These differences were not observed in normal human brains from the same data set. Our analysis revealed several features of the human DS brain transcriptome, and increased our understanding of the pathogenesis of this disease.

Research supported by: USF College of Pharmacy start-up grant

Abstract #: 194

Presented by: Jiang Cheng, MD, Faculty

Polymer Micelle-encapsulated Mutant Aβ fragment as Alzheimer's Disease Vaccine Targeting Oligomeric Aβ <u>Jiang Cheng ^{1,2},' Ningkui Niu ^{1,2}, Chuanhai Cao ¹, and Shu-Feng Zhou ¹</u> ¹Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tamla, FL, ²Department of Neurology, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, China

Keywords: Alzheimer's disease; β-Amyloid; Vaccine; efficacy; Safety.

Objective: Alzheimer's disease (AD) has a high disability rate and has no effective drugs now. Though FDA suspended the famous Elan's AN-1792 amyloid beta (A β) vaccine in phase IIb clinical trials because 6% participants suffered from severe meningoencephalitis, participants who continued to be followed showed a slower decrease in cognition, and the autopsy from one participant suggested that the treatment was successful in brain A β 1-42 clearance. We consider that a potent T cell epitope in Elan's A β vaccine is likely the main reason of the severe side effect. In this study, we have designed the polymer micelle-encapsulated mutant A β fragment as AD vaccine and then evaluated its efficacy and safety in vitro and mouse models.

Methods: The polymer micelles encapsulated A β 1-35 peptide and then chemically characterized and structures confirmed. The micelles encapsulated with A β 1-35 peptide were used to sensitize mouse dentritic cells (DCs) in vitro. Sensitized DCs will be administered to APP/PS1 mice via intraperitoneal injection. The efficacy and safety will be monitored in mice.

Results: The polymer micelles with encapsulation of A β 1-35 peptide have been successfully synthesized and chemically examined. In mouse DCs, the polymer micelles with encapsulation of A β 1-35 peptide showed low cytotoxicity and no adjuvant effect was observed. The polymer micelles with A β 1-35 peptide induced a conformational specific anti-A β antibody response in mouse DCs. The micelles with A β 1-35 peptide will be evaluated in mouse model to test its efficacy and safety.

Conclusion: The newly synthesized polymer micelles encapsulated with A β 1-35 appear to specifically target oligomeric A β , so it may be a promising vaccine candidate for AD treatment.

Presented by: Kevin Chow, High School Student

Prediction of microRNAs That May Regulate Human Cytochrome P450 Genes

Kevin Chow^{1,2}, Jun Liang², and Shu-Feng Zhou² ¹Freedom High School, Tampa, FL; ²Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: CYP, miRNA, gene.

Objective: miRNAs are involved in the regulation of a number of genes that are involved in development, cell proliferation and apoptosis, and carcinogenesis. There are limited data on how miRNAs regulate drug disposition in humans. This study investigated the miRNAs that probably regulated human CYP genes using a bioinformatic approach.

Methods: TargetScan was used to predict the miRNAs that probably regulated CYP genes.

Results: Among 57 functional human CYP genes, miRNAs regulating each of them were predicted by TargetScan, PicTar, EMBL, EIMMo, Miranda, miRBase Targets, PITA TOP, and mirWIP programs. Among all programs used, only TargetScan gave a comprehensive prediction. Among the 55 predictable CYP genes (no prediction data for CYP2C19 and 26C1), a total of 5,880 matching sites were found, with 106.9 sites for each gene. A total of 787 miRNAs were involved in the regulation of these 55 genes, with 647 (82.2%) miRNA being poorly conserved and 140 (17.8%) being conserved. Each CYP gene was regulated by 14.3 miRNAs. The TargetScan program predicted that CYP1A2, 2A6, 2B6, 2C9, 2C19, 2D6, 2E1, and 3A4 were regulated by 72, 18, 126, 34, 69, 4, 10, and 110 miRNAs, respectively. Conserved miRNAs included miR-16, miR-17, miR-141, miR-1324, let-7a, etc, while examples of poorly conserved ones are miR-100, miR-105, and miR-1178. A single miRNA may regulate different CYP genes.

Conclusion: (1) A small number of the miRNAs that were predicted to regulate human CYP genes have been confirmed by benchmarking studies. These studies provide initial insights into how CYPs genes are regulated by miRNAs.

Abstract #: 196

Presented by: Kevin Cowart, BS, Graduate Student

Using the Multiple-Mini-Interview (MMI) as a Tool to Predict Success in Pharmacy School Kevin Cowart, B.S., Pharm.D. Candidate, Kamila Dell, Pharm.D., BCPS, LaShonda Coulbertson, M.P.H. University of South Florida College of Pharmacy Dept. of Pharmacotherapeutics & Clinical Research

Keywords: multiple mini interviews, pharmacy admissions, grade point average

Objective: To investigate if a student's multiple-mini-interview (MMI) score correlates with grade point average across the didactic years 1-3 in the doctor of pharmacy curriculum.

Methods: We will evaluate MMI scores and overall grade point average across years 1-3 in the doctor of pharmacy curriculum for the first three cohorts of students in the college of pharmacy. SPSS version 20 will be used for statistical analysis and to calculate a pearson correlation coefficient.

Results: We predict that MMI scores will positively correlate to grade point average across all three didactic years in the doctor of pharmacy curriculum. Traditionally, the MMI has been used more in medical school admissions but research has shown that many pharmacy schools are replacing the traditional interview process with the MMI due to its validity and its ability to assess emotional intelligence in applicants.

Conclusion: As the role of the pharmacist changes, the admissions process for pharmacy schools must remain robust in an attempt to assess not only grade point average and PCAT scores. The MMI is a validated tool to assess emotional intelligence and many soft skills needed by pharmacists. Using the MMI in the pharmacy school admissions process is a new trend that is becoming more prevalent and a positive correlation with grade point average may provide a stronger indicator of success in pharmacy school.

Presented by: Danielle Dantuma, BS, Graduate Student

Metformin and Atorvastatin Combination Utilized for Improved Drug Delivery for Patient Compliance.

Danielle Dantuma¹, Vijay K. Sutariya², Ana Groshev¹, Vaibhav Alandikar¹, Matt Greene², Brian McMillan², Todd Daviau², <u>Yashwant V. Pathak¹, Srinivas M. Tipparaju¹</u> ¹Department of Pharmaceutical Sciences, USF College of Pharmacy, Tampa, FL, ²CoreRx, Inc. Myerlake Circle, Clearwater, FL

Keywords: metformin, atorvastatin, anti-diabetic, anti-cholesterol, CoreRX

Objective: Anti-diabetic and anti-cholesterol medications are among the top prescription medications in US. Based on earlier surveys, majority of the treatment outcomes in the disease areas are poor because of patient non-compliance and drug therapy errors. Metformin and atorvastatin can be taken at same time before meal, therefore, the goal is to reposition these drugs as a combination therapy, in a single tablet.

Methods: Combination tablet was manufactured using CoreRx, Pharmaceutical Industry R&D tablet blending and tablet press. Unit processing was performed and six batches of tablets designed with API's and excipients. Tablets were made by direct blend and compression technique using ½ inch standard concave tooling at compression force of 15kN, tooling geometry, compression force, testing methods per current USP guidelines. Tablets were evaluated for friability, disintegration time, dissolution time, hardness, weight variation, and physical dimensions, according to standard guidelines.

Results: Weight, diameter and thickness variations were within USP range (less than 5% RSD). Hardness of all the batches ranged between 3.8 to 4.7 kP. Friability studies were performed at 50 rpm for one minute. The Disintegration time was ranged from 6 to 14 seconds. The dissolution studies showed that 95% drug was released in five minutes.

Conclusion: The data revealed that the formulation characteristics are consistent with the release of the API from the combination tablet. Therefore, this combination can be pharmaceutically utilized for its enhanced use and repositioned for improved patient outcomes with improved patient compliance and efficacy.

Research supported by: USF College of Pharmacy and CoreRX

Abstract #: 198

Presented by: Kamila Dell, PharmD, Faculty

Evaluating Exam Question Writing Practices in a Pharmacotherapeutics Series at a New College of Pharmacy <u>Kamila Dell PharmD BCPS, Gwendolyn Wantuch PharmD BCPS</u> USF College of Pharmacy University of South Florida College of Pharmacy, Dept. of Pharmacotherapeutics & Clinical Research

Keywords: exam question, multiple choice questions, assessment, exam question writing best practices

Objective: 1.Evaluate pharmacotherapeutics exam questions in relation to our best practice guidelines at a new college of pharmacy. 2.Identify the most common faults in exam question writing in a pharmacotherapeutics course.

Methods: A literature search was performed regarding exam question writing guidelines. Our search yielded no consensus guidelines that currently exist regarding this topic. Therefore, we utilized recommendations published by individual institutions to establish a list of thirteen best practices to assess our faculty's exam question writing technique. Two pharmacy practice faculty evaluated exam and quiz questions independently from two pharmacotherapeutics courses. Descriptive statistics were performed on collected data.

Results: A quantity of 628 multiple choice and true/false questions were analyzed against our best practices list. A total of 468 questions, 74.5%, had at least one best practice violation. Therefore, only 25.5% of questions met all best practices. The most common deviation was grammar, punctuation, or spelling (23.6%). Other issues included: stem did not include all and only the information necessary to identify the correct answer (20.5%), stem or answer choices included logical cues (14.3%), and answer options were not similar in verb tense and length (12.8%).

Conclusion: We determined exam question writing technique requires improvement at our new college of pharmacy. Formal training in best practices will be implemented and evaluation of exam questions after the training will occur to benchmark progress.

Presented by: Yonghui Ding, MD, Faculty

Role of the Aurora Kinase A inhibitor, Alisertib, in the Treatment of Ovarian Cancer

<u>Yonghui Ding^{1,2}, Chunxiu Yuan^{1,2}. and Shu-Feng Zhou^{1*}</u> ¹University of South Florida College of Pharmacy, Dept. of Pharmaceutical Sciences, ²Ningxia Medical University

Keywords: ovarian cancer; Aurora A kinase; alisertib; apoptosis; autophagy; EMT.

Objective: Epithelial ovarian cancer (EOC) responds poorly to current chemotherapeutic agents. Frequent Aurora kinase A (AAK, encoded by AURKA) gene amplification and protein overexpression have been observed in many types of cancer. Alisertib (MLN8237) is an investigational small molecule kinase inhibitor that has demonstrated the ability to selectively inhibit AAK and thereby disrupt spindle assembly and induce cell cycle arrest, aneuploidy, polyploidy, mitotic catastrophe, and cell death. The objective of the current study was to determent the therapeutic potential of alisertib (MLN8237) in EOC.

Methods: SKOV-3, OVCAR-3, OVCAR-4, and OVCAR-5 cells were used in this study. After treatment with alisertib, cell survival, cell cycle, programed cell death, EMT, invasion and migration were examined using MTT assay, flow cytometry, Western blotting, and confocal microscopy.

Results: Alisertib inhibited the growth of the cells tested. Treatment of SKOV-3, OVCAR-3, OVCAR-4, and OVCAR-5 cells with alisertib caused G2/M arrest and programed cell death.

Conclusion: Aurora A represent a promising target for the therapy of ovarian cancer. Additional experiments are ongoing to check the anticancer activities of Aur-A inhibitors in the treatment of ovarian cancer in vitro and in vivo.

Abstract #: 200

Presented by: Jendayi Dixon, BS, Staff

Characterization of H358, Non-small Lung Cell Carcinoma using the Electric Cell-substrate Impedance Sensing (ECIS®)

<u>Jendayi Dixon, B.S., Vrushalee Palsule, M.S., Diane Allen-Gipson, Ph.D</u> University of South Florida College of Pharmacy, Dept. of Pharmaceutical Sciences

Keywords: H358 Lung Cancer ECIS

Objective: The single most important risk factor for lung cancer development is smoking, it is estimated that 85-90% of lung cancer is due to cigarette smoking, with 85% of lung cancers being non-small cell lung cancer(NSCLC). Three subtypes exist, squamous, adenocarcinoma (reclassified as bronchioloalveolar) and large cell carcinoma. In spite of the vast improvements made to treatment of NSCLC, its 5 year survival rate continues to remain dismal (12-15%) with the biggest problem being the frequent histologic heterogeneity. To gain a better understanding on the cellular behavior of NSCLC, our lab employed the Electric Cell-substrate Impedance Sensing (ECIS®). The ECIS was used to study the NSCLC cell line H358 (classified as bronchioloalveolar) to characterize its cellular behavior including adhesion, spreading, migration, proliferation and metastasis.

Methods: H358 were inoculated on arrays with a low cell density. For our invasion studies, we employed the H358 cell line and Nuli-1 cells, a human bronchial epithelial cell line, to characterize the metastatic potential of NSCLC. Nuli-1 cells were grown to confluency on arrays and then H358 cells were inoculated to observe their invasive properties.

Results: We observed as the cell number increased, the amount of electrode area covered with the spreading of the cells grown caused the electrode impedance in Ohms or nanofarads (C) verses time.

Conclusion: Collectively, the ECIS® approach is useful in characterizing the invasive nature of cancer cells and provides the mechanisms to better understand the cellular behavior of NSCLC which may be useful in targeting new drug therapies associated with the highly heterogeneity adenocarcinomas.

Research supported by: Supported by the College of Pharmacy Dean's Clinical and Research Award (DAG)

Targeting Na+/K+ ATPase in the Treatment of Prostate Cancer

<u>Cameron Durlacher, Shu-feng Zhou, Zhiwei Zhou</u>, Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: Na+/K+,-ATPase, digoxin, digitoxin, prostate cancer

Objective: Previous studies have shown that Na+/K+ ATPase is overexpressed in many types of cancer. We hypothesize that Na+/K+ ATPase is a potential therapeutic target in prostate cancer therapy.

Methods: PC-3, DU145, LNCAP and VCAP prostate cancer cells are used. The effect of modulation of Na+/K+ ATPase by pharmacological and biological methods on cell cycle, apoptosis, autophagy, invasion & migration, and epithelial-tomesenchymal transition (EMT) was determined using flow cytometry, Western blotting and confocal microscopy. The underlying mechanisms will be examined. Nude mice bearing human prostate cancer xenografts will be used in the tumor growth inhibition and mechanistic studies.

Results: Both digoxin and digitoxin inhibited the proliferation of PC-3 and DU145 cells. The IC50 values for digoxin and digitoxin were 8.1 and 4.3 µM for 24 hr, respectively, and increased to 2.1–2.6 µM when treated for 48 hr. At low levels of each drug, digoxin and digitoxin increased the activity of beclin-1 and LC3 to promote autophagy. Higher levels of both drugs suppressed the expression of the two proteins as well as Bcl-2 and Bcl-xL while the expression of cleaved PARP was increased to promote apoptosis. In addition, digoxin and digitoxin suppressed the phosphorylation of Akt at Ser473 and mTOR at Ser2448, contributing to their autophagy inducing effect.

Conclusion: Chemical inhibition of Na+/K+ ATPase results in inhibition of the growth of PC-3 and DU145 cells and induces programed cell death. Further experiments are ongoing to test our hypothesis that Na+/K+ ATPase is a promising target for prostate cancer treatment.

Abstract #: 202

Presented by: Rania Elmaddawi, BS, Graduate Student

Microgravity Research and Personalized Medicine: A New Challenge to Pharmacists

Rania Elmaddawi¹, Danielle Dantuma¹, Marlise Santos², and Yashwant Pathak¹ ¹Department of Pharmaceutical Sciences, USF College of Pharmacy, Tampa, FL ²Joan Vernikos Aerospace Pharmacy Lab, Pontifical Catholic University of Rio Grande do Sul School of Pharmacy, Rio Grande do Sul, Brazil

Keywords: microgravity, NASA, immunology, genomic medicine

Objective: Most of the contemporary scientific theories and physical phenomena to our experience are all related to earth gravity environment. But just how much gravity is needed to have normal function? Preparation for long –duration (in excess of 1 year) explorations in space will require much research and preparation to ensure that the immune system functions normally throughout the entire mission. Thus there is great emphasis on personalized medicine approach to maintain crew health during the mission. The main objective of the current research review is to study the existing literature on space cell biology to highlight the relationship between gravity and biological responses.

Methods: Review of existing NASA summary reports on Microgravity cell biology research in the space shuttle era and recent published articles on microgravity analog culture systems was conducted to extract an answer to the posed question.

Results: Biomedical researchers rely on cell-based research in a microgravity environment to investigate fundamental life processes, diseases and the effects of drugs. The mathematical basis of the relationship of gravity to biologic function cannot be easily extracted and remains unknown. For levels below 1/10g, immune cells known as lymphocytes have diminished locomotion. Results showed that locomotion was inhibited by more than 80%. If the diminished locomotion is sustained it can contribute to a decline in immune function in space.

Conclusion: If personalized medicine is key to maintain crew health in space, then it will be critical for scientist to keep the microgravity research ongoing to further understand the biological response levels. For pharmacists, this fundamental research is critical in contributing to personalized genomic medicine.

Presented by: Xiaofang Guo, PhD, Postdoctoral Fellow

Development of Acquired Sorafenib Resistance in an In Vivo Model for Human Lung Cancer

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Keywords: Sorafenib, Acquired Resistance, Human Lung Cancer

Objective: Acquired drug resistance is a major obstacle to successful cancer treatment. Historically, studies of acquired resistance have involved the development of a resistant cell line in vitro after exposure to escalating drug concentrations. How well the in vitro model assisting in elucidating the mechanisms of phenotypic drug resistance in vivo remains uncertain. As part of our ongoing effort to examine the underlying mechanisms of acquired resistance to sorafenib in human non-small cell lung cancer (NSCLC), the present study compared the phenotypic resistance patterns of sorafenib-resistant clones of the A549 human NSCLC cell line developed both in vitro and in vivo.

Methods: The in vitro model of acquired resistance to sorafenib was developed by continuous exposure to stepwise increasing concentrations of the drug, while the in vivo model was established by once daily oral administration of 40 mg/kg of sorafenib to athymic nude mice bearing A549 xenografts for 16 weeks.

Results: In terms of the magnitude of resistance determined by the in vitro cytotoxicity assay, the sorafenib-resistant A549 clone selected in vitro exhibited at least 1-fold increase in the mean IC50 value as compared with the A549 parental cells, whereas the sorafenib IC50 values for the in vivo generated sorafenib-resistant lines was about 35% higher than that for their parent line. Nonetheless, the in vivo generated resistant cells demonstrated enhanced invasiveness as measured by transendothelial electrical resistance as well as persistent growth under sorafenib treatment after reinoculation.

Conclusion: The in vivo model of sorafenib resistance was successfully generated and ready to be used to further explore the resistance mechanisms acquired in a therapeutic setting.

Abstract #: 204

Presented by: Hai Li, MD, Faculty

Treatment of Human Colorectal Cancer by Na+/K+ ATPase Inhibitors

<u>Hai Li^{1,2}, Feng Wang^{1,2}, Zhi-Wei Zhou², Chunxiu Yuan^{2,3}, & Shu-Feng Zhou²</u> ¹Department of General Surgery, Ningxia Medical University General Hospital, Yinchuan, Ningxia, China, ²Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL, ³Department of Oncology, Ningxia Medical University General Hospital, Yinchuan, Ningxia, China

Keywords: by Na+/K+ ATPase inhibitor,human colorectal cancer,treatment

Objective: Colorectal cancer is a leading killer of human beings worldwide. Currently available chemotherapeutic agents for the treatment of advanced colorectal cancer have limitations of tumor resistance and severe adverse reactions. Overexpression of Na+/K+ ATPase is often observed in colorectal cancer. This study aimed to investigate whether inhibition of this pump affects the growth, death, invasion and metastasis of colorectal cancer cells

Methods: The human colorectal cancer HT29 and SW620 cells were used. The MTT assay was used to check cell viability. Cell cycle, apoptosis and autophagy were determined by flow cytometry. The levels of proteins were determined by Western blotting analysis

Results: Digoxin and digitoxin inhibited the proliferation of both cell lines. The IC50 values for digoxin and digitoxin were 0.30 and 1.50 μ M in HT cells, and 1.68 and 1.13 μ M in SW620 cells, respectively, when cells were treated with the drug for 24 hr. Digoxin arrested the cells in G2/M for HT29 cells, but digitoxin did not affect the cell cycle distribution

Conclusion: Na+/K+ ATPase may represent a new therapeutic target for the treatment of colorectal cancer. Experiments are ongoing at our laboratory to examine the anticancer activities and underlying mechanisms of Na+/K+ ATPase inhibitors in colorectal cancer

Presented by: Hui Li, MD, Faculty

Brain microRNA Profiling in Spontaneously Hypertensive Rats

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Keywords: microRNA; Brain; Essential hypertension; miR-193; Junctional Adhesion Molecute-1.

Objective: Essential hypertension is the most important risk factor for cardiovascular diseases and remains a global public health challenge. Recent studies have showed that microRNAs (miRNAs) are involved in the regulation of vascular endothelial function and pathogenesis in hypertension. However, little is known about the roles of brain miRNAs in essential hypertension.

Methods: miRNA microarray was performed to compare the miRNA expression profiles in medulla samples from spontaneously hypertensive rats and normal control rats. The predicted target proteins of miRNAs and their enriched signaling pathways were analyzed using bioinformatics methods. The expressions of selected miRNAswere validated independently by qRT-PCR.

Results: we discovered that 23 miRNAs were significantly altered in hypertensive rats compared to the control rats. Among them, 7 miRNAs were down-regulated. Bioinformatics analysis indicated that these miRNAs' targets might be mainly enriched in leukocyte transendothelial migration, MAPK signaling pathway and calcium signaling pathway. Further qRT-PCR assay confirmed 2 down-regulated and 3 up-regulated miRNAs (miR-193, miR-653, miR-153, miR-3585-5p, & miR-742) between hypertensive and normal rats. The target identification of miR-193 are ongoing at our laboratory.

Conclusion: These results have suggested an important role of brain miRNAs in the pathogenesis of hypertension and these miRNAs may represent novel biomarkers and potential therapeutic targets for hypertension.

Research supported by: This project were supported by Natural Science Foundation of Guangdong Province (grant no. S2013010011547), National Natural Science Foundation of China (grant no. 81173349) and University of South Florida College of Pharmacy Startup Fund.

Abstract #: 206

Presented by: Jinping Li, PhD, Faculty

Inhibition of Mitotic Aurora A Kinase in the Treatment of Breast Cancer

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Keywords: breast cancer; Aurora A kinase; alisertib; danusertib; tandutinib; apoptosis; autophagy; EMT

Objective: The mitotic kinase Aurora-A (Aur-A) is a master regulator of centrosome segregation and spindle assemble and abnormal Aur-A expression and mutations are frequently observed in various types of cancer. This contributes to the initiation, growth, invasion, and metastasis of breast cancer. In this study, we will investigate the anticancer activities of Aur-A inhibitors in the therapy of breast cancer and the underlying mechanisms.

Methods: MCF10A, MCF7, MDA-MB-231, BT-474, and SK-BR-3 cells were used in this study. The cell proliferation, cell cycle, apoptosis, autophagy, invasion and migration, and EMT markers were determined using MTT assay, flow cytometry, Western blotting analysis, and confocal microscopy.

Results: Aur-A inhibitors inhibited the proliferation of breast cancer cells. Treatment of MCF7, MDA-MB-231, BT-474, and SK-BR-3 cells with danusertib, alisertib and tandutinib (an FLT3 inhibitor) caused G2/M arrest and programed cell death.

Conclusion: Aurora A may be a useful target for the therapy of breast cancer. Additional experiments are ongoing to check the anticancer activities of Aur-A inhibitors in the treatment of breast cancer in vitro and in vivo.

Role of MicroRNA-21 in the Immune Response and Programed Cell Death of Human Lung Epithelial Cells Exposed to Particulate Matters

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Keywords: particulate matter; miR-21; lung epithelial cells; programed cell death; cytokine

Objective: A number of epidemiological and clinical studies have proved that exposure to inhalable air particles is predominantly attributable to the occurrence of respiratory diseases. However, the exact mechanisms for lung injury due to exposure to air particulate matters are not yet fully understood. This study aimed to investigate the role of miRNA-21 in the immune response and programed cell death to PM-exposed human lung epithelial cells.

Methods: Human lung epithelial BEAS-2B cells were used to investigate the biological effects and miRNA-21 expression induced by PMs. The cell viability was determined by the MTT assay. Apoptosis and autophagy were assessed using Western blotting, and ROS level determined. The levels of cytokines and miRNA-21 were determined using RT-PCR.

Results: PMs induced cell death with strong oxidative stress response. The ROS was increased in a time- and dosedependent manner. PMs up-regulated the expression of pro-apoptotic proteins (Bax & Bad) and down-regulated the antiapoptotic proteins (Bcl-2 & Bcl-xI), resulting in caspase 9 and caspase 3 activation and finally cell apoptosis. In the meantime, cellular autophagy was confirmed by confocal microscopy as indicated by LC-3 and berclin-1 expression. The expression of IL-1 β , II-6, IL-8, and TNF- α were induced with PMs with p38 MAPK and NF-kB signal pathway activation. miR-21 was significantly up-regulated by PMs over 24 hr.

Conclusion: PMs can induce apoptosis, autophagy and inflammation in human lung epithelial cells and miR-21 might play a role in these processes. Further studies with loss/gain of function of miR-21 will be performed to study the role of miR-21 in PM-induced respiratory epithelial injuries.

Abstract #: 208

Presented by: Minghua Li , PhD, Postdoctoral Fellow

MiR-299 Suppresses the Growth of Ovarian Cancer Cells Through Targeting the CA-125 (MUC16) Gene <u>Minghua Li, Shu-Feng Zhou</u>, Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: ovarian cancer; miR-299; CA-125 (MUC16); cell growth; cell adhesion.

Objective: The serum level of CA-125(Muc16) is the most frequently used biomarker for ovarian cancer detection, but its role in the initiation, growth, invasion and migration of ovarian cancer is unknown. In the current study, we investigated the role of miRNA-299 (miR-299) in the regulation of CA-125 and whether this would alter ovarian cancer cell viability.

Methods: Human epithelial ovarian cancer cell lines SKOV3, OVCAR-3, and SW626 were used. Gain-of-function and loss-of-function assays were conducted

Results: Bioinformatics analysis showed that the CA-125 gene is a likely target of miR-299. We found that the relative expression level of miR-299 in CA-125 positive OVCAR-3 cells was significantly lower than that in CA-125 negative SKOV3 and SW626 cells. Treatment of the cells with a miR-299 mimic significantly inhibited the CA-125 3'-UTR reporter gene activity, CA-125 mRNA and protein levels compared with the vector controls. We also analyzed the cellular effects linked to oncogenesis in terms of cell proliferation, cell cycle and apoptosis after transfection with miR-299 mimic in OVCAR-3 and SKOV-3 cells. The growth of CA-125 positive OVCAR-3 cells was significantly inhibited by miR-299 mimic treatment. Flow cytometry analysis showed a significant induction of apoptosis by miR-299 mimic treatment. Furthermore, cell adhesion, migration, and invasion ability of ovarian cancer cells were significantly inhibited by miR-299 mimic treatment. In contrast, these effect were opposite by miR-299 inhibitor treatment.

Conclusion: These results have shown that miR-299 regulates CA-125 in ovarian cancer cells and consequently alters their growth, adhesion, migration, and invasion. CA-125 may represent a new therapeutic target in the treatment of ovarian cancer.

Novel Polymeric Nanoparticles Containing tanshinone-IIA from Chinese Herbal Medicine: Preparation, Characterization, and Antitumor Activity

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Keywords: Nanoparticles, tanshinone IIA, PLA, hepatoma.

Objective: We have synthesized novel polylactic acid nanoparticles containing tanshinone IIA (TS-PLA-NPs) using a single oil-in-water emulsion/solvent evaporation method. In this study, we aimed to characterize the properties of these particles.

Methods: The optimized nanoparticles were characterized for morphology, mean particle size, zeta potential, entrapment efficiency, drug-loading content, X-ray diffractometer measurement, and in vitro release kinetics. The effect of TS-PLA-NPs on hepatoma in mice was also performed.

Results: The obtained nanoparticles were spherical and intact. The mean particle size was 192.5 nm with polydispersity index being 0.029 and zeta potential of 226.27 mV. The mean entrapment efficiency and loading of TSIIA in TS-PLA-NPs were 86.35 and 1.61%, respectively. The mean in vitro cumulative release percentage of TSIIA from TS-PLA-NPs vs. time curve fitted well with the Higuchi Equation. In pharmacokinetics and tissue distribution studies, the concentrations of TSIIA were higher in hepatoma and lower in blood, heart, kidney, spleen, and lung at 2 hr after TS-PLA-NPs was administered via caudal vein. TS-PLA-NPs were effective in destroying the human liver cancer cells in a concentration- and time-dependent manner. Mice studies showed TS-PLA-NPs were markedly more effective than both of TSIIA and blank PLA nanoparticles in preventing tumor growth and increasing survival time of mice with hepatoma.

Conclusion: This study provided support for the new paradigm, the application of TSIIA for the treatment of hepatoma.

Abstract #: 210

Presented by: Jun Liang, BS, Staff

Current Therapeutic Targets for Type 2 Diabetes Mellitus (T2DM): A Bioinformatic Study

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Keywords: T2DM, target, PATHER, biguanide, sulfonylurea, insulin, DDP-4.

Objective: Type 2 diabetes mellitus (T2DM) is caused by insulin resistance and characterised by progressive pancreatic β cell dysfunction. This article aimed to analyse current therapeutic targets for T2DM based on data from the literature and drug target related databases. Identified targets were further analysed with a bioinformatics approach using the Protein Analysis through Evolutionary Relationships (PANTHER) program.

Methods: Data on current clinical drugs for T2DM treatment were extracted from the US Food and Drugs Administration website (to December 2013). Candidate targets of T2DM were extracted from three online databases: Drugbank, Therapeutic Target Database and Potential Drug Target Database (all from inception to December 2013).

Results: A total of 34 clinical protein targets for T2DM were identified; these mainly include nuclear hormone receptors and nucleic acid binding proteins (PPARA and PPARG), transcription factors (PPARA & PPARG), voltage gated K+ channels (KCNJ1, 5, 8, & 11), glucosidase, amylases (AMY1, AMY2, & AMY3), G-protein coupled receptors (ADRA1A, ADRA1B, ADRA1D, ADRA2A, ADRA2B, ADRA2C, DRD2, etc.), non-receptor serine/threonine protein kinases (PRKAA1, PRKAA2, PRKAB1, PRKAB2, PRKAG1, etc.), and serine protease (DDP4). Current T2DM treatment focuses on the reduction of blood glucose level via different mechanisms involving nuclear hormone receptors, nucleic acid binding proteins, transcription factors, voltage gated K+ channel, glucosidase, G-protein coupled receptor and non-receptor serine/threonine protein kinase.

Conclusion: Extensive efforts should be taken to discover and develop the novel therapeutic agents, which may provide alternative therapies to overcome the current shortcomings and achieve therapeutic goals.

Presented by: Zhang Lifang, MD, Faculty

Effect of Melatonin in Combination with Caffeine on β-amyloid Production in N2a App Cells

Lifang Zhang¹, Chuanhai Cao², & Shu-Feng Zhou² ¹Department of Neurology, Ningxia Medical University General Hospital, Yinchuan, Ningxia, China, ²Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: Melatonin; caffeine, A beta, AD.

Objective: Our previous AD mouse studies have demonstrated that melatonin improved mitochondrial function and directly binds to $A\beta$ to inhibit $A\beta$ aggregation and that caffeine served as a blocker of β and γ secretase that reduced $A\beta$ production. Since melatonin and caffeine appear to act through different mechanisms, we hypothesize that a combined use of these two compounds will produce a synergistic or additive effect on A generation in neurons. The present study aimed to investigated the effects of melatonin in combination with caffeine on cell viability & programed cell death, $A\beta$ level, and cytokine production and in wild-type murine neuroblastoma N2a and N2a stably transfected with amyloid precursor protein cell lines.

Methods: The study used the MTT assay, Sandwich ELISA, immunocytochemistry and Western blots techniques. AD mice will be used to examine if the combination of melatonin and caffeine can improve the symptoms of AD and the underlying mechanisms.

Results: The results showed that melatonin plus caffeine increased cell viability and slightly changed the morphology of N2a/N2a App cells. Melatonin alone increased A β levels. The combination of melatonin with caffeine most significantly increased A β levels compared with cells treated with melatonin or caffeine alone. Studies are ongoing to investigate the underlying mechanisms.

Conclusion: The combined use of melatonin with caffeine produces an additive effects on A generation in vitro, probably through inhibition of A aggregation

Research supported by: Shufeng-Zhou, Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL 33612 szhou@health.usf.edu

Presented by: Ruijuan Luo, PhD, Postdoctoral Fellow

Metabonomic Response to the Treatment of Tyrosine Kinase Inhibitors in Human Hepatocarcinoma Cells <u>Rui-Juan Luo, and Shu-Feng Zhou</u> Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: TKI, HCC, Metabonomics

Objective: The molecular pathogenesis of hepatocellular carcinoma (HCC) is complicated, involving multiple signaling pathways and altered cellular behavior. However, early and timely diagnosis of HCC is difficult due to lack of selective biomarkers and specific clinical symptoms. In HCC, there is often increased expression of angiogenic factors including VEGFs, EGFs, and PDGF, which represent useful therapeutic targets that can be hit by tyrosine kinase inhibitors (TKIs). Metabolite profiles represent sensitive biomarkers of both genomic and phenotypic changes. We looked to metabonomic methods to find novel biomarkers and aid in TKI based drug development for HCC.

Methods: An HPLC-MS based metabonomics method was applied to monitor the endogenous metabolite profiling in HCC cell lines, HepG2, Hep3B and SK-HEP-1 upon treatment with commonly used TKIs.

Results: TKI drugs and their metabolites were quantified to establish pharmacokinetic concentration at cellular levels to clarify the effect of drug metabolism on therapeutic outcome and establish concentration-response relationships.

Conclusion: Concentration-response relationships were determined for each TKI tested. Our research shows metabonomics as a powerful methods to determine pharmacokinetic and therapeutic properties of TKI's for HCC.

Research supported by: by a Startup Fund from the College of Pharmacy, USF.

Presented by: Matthew MacPherson, BS, Graduate Student

Formulation Development Strategies for Improved Patient Compliance Via Single Tablet Combination of Metformin and Atorvastatin

Matthew MacPherson^{1,} Vijaykumar B. Sutariya^{2,} Yashwant V. Pathak^{2,} Janice Cacace^{3,} Venkat Bhethanabotla¹, Todd Daviau³, Matt <u>Greene³, Brian McMillan³, Srinivas M. Tipparaju²</u> ¹Department of Chemical Engineering, University of South Florida College of Engineering, ²Department of Pharmaceutical Sciences, USF College of Pharmacy, ³CoreRx, Inc.

Keywords: Metformin, Atorvastatin, tablet, combination, patient compliance

Objective: To successfully formulate a single tablet that combines Metformin, a biguanide used as anti-hyperglycemic drug, and Atorvastatin, a HMG-CoA reductase inhibitor (anti-cholesterol). Combination therapy reduces the need for number of medications taken by the patient, which in turn can increase patient compliance.

Methods: Active pharmaceutical ingredients (Metformin and Atorvastatin) and excipients were passed through a fine mesh screen, proportioned, and mixed using a Turbula mixer. The mixture was loaded into a gravity fed hopper, which fed an automated tablet press for final production of tablets. Tablets were compressed using a 1/2inch standard concave mold, at compression settings that ranged from 25-30kN, and mold depths of 8.3-10.3mm.

Results: Previous research from the group evaluated weight variations, hardness, friability, disintegration, and dissolution; did not meet certain expectations. Most recent works substituted the excipients from prior works with different grades and altered the excipient proportions using fractional design approach. The hardness of the tablets increased, which often suggests that the friability will also increase, however, no significant improvement was observed in the overall tablet properties. Alternative formulations with use of Solutrol, and other binders, are underway and will likely improve the over hardness and meet the expected market standards.

Conclusion: The excipients used in both current and prior works are designed to meet the highest standards set by the pharmaceutical industry. The formulation design achieves certain requirements but was unable to comply with other standards. Additional research and development is underway for overcoming formulation development challenges.

Research supported by: Florida High Tech Corridor grant

Abstract #: 214

Presented by: Malathi Narayan, PhD, Postdoctoral Fellow

Withaferin A regulates Parkinson's Disease-associated protein LRRK2

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Keywords: Parkinson's Disease (PD), LRRK2, Withaferin A, chaperone, inflammation

Objective: Leucine-rich repeat kinase 2 (LRRK2) is a large, multi-domain protein that is mutated in patients with familial and sporadic Parkinson's disease (PD). Functions of LRRK2 are still unclear, but mutations in LRRK2 (e.g. G2019S) are associated with adverse gain-of-function activities such as increased kinase activity leading to inflammation. Consequently, we hypothesized that exploring mechanisms to decrease levels of LRRK2 by pharmacological inhibition would be advantageous. This study explores the effect of the anti-inflammatory withanolide withaferin A (WA) on levels of LRRK2 and the molecular mechanism that leads to decrease in LRRK2 levels.

Methods: LRRK2 levels were analyzed by western blotting in several cell lines. N9 mouse microglial cells were used for subsequent drug treatments. SHSY-5Y cells were used for transfection with the G2019S LRRK2 mutant. Interaction between LRRK2, Hsp90 and Cdc37 was analyzed by immunoprecipitation (IP).

Results: N9 cells showed the highest levels of LRRK2 expression. Treatment with WA decreased LRRK2 levels in a doseand time-dependent manner. WA treatment also decreased levels of G2019S LRRK2. The interaction between Hsp90, Cdc37 and LRRK2 has been shown to stabilize LRRK2. IP data showed that WA treatment decreases the interaction between Hsp90, Cdc37 and could be regulating LRRK2 via this mechanism.

Conclusion: We report that WA drug treatment causes dramatic reduction in both endogenous WT LRRK-2 and PD associated mutant LRRK2 in cellular models. Our data also suggests that WA might be regulating LRRK2 levels via disrupting the interaction between Hsp90 and its co-chaperone Cdc37. Further studies with in vivo models of PD such as C.elegans will address therapeutic potential of WA for the treatment of PD.

Presented by: Ningkui Niu, MD, Faculty

Synthesis and biological evaluation of novel targeted PEGylated liposomes conjugated with four anti-tubercular drugs & siRNA complexes in the treatment of TB

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Keywords: PEGylated; liposomes; siRNA; anti-tubercular drug; TB

Objective: TB is still a public health issue in developing countries and its chemotherapy is compromised by drug resistance and severe side effects. This study aimed to synthesize a targeted and PEGylated liposomes encapsulated with four commonly used anti-tubercular drugs (SM, INH, RIF, and PZA) and siRNA against TGF- β 1 and then evaluate the efficacy and safety in human macrophages affected with Mycobacterium tuberculosis.

Methods: The nanoparticles were synthesized and chemically characterized. We would further examined the anti-bacterial effect of the nanoparticles in human macrophages infected with MTB H37Rv. Streptomycin (SM) was modified by the polyethylene glycol (PEG) to reduce its cell toxicity. The liposomal formulation prepared with the cationic lipid DOTAP and cholesterol, and it encapsulated other three anti-tubercular drugs including isoniazid (INH), rifampicin (RIF), and pyrazinamide (PZA). We also described a method for the complexation of siRNA with the cationic liposomes. Finally, we compared the anti-tubercular effect with monotherapy, anti-tubercular drug –PEG-liposomes, and also evaluate the gene silencing of transforming growth factor- β 1 (TGF- β 1) by siRNA.

Results: The nanoparticles were successfully synthesized and chemically characterized. The nanoparticles with four antitubercular drug–PEG-liposomes showed little cytotoxicity towards human macrophages infected with MTB and did not affect the cell cycle of MTB-infected macrophages. Other experiments are ongoing to further assess the efficacy and safety of the newly synthesized nanoparticles for TB treatment.

Conclusion: The newly synthesized nanoparticles target MTB-infected human macrophages with a low cytotoxicity, representing a promising delivery system for anti-TB drugs.

Abstract #: 216

Presented by: Misty Ochotny, BS, Graduate Student

Role of Sirolimus in Post-Cardiac Transplantation When Compared to Standard Immunosuppressive Therapies: a Systematic Review

<u>Misty Ochotny¹, Minal Shah¹, Alexis Ngo¹, Dr. Christina Doligalski², Dr. Kamila Dell³</u> ¹University of South Florida College of Pharmacy, ²Tampa General Hospital, ³USF College of Pharmacy, Department of Pharmacotherapeutics & Clinical Research

Keywords: renal dysfunction, calcineurin inhibitors **Objective:** T duction of the progression a nmunosuppression for hdraw post-cardiac sfunction (RD) in patients that used SR Methods: A onal studies, review articles, and exposure, outcomes, and inclusion nts and renal function.

Results: The Conversion to tx was deem CNI doses po Oral Presentation Only hown to cause RD. SRL therapy post-cardiac owered or discontinued

Conclusion: SRL can benefit cardiac tx rejection therapeutic treatments to reduce the progression and prevention of CAV and RD. There is a lack of literature regarding the use of SRL in post-cardiac tx patients. A future direction of research should include more longitudinal studies utilizing SRL as primary or adjunct treatment in post-cardiac tx recipients.

Chemical Characterization and Cytotoxicity of Electronic Cigarette Refill Cartridge Fluid

<u>Vishwani Persaud-Sharma, Juan-Juan Yin, Zhi-Wei Zhou, Jun Liang, Shu-Feng Zhou</u> Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: Electronic Cigarette, Refill Fluid, Cytotoxicity, HPLC, LC/MS, TEM.

Objective: Cigarette smoking continues to cause medical concern around the world, and the search for safe alternatives permeate the global consumption industry. One such alternative is that of the electronic cigarette (EC) with claims as a healthful substitute for smoking consumers. The purpose of this study was to experimentally examine the components of the EC fluid and its potential cytotoxicity towards lung epithelial cells.

Methods: The EC fluid was analyzed by HPLC, LC/MS, and TEM. Human adenocarcinoma alveolar basal epithelial cells (A549) were used to assess the cytotoxicity of EC fluid at varying concentrations. The apoptosis-inducing effect of EC fluid was determined using flow cytometry.

Results: Sample analysis via both LC/MS and HPLC methods yielded similar results in which one the predominant substances was identified as coenzyme Q10. As observed by TEM analysis, the particle size of the flavored EC samples ranged from 0.90 to 1.70 nm in size and the zeta potential was obtained at a range of -46.89 to 27.69. Results have indicated that the lower dose range of 5 to 40 percent of a 1% dissolved EC solution yielded optimal cellular growth and proliferation conditions.

Conclusion: Results obtained serve as the scientific basis leading towards the critical parameters that govern EC quality and ultimately safety profiling. While further investigation is necessary to establish the specifications required to assess nanoformulation and modification, these results provide sufficient background to move forward in sample characterization. The EC fluid tested appears to have minimal toxicity.

Research supported by: This project is supported by Dekang Biotechnology Inc., Shenzhen, China.

Abstract #: 218

Presented by: Jiazhi Sun, MD, Faculty

Crizotinib Induces Tumor Suppressor miR-146a and p21Waf1/Cip1 by Alternative Targeting Non-TK Target AktmTOR-Foxo Axis

<u>Jiazhi Sun^{1,} Lun Yang^{2,} Minghua Li^{1,} Ian E. Heller¹, Isaac Raplee¹, Steven Guzman¹, John P. Pasciak^{1,} Anand K. Prasad¹, Feng Cheng¹, <u>Lamere Buchanan¹, Daniella Roehm¹, Leah Finn¹, Kevin B. Sneed^{3,} Lin He² and Shu-Feng Zhou¹</u> ¹Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida; ²Bio-X Center, Shanghai Jiao Tong University, Shanghai, China; and ³Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, University of South Florida</u>

Keywords: Crizotinib, miR-146a, p21Waf1/Cip1, TKI, Foxo

Objective: Crizotinib, a first ever ALK /MET tyrosine kinase inhibitor for the treatment of ALK-rearranged NSCLC patients. We hypothesize that crizotinib acts on other molecular targets in addition to tyrosine kinases ALK/MET and may play critical role given that there is a complex network of kinases that work together to regulate a number of important cellular processes and different disease signature.

Methods: Approaching with a established chemical-protein interactome (CPI), we have discovered 301 PDB-deposited proteins corresponding to 353 ligand binding pockets among a total of 1,780 PDB-deposited human protein entries. Systemic pharmacology approach also applied including validation the molecular target(s) of TKIs in vitro. Oncogenic signaling study, luc-reporter, autophagy, apoptosis assay and NGS analysis applied.

Results: Crizotinib had a high CPI binding score (ZZ_score) of -2.2778 against tyrosine kinase Lck, also had -1.4672, -1.1242, -0.7033 and -1.5384 against MAPK3, S6K, GSK-3β and HDAC 7A. Our preliminary studies have showed that the crizotinib induced autophagy by activated LC3 and inhibited oncogenic Akt/mTOR signaling in melanoma cells resulting in G2/M cell cycle arrest. Furthermore, crizotinib increased p21Waf1/Cip1 and Foxo3A expression and tumor suppressor miR-146a in melanoma cells.

Conclusion: Taken together, crizotinib induces miR-146a, autophagy and p21 waf1/cip1 may potentially treat other type of human cancer by concurrently targeting tyrosine kinase, Akt/mTOR/Foxo axis, shedding a light for future both anti-cancer and anti-metabolic disorder drug discovery and development. This is the first CPI-based systemic study on leading discovery of crizotinib off-target phenotypic importance.

Research supported by: State funding

The Effect of the antitumor drug DMXAA On The Nuclear Orphan Receptor Nur77

Chia Thach and Shufeng Zhou, Department of Pharmaceutical Sciences, University of South Florida College of Pharmacy

Keywords: Cancer, pharmaceutical drugs, apoptosis

Objective: To investigate the early mechanism of 5,6-dimethylxanthenone-4-acetic acid (DMXAA) on Nur77 prior to apoptotic events.

Methods: Human esophageal cancer cells, EC109, and epithelial cancer cell, A549, were exposed to 10 µM DMXAA at 0, 15 m, 30 m, 1 h, 2 h, and 4 h. Nuclear and cytoplasmic extractions were collected from both cell lines. Western Blotting was used to evaluate apoptotic proteins and Nur77 proteins. Time point experiments were ran on chamber slides. Cells were stained for Nur77 proteins, the mitochondria protein HSP60 and endothelium reticulum protein PDI (protein disulfide isomerase). Translocation of Nur77 into the cytoplasm was determined by confocal microscopy.

Results: Confocal microscopy showed that Nur77 translocates into the cytoplasm and colocalize with HSP60. Nur77 did not colocalize with PDI. Western Blot showed a significant reduction of Nur77 between 1 h to 4 h from the nucleus. Cytoplasmic Nur77 increased after 30 m and decrease at 4 h. The apoptotic protein Bax showed an increase and anti-apoptotic protein Bcl-2 showed a decrease in cell treated with DMXAA.

Conclusion: DMXAA induces apoptosis of cancer cells by inducing the nuclear orphan receptor Nur77 translocation into the cytoplasm. Nur77 colocalize with the mitochondria and induce apoptotic events through Bax activation and Bcl-2 reduction.

Abstract #: 220

Presented by: Feng Wang, MD, Faculty

Plumbagin Induces Programed Cell Death in Human Pancreatic Cancer Cell Lines

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Keywords: plumbagin,autophagy,apoptosis,pancreatic cancer cell,

Objective: Pancreatic cancer is a major killer of human beings worldwide. There are no good chemotherapeutic drugs for the therapy of advanced pancreatic cancer due to tumor resistance and severe side effects. This study aimed to examine the role of plumbagin (PLB), a natural anticancer compound, in the treatment of pancreatic cancer using cell models.

Methods: Human pancreatic cancer lines PANC-1 and BxPC-3 were used. The cell viability was examined using the MTT assay. Cell cycle was determined using flow cytometry. Apoptosis and autophagy were detected with annexin V: PE apoptosis detection kit and Cyto-ID® autophagy detection kit, respectively. Western blotting was used to assess the expression of proteins.

Results: Plumbagin suppressed the growth of both PANC-1 and BxPC-3 cells in a dose-dependent manner. The IC50 value for PLB was 8.96 μ M in PANC-1 cells and 5.94 μ M in BxPC-3 cells when treated with PLB for 24 hr. PLB significantly increased the proportion of the sub-G1 population in both PANC-1 and BxPC-3 cells but no effects on cell populations in G1, S, and G2/M phases. Other experiments are ongoing to evaluate the effects of PLB on the programed cell death of pancreatic cancer cells.

Conclusion: Plumbagin shows potent anti-proliferative effect on human pancreatic cancer cells

Research supported by: The study was supported by Dr Shufeng, zhou with the Startup Fund of the College of Pharmacy, University of South Florida, Tampa, FL 33612

Presented by: Jiayou Wang, PhD, Faculty

Role of microRNAs in Acupuncture Treatment in Hypertensive Rats

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Keywords: microRNA; acupuncture; hypertension; miR-339; Sirt2.

Objective: Acupuncture has been used to treat hypertension with promising clinical efficacy and excellent safety, but the molecular mechanism is unknown. MicroRNAs (miRNAs) are a group of endogenous noncoding RNA that play important roles in many biological processes. This study aimed to check if miRNAs were involved in the response to acupuncture therapy.

Methods: miRNA microarray were performed to compare the miRNA expression profiles of medullas in hypertensive rats treated with or without acupuncture.

Results: 23 miRNAs with significant difference were identified in acupuncture-treated samples compared with untreated control sample, and their target proteins were narrowed down to 920 proteins, including 3 proteins (Sirt2, HSP90, & SOD) which were screened by our earlier study. Subsequent KEGG analyses indicated that the 920 proteins were enriched in 9 signaling pathways. Further qRT-PCR assay confirmed 4 up-regulated miRNAs (miR-339-5p, miR-223, miR-141, & miR-451) between acupuncture and control or sham acupuncture. MiR-339-5p mimic inhibited Sirt2 expression and miR-339-5p inhibitor enhanced Sirt2 expression in rat and human neurons. Finally, gain–of-function or loss-of-function studies showed that over-expression of miR-339-5p down-regulated Sirt2 expression.

Conclusion: This study provides initial evidence that miRNAs play a role in response to acupuncture therapy, which will better our understanding of how acupuncture elicits beneficial effects on hypertension

Research supported by: This project were supported by Natural Science Foundation of Guangdong Province (grant no. S2013010011547), National Natural Science Foundation of China (grant no. 81173349) and University of South Florida College of Pharmacy Startup Fund.

Abstract #: 222

Presented by: Yanyang Wang, MD, Staff

CDDO-Me, an Nrf2 Agonist, Induces Apoptosis and Autophagy of Esophageal Squamous Cell Carcinoma by Inhibiting Akt/mTOR and Activating p38-MAPK

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Keywords: esophageal squamous cell carcinoma; CDDO-Me; G2/M arrest; apoptosis; autophagy; Akt/mTOR pathway

Objective: CDDO-Me, a synthetic analog of oleanolic acid, is an Nrf2 agonist and used for the treatment of chronic renal disease. We have investigated the anti-proliferative effect of CDDO-Me on human esophageal squamous cell carcinoma (ESCC) and the underlying mechanisms.

Methods: The cell cycle distribution, apoptosis and autophagy of ESCC cells were detected using the MTT test, flow cytometry, confocal fluorescence and electronic microscopy. Western blotting was performed for detecting changes of protein levels.

Results: CDDO-Me exhibited an anti-proliferative activity toward Ec109 and KYSE-70 cells in a dose-dependent and timedependent manner. CDDO-Me induced cell cycle arrest at G2/M phase via down-regulating CDK1 and cyclin B1 and upregulating p21 and p53. Treatment with CDDO-Me caused the down-regulation of Bcl-2 expression, up-regulation of Bax, Puma, cytochrome c, cleaved caspase-9, and cleaved PARP-1 expression. In addition, exposure to CDDO-Me increased the ratio of LC3-II/LC3-I and beclin 1 expression. Finally, CDDO-Me reduced the phosphorylation of Akt Ser473 and mTOR Ser2448 and activation of p38-MAPK at Thr180/Tyr182 in both cell lines.

Conclusion: Our findings show that CDDO-Me not only inhibits cell growth, but also induces apoptosis and autophagy in ESCC cells, suggesting that CDDO-Me may be a potential candidate for cancer therapy against esophageal cancers.

Presented by: Zhi-Xin Wang, MS, Graduate Student

Bioinformatic Prediction of the microRNAs That Regulate ABC transporter Genes

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Keywords: miRNA, transporter, gene.

Objective: MicroRNAs (miRNAs) are a class of minute RNA molecules (approx. 22 nucleotides long) which act as posttranscriptional regulators. By targeting specific mRNA sequences, miRNAs regulate gene expression through RNA interference. Multiple studies have shown that miRNAs are responsible for the regulation of 30% of the human genome. The genes being regulated by miRNAs involve cell development, carcinogenesis, and apoptosis. Recently, there has been a limited amount of data regarding miRNA's role in the regulation of ATP-binding cassette transporters (ABC family). ABC transporters can carry many types of sterols, lipids, and drugs across membranes. This study has predicted the miRNAs which are responsible for regulating the ABC transporter genes using a bioinformatic approach.

Methods: The computer program TargetScan was in this study.

Results: Among the 48 predicted ABC transporter genes, a total of 5,428 matching sites were found, which means there were around 113 candidate miRNAs for each gene. From the TargetScan data, ABCA4, ABCB2, ABCB9, ABCC3, ABCE2, and ABCG4 were regulated by 38, 132, 89, 181, 124 and 219 miRNAs, respectively. Conserved miRNAs included miR-124, miR-1271, miR-96, miR-182, and miR-495, while examples of poorly conserved ones are miR-17, miR-155, miR-23, miR-205 and miR-186. Also, it was shown that a single miRNA might regulate different ABC transporter genes. For example, miR-383 could regulate ABCA9, ABCC10, ABCC11, ABCG1, and ABCG5, as well as miR-1227 might regulate ABCA9, ABCA10, ABCB10, ABCC5, ABCG4, and ABCG8. Totally 682 miRNAs were involved in the regulation of these 48 ABC transporters genes.

Conclusion: Benchmarking studies are undergoing to validate our computational data.

Abstract #: 224

Presented by: Yan Xu, MPH, Graduate Student

TIBS: A Web Database to Browse Gene Expression in Irritable Bowel Syndrome

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Keywords: IBS,UC,microarray,Database,TIBS

Objective: Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder. Its symptoms include chronic abdominal pain, bloating gas, diarrhea or constipation. The prevalence of IBS in Europe and North America is about 10-15%. The high prevalence of IBS and its unpleasant symptoms significantly lowers patients' life quality and makes IBS a disease with a high social cost. The pathophysiology of IBS is considered as multifactorial and the exact cause of the disease remains poorly understood. Recently, genome-wide expression microarray technique has been applied to investigate the possible mechanisms of IBS. However, a user-friendly database that allows scientists to query these data sets has not yet been established.

Methods: 198 samples in four published microarray sets from the NCBI Gene Expression Omnibus (GEO) repository were integrated into an online database called TIBS (Transcriptome of Irritable Bowel Syndrome) to compare gene expression difference between two unpaired groups (IBS vs. healthy volunteers, and IBS vs. UC patients).

Results: Users can query the gene expression change in IBS patients comparing to healthy volunteers or UC patients by gene symbols. Sex difference in IBS patients was also shown in the database. The current version of TIBS database contains 20968 annotated gene probe sets represented on the Affymetrix Human Genome U133A.

Conclusion: TIBS will be an invaluable resource for a better understanding of pathogenesis and progression of IBS at the molecular level and for drug development against IBS. The TIBS database is available online at http://www.chengfeng.info/tibs_database.html.

Research supported by: The start-up grant from the College of Pharmacy at the University of South Florida

Presented by: Juanjuan Yin, PhD, Postdoctoral Fellow

Development of a Novel cyclodextrin-fullerene Supramolecular Complex for Targeted siRNA Delivery

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Keywords: fullerene dimer; amphilic cyclodextrin; siRNA; breast cancer.

Objective: Targeting amphiphilic cyclodextrin-fullerene based supramolecule can serve as siRNA delivery vehicles, and the multifunctional nano-system is aimed to elicit synergistic effect and deliver siRNA to diseased site preferentially. This may represent a promising strategy for siRNA-based therapies.

Methods: Persubstituted cyclodextrins, cationic cyclodetrins, and fullerene dimer have been synthesized in this study. siRNA is compressed and packed in the self-assembling supramolecule for the targeted delivery. The transfection ability of the cyclodextrin-fullerene based complex were compared with naked siRNA at the cellular level.

Results: Bromine persubstituted cyclodextrins, cationic cyclodetrins and fullerene dimer have been synthesized successfully, and characterized through spectral methods. The self-assembling of the supramolecule was confirmed using TEM and SEM. The transfection ability of the cyclodextrin-fullerene was enhanced with improved efficiency.

Conclusion: The ability of fullerene dimmer to complex with amphilic cyclodextrin and the possible synergistic effects of fullerene's free radical scavenging activity make a fullerene-based linker a great candidate for the proposed delivery system. Fullerene dimmer can effectively complex with amphilic cyclodextrin to compress siRNA. The fullerene dimmer and amphilic cyclodextrin complex represent a promising delivery vector for siRNA. Additional experiments are ongoing to check the transfection effect in the treatment of breast cancer in vivo.

Research supported by: The College of Pharmacy, USF

Abstract #: 226

Presented by: Chunxiu Yuan, MD, Faculty

Targeting Mitotic Aurora A Kinase in the Treatment of Gastric Cancer

<u>Chunxiu Yuan^{1,2}, Yonghui Ding^{1,2}, and Shu-Feng Zhou¹</u> ¹University of South Florida College of Pharmacy, Department of Pharmaceutical Sciences, ²Ningxia Medical University

Keywords: gastric cancer; Aurora A kinase; alisertib; apoptosis; autophagy; EMT.

Objective: The mitotic kinase Aurora-A (Aur-A) plays a critical role in regulating centrosome segregation and spindle assemble and the dysregulation of Aur-A is often observed in various types of cancer. Aur-A plays an important role in the initiation, growth, invasion and metastasis of gastric cancer. This study aimed to investigate whether Aur-A inhibitors affect the growth, invasion and metastasis of gastric cancer.

Methods: AGS and NCI-N78 cells were used in this study. The cell cycle, apoptosis, autophagy and EMT markers were determined using flow cytometry and Western blotting analysis.

Results: Treatment of AGS and NCI-N78 cells with alisertib caused G2/M arrest and apoptotic cell death.

Conclusion: Aurora A represent a promising target for the therapy of gastric cancer. Additional experiments are ongoing to check the anticancer activities of Aur-A inhibitors in the treatment of gastric cancer in vitro and in vivo.

A Novel, Multi-Component, Multi-Targeted "Cocktail" from Natural Products for the Treatment of Alzheimer's Disease

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Keywords: natural compound, Alzheimer's disease, drug.

Objective: As Alzheimer's disease (AD) is a multifactorial, heterogeneous disorder involving multiple biochemical pathway changes, and a number of potential targets and signaling molecules have been identified as possible drug targets. Our approach focuses the discovery of a novel multi-component therapeutic ('cocktail') targeting multiple pathways for AD. Amyloid (A β), Tau hyperphosphorylation, and inflammation are considered to play a central role in the pathogenesis of AD. We postulate that targeting multiple pathogenic AD pathways will result in a synergistic effect, resulting in a treatment with better efficacy.

Methods: Panels of natural compounds were examined for their effect on AD using cellular (N2A APP Cells) and mouse AD models (P57/APP). ELISA, MTT Assays, and Western Blot were used to determine effect of drug on cellular conditions.

Results: Four compounds (galangin, berberine choride hydrate, indirubin-3'-monoxime, and honokiol) showed modulatory effects on the expression of A β in N2a APP cells and were suitable for drug use based on ELISA and MTT assays. These four compounds were further tested on their effects on the inhibition of A β aggregation, the Th1-related IL-12, IFN- γ and TNF- α production, and Th2-related IL-4 and IL-10 secretion. Western blot analysis was applied to check the change of JNK, p38 MAPK, Erk, PKC θ , and NF- κ B.

Conclusion: Based on these results, various combinations of the four natural compounds will be investigated in N2a APP to determine the ratios that maximally suppress the expression of $A\beta$ while beneficially modulating the immune response. Our natural compound library will be expanded and screened. The optimal cocktail will be further tested on the animal model of AD.

Abstract #: 228

Presented by: Zhiwei Zhou, PhD, Postdoctoral Fellow

Induction of Apoptosis and Autophagy and Suppression of EMT via Sirt1-Mediated Pathway by Plumbagin in Human Prostate Cancer Cells

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Keywords: Plumbagin; prostate cancer; apoptosis; autophagy; EMT; Sirt1

Objective: Plumbagin (PLB) has shown good anticancer activities, but the role of PLB in the treatment of prostate cancer is unclear. This study aimed to investigate the effects of PLB on the growth, apoptosis, autophagy, and epithelial to mesenchymal transition (EMT) of human prostate cancer PC-3 and DU145 cells and the underlying mechanisms.

Methods: Cell proliferation was evaluated by the MTT assay. Intracellular ROS level was measured using CM-H2DCFDA. Cell cycle distribution, apoptosis, and autophagy were determined using flow cytometry. Intracellular autophagy-associated signals were observed and quantified by confocal microcopy. The levels of proteins were quantified by Western blotting assay.

Results: The results showed that PLB had a potent growth-inhibitory, pro-apoptotic, pro-autophagic, and EMT inhibitory effects on both cells. PLB arrested PC-3 cell in G2/M and DU145 cells in G1 phase and significantly increased the intracellular level of ROS. PLB induced mitochondria-mediated apoptosis and autophagy in both cells. PLB suppressed PI3K/Akt/mTOR and p38 MAPK pathways and activated AMPK, contributing to the autophagy-inducing activities of PLB. Modulation of autophagy altered the apoptosis of both cells. Furthermore, PLB suppressed EMT-like phenotypes in both cells by restoring the balance of E-cad and N-cad. PLB down-regulated Sirt1 and inhibition of Sirt1 enhanced autophagy, whereas induction of Sirt1 abolished PLB-induced autophagy in both cells. In addition, inhibition of Sirt1 restored the balance of E-cad and N-cad. PBEF in both cells.

Conclusion: These findings indicate that PLB promotes cellular apoptosis and autophagy but inhibits EMT in prostate cancer cells involving PI3K/Akt/mTOR and Sirt1-mediated pathways.

Oxymatrine Improves Intestinal Barrier Function in Hepatic Cirrhosis by Inhibiting Activation of NF-kB p65 <u>Fang-Qing Zhu¹, Zhi-Wei Zhou², Shu-Feng Zhou², and Jian-Bo Wen¹</u> ¹Department of Gastroenterology, the Affiliated Pingxiang Hospital of Southern Medical University, Pingxiang 337000, Jiangxi, China, ²Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL

Keywords: Oxymatrine; Cirrhosis; Intestinal epithelial barrier; NF-B p65.

Objective: Intestinal epithelial barrier has an important role in the pathogenesis of chronic liver diseases and the development of complications of hepatic cirrhosis. Here we investigated the effect of oxymatrine on intestinal epithelial barrier function and the underlying mechanism in the small intestine of cirrhotic rats.

Methods: In rats with carbon tetrachloride (CCl4)-induced cirrhosis, thirty rats were randomly divided into two groups: treatment group, who received oxymatrine treatment (63 mg/kg); and non-treatment group, who received the same dose of 5% glucose solution. Another 10 healthy rats served as a normal control group. A piece of terminal ileum was sampled for histopathologic examination. The expression level of NF-B p65 in ileum tissue was evaluated with immunohistochemistry. The expression level of TNF-alpha and IL-6 mRNA and concentration of TNF-alpha[] and IL-6 in ileum tissue were analyzed using RT-PCR and ELISA, respectively.

Results: In comparison to the normal group, the results showed that intestinal mucosal villi in the non-treatment group were atrophic, shorter and fractured, and inflammatory cells were infiltrated into the lamina propria and even muscular layer. The swell of villi was serious and structure of mucous membrane became loose. Whereas, oxymatrine reversed the histological changes and restored the intestinal barrier function. Moreover, oxymatrine reduced the expression level of NF-B p65 and TNF-D and IL-6 which were elevated in non-treatment group. In addition, the serum endotoxin level significantly declined after oxymatrine treatment.

Conclusion: The results indicate that oxymatrine improves intestinal barrier function by inhibiting NF-κB p65 activation to reduce multiple pro-inflammatory cytokines expression.

Abstract #: 230

Presented by: Jennifer Bleck, MPH, Graduate Student

Gender and Racial Differences in the Co-Occurrence of ADHD and Disordered Eating Behaviors Jennifer R. Bleck, MPH¹, Rita D. DeBate, PhD, MPH, FAED Professor¹, Roberto Olivardia, PhD Clinical Instructor² ¹Department of Community and Family Health College of Public Health University of South Florida, ²Department of Psychiatry Harvard Medical School

Keywords: ADHD, eating disorders, comorbid, mental health

Objective: While emerging evidence suggests comorbidity of ADHD and eating disorders, little is known regarding racial and gender differences. As the prevalence and manifestation of each disorder differs by gender and race, further investigation is needed to increase our understanding of these co-occurring disorders.

Methods: The current study consists of a secondary analysis of data from the National Longitudinal Study of Adolescent Health (n=9,387; 50% female). Logistic regressions were used to identify the relationship between childhood ADHD behaviors and disordered eating behaviors in adulthood, stratified by gender and race. Analyses controlled for age and socioeconomic status and proper sample weights were applied.

Results: Results revealed that childhood ADHD behavior was associated with: a) adult binging and/or purging behaviors among Caucasian males (OR: 2.1, 95% CI: 1.3, 3.3) and females (OR: 1.7, 95% CI: 1.2, 2.4), African American males (OR: 2.2, 95% CI: 1.0, 4.8) and females (OR: 2.0, 95% CI: 1.0, 4.0), and Hispanic males (OR: 2.9, 95% CI: 1.2, 7.1); and, b) adult restrictive behaviors among Caucasian females (OR: 1.5, 95% CI: 1.1, 2.1), and Asian males (OR: 4.3, 95% CI: 1.2, 15.3).

Conclusion: The current study provides additional evidence that supports the co-occurrence of ADHD and disordered eating behaviors. Results depict novel findings both supporting the existence of this co-occurrence in diverse populations as well as differences in the associated disordered eating behavior across gender/racial groups. Implications include monitoring males and racial minorities with ADHD for disordered eating behaviors in order to address the growing concerns regarding eating disorders within these at-risk populations.

Presented by: Humberto López Castillo, MD, Graduate Student

Does Maternal Age Have a Role in Neonatal Weight? A 13-year Secondary Analysis of Panamanian Data

Humberto López Castillo, MD, MEd, MSc¹, Martín Lasso Bonilla, MD, MSc², Arlene A. Calvo, PhD, MPH, CHES^{1,3} ¹Department of Community and Family Health, College of Public Health, University of South Florida, Tampa, FL, ²Department of Neonatology, Dr. Arnulfo Arias Madrid Metropolitan Hospital Complex, Social Security Fund, Panama City, Republic of Panama; ³USF Health International Foundation, City of Knowledge, Republic of Panama.

Keywords: maternal age, birth weight, regression study

Objective: To assess the correlations between maternal age and birth weight of live singleton births from 2001 to 2013.

Methods: Secondary data analysis of the 2001-2013 birth registry of the Neonatology Unit of the Dr. Arnulfo Arias Madrid Metropolitan Hospital Complex—the Social Security Fund's largest delivery hospital in Panama City. The database was pooled and analyzed using a linear regression model in SPSS v. 21 (Cary, NC) for the independent variable maternal age, the dependent variable newborn birth weight, and the confounding variables newborn's gender and gestational age, mother's parity, and delivery method.

Results: Among the 53,832 live births in the registry, 50,201 (93.3%) corresponded to singleton births, 62.1% of which were vaginal deliveries. There were significantly (χ 2=41.6, 2 df, P<.001) more males (49.2%) than females (46.4%) born. Overall, mean (SD) gestational age was 38.4 (2.1) weeks and birth weight was 3175.5 (598.9) g. The respective mean (SD) gestational ages and birth weights were significantly (P<.001) different between vaginal (38.6 [1.8] weeks, 3196.3 [505.6] g) and Cesarean (38.0 [2.5] weeks, 3146.4 [718.9] g) deliveries. Controlling for the four confounders in the model, increased maternal age was significantly correlated to an increased birth weight (R=.600, P=.001).

Conclusion: Taking confounders into account, maternal age has significant effects on singleton newborn's weight. This finding must be taken into account by family planning and prenatal care programs, as well as adjusting local delivery guidelines for newborn risks associated to maternal age.

Research supported by: Panama's National Secretariat for Science, Technology, and Innovation (SENACYT).

Abstract #: 232

Presented by: Jeannese Castro, BA, Graduate Student

Breastfeeding and the Prevalence of Asthma

<u>Jeannese Castro¹, Russell Kirby²</u> ¹University of South Florida College of Public Health, ²USF College of Public Health Professor and Marrell Endowed Chair, Department of Community & Family Health

Keywords: Exclusive Breastfeeding, Non-exclusive Breastfeeding, Asthma, Secondhand smoke

Objective: To determine if exclusively breastfeeding an infant for six months is a protective factor against the development of childhood asthma among children under the age of five.

Methods: Data from the 2011 National Survey of Children's Health for children under age 5 was analyzed using Statistical Analysis Software (SAS 9.3) procedures for complex survey data. Bivariate logistic regression was conducted to test the independent variable, breastfeeding, against the dependent variable, asthma, which was used as the model to compare with the control variable, secondhand smoke. Multivariate logistic regression was conducted to examine the role of the covariates poverty, gender, and race/ethnicity.

Results: Compared to exclusively breastfed infants, for infants breastfed non exclusively for the first six months the odds ratio of having current childhood asthma was 1.44 (95% CI: 1.05-1.98); this compares to an odds ratio of 2.36 (95% CI 1.67-3.38) for those infants never breastfed. When a bivariate weighted analysis was conducted against the control variable, tobacco, the odds ratio that tobacco in the household will cause asthma is 1.33 (95% CI: 1.11-1.60) (pvalue 0.0016).

Conclusion: Exclusive breastfeeding appears to protect against development of childhood asthma. Environmental factors are also predictors of childhood asthma. Secondhand smoke in the child's household significantly increases the odds that the child will develop asthma. Future research is needed in the health disparities that relate to breastfeeding and how to promote breastfeeding practices among the populations who are at risk for childhood asthma.

Research supported by: Abstract developed in PHC 6197, Secondary Data Analysis, Fall 2013.

Best Practices for Insuring Hard-to-Reach Populations: A Case Study Evaluation

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Keywords: health care coverage, rural health, case study evaluation

Objective: Assess the outreach and enrollment strategies implemented by Florida Community Health Centers, Inc. (FCHC) to enroll eligible but not insured community members in Medicaid and other benefits programs.

Methods: Researchers conducted semi-structured interviews with 24 staff members and patients, conducted ethnographic observations, administered a short staff survey, and collected outreach related print materials for analysis. FCHC, Inc. provided enrollment numbers to compliment qualitative interview data about the program's impact. Data were analyzed using Atlas.ti.

Results: Results suggest that FCHC's outreach and enrollment model increases healthcare access for eligible, low-income and hard-to-reach patients in their service area who face barriers to enrollment. 87% of patient participants reported facing more than one barrier to enrollment and 100% of the Spanish speaking participants reported concurrently facing three or more barriers to enrollment. 80% of patient participants reported that they had, at one time, tried and failed to apply for Medicaid or other benefits as a result of encountering least one of these barriers. By using tailored, culturally appropriate in-reach and outreach strategies, providing application assistance, and employing culturally competent outreach coordinators, FCHC has reduced their uninsured rate to 16.2% (8% lower than Florida and 2% lower than the U.S.). In addition, 97% of the patients who worked with FCHC were approved for benefits and 100% of patients interviewed regularly used benefits.

Conclusion: We suggest that these promising practices could be replicated in other similar contexts by CHCs with "hard-to-reach" populations who are more likely to be uninsured.

Abstract #: 234

Presented by: Sarah Fishleder, BS, Graduate Student

Pathways in The Villages: An Analysis of Unhealthy Drinking Utilizing Structural Equation Modeling Sarah Fishleder¹, Carla Vandeweerd², Jaime Corvin³, Larry Schonfeld⁴, Donna Petersen⁵

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Keywords: Structural Equation Modeling, Substance Abuse, Older Adults

Objective: The population of older adults in the US is increasing rapidly. Now one of the largest subpopulations in the US, this group is also one of the fastest growing demographics of substance abusers. Problem drinking has been linked to cardiovascular disease, stroke, cancer, mental health problems, and kidney and liver damage. The purpose of this study is to map the strongest pathways in which unhealthy drinking manifest, thereby adding to knowledge about the factors that lead to unhealthy drinking in older adults.

Methods: The Villages, a large senior community in central Florida with a focus on healthy, active living, is home to almost 90,000 adults over the age of 55. In 2012, a population-based needs assessment was implemented in partnership with USF Health. Assessments were mailed to all residents of The Villages; 33,119 were returned. Unhealthy alcohol use was identified via the AUDIT-C, a subscale employed on the assessment. Structural equation modeling was utilized to analyze responses from those individuals who reported problem drinking to determine pathways towards misuse.

Results: Problem drinking was reported in n=1,600 (15.4%) of respondents, rates slightly higher than the general population of older adults, which has been shown to be around 10%. Theoretically relevant factors including gender, marital status, social factors, physical activity, retirements, accessibility to care, and mental health factors were examined for their role in problematic drinking.

Conclusion: Examining substance misuse from this perspective is a novel approach and enables insights that biomedical and individual approaches have long overlooked. Understanding the underlying reasons for addiction may enable successful management of substance use.

Presented by: Elisabeth Franzen, BS, Graduate Student

Preliminary Sexual Behavior and Contraceptive Differences among Youth Participating in a State-Wide Positive Youth Development Program Evaluation

Elisabeth Franzen, BS¹, Elizabeth V. Powers, BA^{1, 2}, Helen Mahony, MPH¹, Sarah B. Maness, MPH¹, Shireen M. Noble, BASc¹, Charlotte Noble, MA, MPH^{1,2}, Ashley Singleton, MPH¹, Wei Wang, PhD³, Rita DeBate, PhD¹, Stephanie L. Marhefka, PhD¹, Ellen M. Daley, PhD¹, Kay Perrin, PhD¹, Eric R. Buhi, MPH, PhD¹ ¹University of South Florida College of Public Health, Department of Community and Family Health, ²USF College of Arts & Sciences, Graduate Program in Applied Anthropology, ³USF College of Public Health, Department of Epidemiology and Biostatistics

Keywords: Adolescents, Positive Youth Development, Sexual Behavior

Objective: The purpose of this research was to identify preliminary sexual behavior and contraceptive use differences between youth participating in an evidence-based positive youth development program (PYD), the Teen Outreach Program (TOP), and a matched control group, from baseline (time 1) to post-intervention (time 2).

Methods: This project involved a randomized controlled trial in 28 high schools in 12 Florida counties in the 2012-2013 academic school year. Treatment and comparison youth completed a survey at time 1 (n=1812 [82%] and 2177 [84%], respectively) and time 2 (n=1498 [68%] and 1909 [74%]). Participants were asked about sexual intercourse, sexual intentions, and contraceptive/condom use. Multilevel modeling was conducted and odds ratios (OR) and their corresponding 95% confidence intervals (CIs) were reported. The covariates of age, gender, and race/ethnicity were included in the model. Data were analyzed with S-PLUS version 8.1.

Results: After controlling for baseline risk, preliminary results showed youth in the treatment group were less likely to report ever having sex, compared to the control group (OR: 0.64, 95% CI: 0.48-0.86, p=0.0025). Treatment youth were less likely to report future intention, compared to control youth (OR: 0.71, 95% CI: 0.44-0.98, p=0.02). These results remained statistically significant after controlling for covariates.

Conclusion: Data support decreased incidence of sexual behavior and intentions of having sexual intercourse versus comparison group. Limitations include potential self-report bias and survey attrition. Strengths include large sample size and ethnic/racial diversity of participants. These preliminary findings lend support for PYD programs, such as the TOP.

Research supported by: Office of Adolescent Health, USDHHS

Abstract #: 236

Presented by: Beatrice Frempong, MPH, Graduate Student

Presence of Neighborhood Amenities and Physical Activity in Children

Beatrice Frempong University of South Florida, College of Public Health, Department of Community & Family Health

Keywords: Physical Activity Children Wellness

Objective: Research suggests that community features and the built environment have an effect on levels of physical activity. We examines the association between presence of neighborhood amenities and level of physical activity in children using a national representative sample.

Methods: The 2011 National Survey of Children's Health included participant's children ages 6-17 years old (N = 62,380). The dependent variable was physical activity (participating in physical activity at least 4 times a week or 4-7 times a week). Independent variables included supportive neighborhoods, sidewalks, parks, recreation center, library, and number of amenities in the neighborhoods. Weighted crosstabulations, crude and multivariable logistic regression analyses were used to examine associations between the presence of neighborhood amenities and physical activity in children.

Results: While there was no association between participation in physical activity <4 times a week and one or two neighborhood amenities versus no amenities, an association between all four amenities vs. no amenities in physical activity less than four times a week (OR:0.736, 95% CI:0.591-0.916) in the unadjusted analysis. The adjusted analysis identified an association between three amenities vs. no amenities when participating in physical activity less than four times a week (OR: 1.129, 95% CI: 1.007-1.265) as well as all four amenities vs. no amenities (OR: 0.760, 95% CI: 0.618-0.935).

Conclusion: Physical activity among children was increased in neighborhoods that had all four amenities. Future research should examine the roles of family and child characteristics as well as other neighborhood factors that may influence a child's overall physical activity rates.

Presented by: Pamela Guevara, MPH, Graduate Student

Participant Cohesion and Comfort in a Video-Group Intervention for Women Living with HIV

<u>Guevara, P., Merrell, L., Lynn, V., Lockhart, E., Green, S., Johnson, A., and Marhefka, S</u>. Department of Community and Family, College of Public Health, University of South Florida

Keywords: HIV/AIDS; social support; telehealth; behavioral intervention

Objective: Behavioral interventions are usually delivered in-person, which is not always feasible. Video-conferencing technology is an innovative way to deliver group interventions. However, there is little information regarding participants' experiences with video-group (VG) interventions, and particularly whether group cohesion can be achieved through VGs. We adapted a CDC approved Effective Behavioral Intervention, Healthy Relationships, for delivery via video-phones to women living with HIV (WLH). The adapted 6-session program was delivered as part of a feasibility randomized controlled trial. This mixed methods study looks at participants' perceived cohesion.

Methods: 71 WLH participated (n=36 immediate intervention; n=35 wait-list control) from 4 Florida counties. Groups consisted of 3-7 participants. Each group met twice a week for 3 weeks. Most participants completed a group cohesion questionnaire after their last session (n=50) and a sub-sample (n=21) completed open-ended interviews.

Results: Participants (M age=43.5; SD=8.304; 56% African-American/Black; 22% Caucasian; 16% Hispanic) reported group members respected the agreement of confidentiality (96%) and a positive relationship among the group members (96%). Participants also reported feelings of unity and togetherness among group members (94%) and they felt free to share information (94%). In the qualitative interviews women reported they enjoyed the VGs, noting increased knowledge and support received.

Conclusion: Findings from this study indicate WLH felt connected in a VG intervention. VGs are promising strategy for delivering behavioral interventions for WLH. VG interventions can be used to derive meaningful relationships among participants.

Research supported by: NIH R34MH092207 (PI: Marhefka)

Abstract #: 238

Presented by: Mahmooda Khaliq, MHS, CPH, Graduate Student

A Systematic Review of Community Contextual Factors and Modern Contraception Use in Low-Middle Income Countries

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Keywords: Community Contextual Factors, Contraception, Multilevel, Demographic Health Survey

Objective: Globally, 32% of women use modern contraception and an estimated 222 million women have an unmet need for modern contraception. To understand the factors that influence modern contraception use a better understanding of existing research on individual and community contextual factors is necessary.

Methods: This paper summarizes the results of a systematic review that examines how the Demographic Health Survey and multilevel modeling have been used to investigate community contextual factors and their impact on modern contraception. Using PRISMA and the Matrix Method, this study conducted a review of literature in four electronic bibliographic databases, which yielded a total of 11 articles for abstraction.

Results: At the individual level factors that influence modern contraceptive use are age, parity, media exposure, access to family planning services, discussion of family planning with partner, migration status, education and wealth. Marriage, ideal family size and religion were not shown to be predictors of modern contraception use. At the community level, level of approval by women for family planning, discussion of family planning with partner and residence in an urban community were found to be predictors of modern contraceptive use.

Conclusion: The systematic review revealed that a theoretical/conceptual framework does not exist for guiding research and that most research has focused on the African sub-continent. The existing geographic focus, misses the significant need for contraception in Asia and South Asia, where 131 million women with unmet need reside. Future research should focus on Asian nations, and should conduct in-depth country level analysis using longitudinal data.

Presented by: Nolan Kline, MA, Graduate Student

Multilevel Health-Related Impacts of Immigration Policy: Implications for Immigrant Health, Providers, and the Affordable Care Act

Nolan Kline, MA¹⁻², Heide Castañeda, PhD, MPH², Angela Stuesse, PhD² ¹University of South Florida College of Public Health, Department of Community and Family Health, ²University of South Florida College of Arts and Sciences, Graduate Program in Applied Anthropology

Keywords: Immigrant Health, Health Policy, Social Determinants of Health

Objective: In 2010, the Georgia legislature passed an immigration law prohibiting undocumented immigrants from receiving publically financed health services and prohibiting health professionals from providing non-emergency services to undocumented patients. This qualitative study explores how state-level immigration policies intersect with federal immigration laws and local police practices to impact undocumented immigrants' health seeking behaviors and health providers' practices. This research further examines intersections of immigration and health policies that impact the broader health care system.

Methods: This research employs the social ecological model of health to guide semi-structured interviews with state legislators, government agency workers, health providers, non-government organization leaders, immigrant rights leaders, and undocumented immigrants. Interview data were triangulated by participant observation experiences with immigrant rights organizations and a media analysis of Georgia's print media outlets.

Results: Findings demonstrate that some undocumented immigrants alter preventive behavioral health practices and fear seeking health services in response to immigration laws. Providers discussed conflicting ethical perspectives regarding treating undocumented immigrants, recognizing a professional ethical duty to treat patients regardless of immigration status. Findings further underscore how policies targeting undocumented immigrants may ultimately result in negative consequences for the larger health system.

Conclusion: Social science research and health policy research must pay specific attention to the health-related consequences of laws seemingly beyond the scope of health domains, such as immigration laws.

Abstract #: 240

Presented by: Karen Liller, PhD, Faculty

Analysis of Florida High School Athlete's Sports Injury Data for 2012-2013

Karen D. Liller, PhD¹, Barbara Morris, DHSc², Siwon Jang, PhD¹, Siew Wong, MA¹ ¹University of South Florida College of Public Health, Department of Community & Family Health, ²Sports Medicine & Athletic Related Trauma (SMART) Institute, Department of Orthopaedics and Sports Medicine, Morsani College of Medicine, University of South Florida

Keywords: sports injury, high school, injury surveillance

Objective: The purpose of this study was to provide the latest surveillance data (2012-2013) for injured high school athletes from 11 large public and private high schools in west-central Florida and to propose targeted injury prevention interventions.

Methods: The SMART Injury Registry was developed by the Sports Medicine and Athletic Related Trauma (SMART) Institute of the University of South Florida in 2007. For the 2012-2013 academic year, sports-related injuries were collected and reported by the certified athletic trainers (ATCs) hired by SMART at 11 west-central Florida high schools through the national Reporting Information Online (RIO) system.

Results: A total of 503 injuries were reported by the ATCs, the majority of which were related to football (N=215). The leading rate of injury per 1000 athlete-exposures for practices was for football at 2.57, followed by wrestling at 2.30, and other sports at 2.24. For competitions, the injury rate per 1000 athlete-exposures was greatest for football at 15.9 followed by women's soccer at 8.52 and men's soccer at 5.18. The leading type of injury for all sports overall was a ligament sprain (27.29%) followed by a concussion (19.12%) and a muscle strain (16.33%). The principle body parts injured (for all injuries) were the head/face (20.28%), followed by the ankle (17.89%) and the knee (15.71%).

Conclusion: As in previous years, football showed the highest injury rate for both practices and competitions for the 2012-2013 academic year. Concussions were the leading cause of injury for football, baseball, and softball. These results allow for the development of targeted injury interventions and enforcement of related policies for these athletes that should lead to reductions in injuries.

Presented by: Elizabeth Lockhart, MPH, Graduate Student

Reporting Sexual Behaviors Using ACASI: Can Women Living with HIV be Honest and Comfortable or is There Social Desirability Bias?

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Keywords: ACASI, HIV/AIDS, mixed methods, evaluation and sensitive questions

Objective: Little is understood about how honest participants are when answering research questions via audio computer assisted self-interview (ACASI) software. ACASI assessments could reduce stigma and increase honesty for participants, due to the sensitive nature of sexual behavior questions. This mixed methods study assesses the self-reported honesty of women living with HIV (WLH) that participated in an adapted CDC approved Effective Behavioral Intervention, Healthy Relationships, for delivery via video-phones. Participant responses at 6-months post intervention and specific facilitators and barriers to completing research assessments via ACASI were examined.

Methods: 71 WLH participated (n=36 immediate intervention; n=35 wait-list control) from 4 Florida counties. A subset of 21 semi-structured interviews was completed with intervention participants. The quantitative responses for those interviewed were subsequently analyzed. 6 questions to assess different aspects of honesty were evaluated, while grounded theory was used to examine the qualitative data for specific reasons in self-reported honesty data.

Results: Overall participants reported being honest in answering questions via ACASI (95% report being mostly or completely honest) and comfortable participating in ACASI assessments (90% report feeling good or very good). The factors that participants cited for using ACASI include comfort in answering questions, privacy and security and ease of use.

Conclusion: Findings indicate that ACASI can be used to obtain honest answers from WLH with regards to sexual behavior. ACASI is a promising assessment tool to use for sexual health research. Future research can utilize ACASI as a method to increase honesty.

Research supported by: NIH grant R34MH092207 (PI: Marhefka)

Abstract #: 242

Presented by: Sabrina Luke, MPH, Graduate Student

The impact of Assisted Reproductive Technology (ART) on Live Births: Three States

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Keywords: ART, preterm, SGA, multiples, state

Objective: Assisted reproductive technology (ART) has been successfully used to treat infertility for the past 30 years. Questions remain about the potential health risks associated with ART use and whether these vary by state. We examined the prevalence of poor birth outcomes in women using ART in Florida, Massachusetts and Michigan. The associated effects of ART were examined across states to identify associations by population characteristics and geographic location.

Methods: Data from the CDC's National ART Surveillance System (NASS) were linked to Massachusetts, Florida and Michigan state vital records for the period of 2000 to 2006. Bivariate analyses were conducted to compare rates of multiples, preterm births (32 and 37 weeks), and small-for-gestational-age infants (<5th and <10th percentiles) by maternal characteristics and ART procedures used. Logistic regression was conducted to identify increased risks of adverse birth outcomes by ART use and by state.

Results: No statistically significant associations were found for ART use and increased risk of SGA within states, however, differences were found between states. ART use in Florida resulted in an 18.5% increased risk of delivering a SGA infant in the 10th percentile when compared to women using ART in Massachusetts. Statistically significant associations were found between ART use and increased risk of preterm birth (32 and 37 weeks) within Michigan and Massachusetts but not within Florida. Florida did experience higher rates of preterm births.

Conclusion: Variations in adverse birth outcomes by state may be due to differences in procedures used or to regional variability of factors that predispose women to be more at risk for adverse outcomes.

Research supported by: CDC,FDOH,USF

The 5 Cs Model of Positive Youth Development: A Preliminary Confirmatory Factor Analysis and Assessment of Measurement Invariance

Sarah B. Maness, MPH¹, Helen Mahony, MPH¹, Sarah B. Maness, MPH¹, Shireen M. Noble, BASc¹, Elisabeth Franzen¹, Elizabeth V. Powers, BA^{1,3}, Charlotte Noble, MA/MPH¹, Ashley Singleton, MPH¹, Rita DeBate, PhD¹, Stephanie L. Marhefka, PhD¹, Wei Wang, PhD², Ellen M. Daley, PhD¹, Kay Perrin, PhD¹, Eric R. Buhi, MPH, PhD University of South Florida College of Public Health, ¹Department of Community and Family Health ²Department of Epidemiology and Biostatistics; and, ³USF College of Arts & Sciences Graduate Program in Applied Anthropology

Keywords: Adolescents, Positive Youth Development, Measurement

Objective: Although adolescents have historically been studied using a deficit-based approach, a focus on youth assets has recently gained popularity. One widely used model of Positive Youth Development (PYD) is the 5 Cs model, which includes Character, Competence, Caring, Connection, and Confidence. The goal of this study was to assess validity and reliability of two constructs, Caring and Connection, comprising the 5 Cs.

Methods: Data were collected as part of the USF-led evaluation of the Teen Outreach Program (TOP). This study uses baseline data of study participants (N=3989) from 28 Florida public high schools. A confirmatory factor analysis of the scales within Connection and Caring was conducted and potential measurement invariance between Hispanic and non-Hispanic youth was explored using Mplus Version 7.

Results: Results yielded valid and reliable scores related to the Connection scale (RMSEA=0.054, CFI=0.965, SRMR=0.041, χ 2=1248.821, df=101, α =.919). Data from the Caring scale also yielded valid and reliable scores (RMSEA=0.082, CFI= 0.940, SRMR=0.043, χ 2=752.903, df=27, α =.845). There was good model fit when examining measurement invariance between Hispanic and non-Hispanic youth.

Conclusion: This analysis indicated that Caring and Connection were valid and reliable in this sample. Measurement invariance indicates the same construct is being measured across groups. This analysis provides a foundation to continue measurement of remaining components of the 5 Cs model of PYD and contributes to the literature by validating this model in a racially and ethnically diverse sample. This will allow PYD programs to be effectively evaluated to determine their impact on public health.

Research supported by: Office of Adolescent Health, U.S. Department of Health and Human Services

Abstract #: 244

Presented by: Laura Marsh, MPH, Staff

Changes in Developmental Assets and Physical Activity Frequency among 3rd-5th Grade Girls Participating in a Positive Youth Development Program

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Keywords: positive youth development, physical activity, program evaluation, pre-adolescent girls

Objective: Despite the benefits of physical activity on mental, social, and physical health, across all ages, females are less active. Positive youth development through sport programs may offer the unique blend of sport and life skills that address girl-specific physical activity determinants, and encourage a physically active lifestyle. The purpose of this study was to assess the short-term outcomes of a sport-based positive youth development program for girls.

Methods: A secondary analysis of pre-post intervention evaluation data was conducted to assess developmental assets, overall positive youth development, and physical activity among first-time intervention participants (n=150). Data analyses included descriptive statistics and paired sample t-tests to determine pre- to post-intervention changes as well as overall sustainability two months post-intervention exposure.

Results: Results revealed significant improvements in confidence and connectedness developmental assets as well as overall positive youth development and physical activity frequency. The average overall score was maintained two months post-intervention among seven repeat participants.

Conclusion: Findings suggest that the Girls on the Run program may produce improvements in targeted developmental assets and physical activity frequency with the potential for sustained impacts post-intervention exposure. This exploratory study provides preliminary data to support future studies examining the short and long-term effectiveness of sport-based positive youth development programs.

Presented by: Shireen Noble, BASc, Graduate Student

Lessons Learned from a School-Based Randomized Control Trial Evaluation of a Positive Youth Development Program: Successes, Challenges, and Solutions

Shireen M. Noble, BASc¹, Ashley Singleton, MPH^{1,} Cameron R. Chambers⁴, Elisabeth Franzen, BS¹, Helen Mahony, MPH¹, Sarah B. Maness, MPH¹, Charlotte A. Noble, MA, MPH^{1,2}, Elizabeth V. Powers, BA^{1,2}, Wei Wang, PhD³, Rita DeBate, PhD¹, Stephanie L. Marhefka, PhD¹, Ellen M. Daley, PhD¹, Kay Perrin, PhD¹, Eric R. Buhi, MPH, PhD¹ ¹ University of South Florida College of Public Health, Dept. of Community & Family Health, ² USF College of Arts and Sciences, Graduate Program in Applied Anthropology ³USF College of Public Health, Dept. of Epidemiology and Biostatistics, ⁴USF College of Public Health

Keywords: sexuality education, adolescents, randomized control trial, lessons learned

Objective: The purpose of the research is to describe the experiences of the Teen Outreach Program (TOP) evaluation team, after one year conducting a school-based randomized controlled trial evaluation of the TOP, a positive youth development (PYD) program. Topics reviewed include the successes, challenges, solutions, and lessons learned.

Methods: Through a partnership between an evaluation team at USF and the Florida Department of Health (DOH), 28 high schools in 12 non-metropolitan Florida counties participated in this project. Responsibilities of the evaluation team included conducting pre- and post-intervention surveys, as well as 1 and 2 year follow-ups. The first year included 3989 youth, despite challenges related to the complexity of the research design, sensitive nature of the topic (e.g., sexual behavior), and working with multiple school districts.

Results: Success was achieved through use of a passive parental permission process, allowing for the inclusion of more youth (which can lead to better external validity). Challenges included misunderstanding of survey questions and missing data, though procedures were adapted to help combat that loss. An early partnership with the DOH provided credibility to the project with school districts. Finally, issues have arisen around school attrition, but they have been addressed through better communication with school administrators.

Conclusion: Researchers conducting similar evaluations can learn from our experience. Being able to adapt to the needs of each school is essential, and creating personal relationships with school personnel to proactively address issues helps reduce problems. Finally, the opt-out permission process can be used to increase survey participation.

Research supported by: Office of Adolescent Health, USDHHS

Abstract #: 246

Presented by: Funmilayo Olaoye, MPH, Graduate Student

The Association between Childhood Exposure to Family Violence and Bullying.

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Keywords: Bullying, family violence

Objective: To examine the relationship between childhood exposure to family violence and bullying and the role of other sociodemographic factors.

Methods: A secondary data analysis was done using the 2011-2012 National Survey of Children's Health (NSCH) dataset. The children aged 6 to 17 years in the United States were selected for the study (N=65,680). The dependent variable was bullying; independent variables were domestic violence, neighborhood violence, race/ethnicity, poverty level and Children with Special Health Care Needs (CSHCN). Weighted chi-square bivariate analysis and adjusted weighted multivariable logistic regression analyses were performed.

Results: Childhood exposure to family violence is significantly associated with bullying. Children exposed to family violence have almost 2-fold increased risk OR=1.95, 95% CI (1.55 -2.45) of bullying others compared to children who are not exposed to bullying. Children exposed to neighborhood violence are at higher risk [OR=1.40(1.13-1.74)] of bullying compared to children who are not exposed. African American non-Hispanics [OR=1.42(1.13-1.77)] are at higher risk [OR=1.42(1.13-1.77)] of bullying compared to children who are not exposed to bullying increased with decreasing strata of family income below the Federal Poverty Level compared to families at 400% of FPL. Children with Special health Care Needs have about 2-fold increased risk [OR=1.75(1.52-2.03)] of bullying compared to CSHCN. No association exists between gender and bullying.

Conclusion: An association exists between family violence and childhood exposure to bullying after controlling for age, gender, race and ethnicity. For future research, it may also be interesting to examine the role of other familial, child, and socio-demographic factors.

Presented by: Elizabeth Powers, BA, Graduate Student

The Effects of an Evidence-Based Positive Youth Development Program on Academic Outcomes in Non-Metropolitan Florida: A Preliminary Analysis

Elizabeth V. Powers, BA, ^{1,2;} Elisabeth Franzen, BS, ^{1;} Helen Mahony, MPH, ^{1;} Sarah B. Maness, MPH, ^{1;} Shireen M. Noble, BASc, ^{1;} Charlotte Noble, MA, MPH, ^{1,2;} Ashley Singleton, MPH, ^{1;} Wei Wang, PhD, ^{3;} Rita DeBate, PhD, ^{1;} Stephanie L. Marhefka, PhD, ^{1;} Ellen <u>M. Daley, PhD, ^{1;} Kay Perrin, PhD, ^{1;} Eric R. Buhi, MPH, PhD, ¹¹ USF</u> Department of Community and Family Health ² USF Department of Applied Anthropology ³ USF Department of Epidemiology and Biostatistics University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Adolescents, Positive Youth Development, Academic Failure

Objective: The purpose of this research was to compare preliminary academic outcomes between treatment youth participating in an evidence-based positive youth development program (the Teen Outreach Program [TOP]) and comparison youth from baseline (time 1) to program exit (time 2).

Methods: This project involved a randomized controlled trial (RCT) in 28 high schools in 12 Florida counties. Treatment and comparison youth completed a survey at time 1 in September 2012 (n=1812 [82%] and 2177 [84%], respectively) and time 2 in May 2013 (n=1498 [68%] and 1909 [74%]). Survey items measured four academic outcomes: course failure, failing grades, school suspension, and cutting class. A multilevel model analysis was conducted with age, gender, and race/ethnicity as covariates. Data were analyzed with S-PLUS 8.1, and odds ratios (OR) with corresponding 95% confidence intervals (CI) were reported.

Results: After controlling for baseline risk, preliminary results showed no statistically significant difference between treatment and comparison group youth for course failure (OR: 1.04, 95% CI: 0.68-1.58), failing grades (OR: 0.82, 95% CI: 0.55-1.21), school suspension (OR: 0.98, 95% CI: 0.66-1.47), or cutting class (OR: 1.08, 95% CI: 0.64-1.82).

Conclusion: Preliminary results suggest that the TOP's immediate effect on academic outcomes is null. This conclusion differs from Allen et al's (1997) study of the TOP, which found statistically significantly less risk for these outcomes among treatment youth compared to comparison youth. While these results are preliminary and reflect changes in one cohort of participants, our study will go beyond the Allen et al study to explore longitudinal (1- and 2-years post program) effects with a larger sample.

Research supported by: Office of Adolescent Health, USDHHS

Abstract #: 248

Presented by: Tommi Rivers, BA, Graduate Student

The eBIT Project Needs Assessment: Using Translational Science to Bring Evidence-based Interventions to School Social Workers

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Keywords: School Social Workers, Evidence-based Interventions, Needs Assessment

Objective: To describe the baseline Hillsborough County Public Schools District's (HCPSD's) school social workers (SSWs) needs assessment for evidence-based interventions (EBIs).

Methods: Through a collaborative partnership between HCPSD and the ITRABH, we performed an EBI needs assessment of HCPSD's SSWs. Participants were invited to take a voluntary online survey on October 2013, and then reminded on November 2013. This survey covered aspects of SSWs resources to identify and implement EBIs. Questions used a 1-5 Likert-like scale and their summarized results are presented as percentages.

Results: Among the 107 SSWs participating in the survey (response rate = 83.6%), almost half (49%) have sparely used online intervention databases, Intervention Central, and/or the District Mental Health Toolbox. Most (78%) of the SSWs spend 1 to 4 hours per week researching for behavioral and/or mental health interventions. However, 20% of SSWs do not perform research tasks. When asked about HCPSD-sanctioned EBIs, 18% of SSWs do not feel comfortable using them. Seventy percent of SSWs use EBIs in their practices, while 28% of them could not identify where to find EBIs.

Conclusion: Needs assessment of HCPSD SSW warrant provision of EBIs in a time- and effort-saving, readily available format. These results warrant the use of translational methods to develop, implement, and evaluate an Evidence-based Intervention Toolkit (eBIT)—a custom-made, searchable, online database of Tier 2 EBIs for SSWs, currently underway.

Research supported by: USF's Institute for Translational Research in Adolescent Behavioral Health (Funded through a grant from the National Institute on Drug Abuse (NIDA) 1R25DA031103-01A1NIDA) and Panama's National Secretariat for Science, Technology, and Innovation (SENACYT).

Presented by: Rebecca Saint Fort, BS, Graduate Student

Childhood Adverse Experience: The Association Between Adverse Family Experience and Resiliency in School Aged Children.

Rebecca Saint Fort University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: ACEs, Resiliency, Child Health

Objective: Although many studies have examined factors associated with why children do well or poorly in the face of adversity, less is known about why some children do well. This study examined factors associated with resilience in children who experienced adversity.

Methods: The data from the 2011 National Survey on Children's Health (NSCH) was used to establish the association between the adverse family experiences and resiliency (defined as school attendance and if a child repeated a grade among US Children age 6-17 years) and with the number Adverse Childhood Experiences (ACEs) a child has.

Results: The sample included 65393 children ranging in age from 6 to 17 years. Number of ACEs was associated with school engagement and having repeated a grade. Consequently, certain factors inherent in these environments may have the potential to promote their health and wellness. Nearly half (47.9%) of US children age 0-17 years experienced one or more of the nine ACEs asked about in this survey; a total of 34,825,978 children nationwide. Children between the age 6 to 17 years that experience two or more ACEs were less likely to repeat a grade and are more likely to be engaged in class. Children that have more than two adverse family experiences were more likely to have more resiliency than their counterparts.

Conclusion: There is evidence consistent with children actually benefiting from the experience of some adversity.

Abstract #: 250

Presented by: Montray Smith, MPH, Graduate Student

Duval County Special Needs Coordination During EOC Activation During Tropical Storm Andrea <u>Montray Smith, MSN, RN, LHRM</u> University of South Florida, College of Public Health, Dept. of Community & Family Health

Keywords: Emergency Management, Special Needs, Emergency Operations Center

Objective: The purpose was to collaborate with a multidisciplinary team to provide the best practices for a large metropolitan area with a diverse population.

Methods: Quantitative methodology was used. Regional cross sectional telephone surveys were performed to gather patient census of all local categories 1-2 healthcare facilities on the number of patients that use stretchers or wheelchairs. This information was used to determine the number and type of health care vehicles needed for a possible evacuation to special needs shelters.

Results: The results showed that local ambulances (city and private) were limited and additional resources were needed. As the result, the city's transportation authority were informed to develop plans to provide additional vehicles if needed.

Conclusion: The EOC relies on telephone communication to receive current patient transportation needs; however, the system has not been tested on full scale activation using category 4-5 healthcare facilities. The process also depends on the number of EOC personnel available to manage phone traffic and if communication to the facilities is still maintained during a disaster.

Research supported by: The Florida Division of Emergency Management, JFRD Emergency Preparedness Division

Presented by: Erika Thompson, MPH, Graduate Student

Theory-Based Determinants of Physical Activity during Pregnancy: A Systematic Review

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Keywords: Pregnancy, Review, Physical Activity

Objective: National guidelines recommend that pregnant women engage in ≥30 minutes of moderate exercise most days of the week; yet only 14% report meeting this recommendation. Theory assists in identifying salient determinants of health behavior to guide interventions; however, the application of theory to physical activity among pregnant women has not been examined cohesively among the multiple levels of influence. This systematic review aims to examine the extent theory has been used to explain or predict physical activity during pregnancy.

Methods: The search produced 223 articles published before September 2013. Inclusion criteria applied: empirical-based; published in a peer-reviewed journal; measured predictors; comprised a pregnant sample; and guided by theory. Studies testing an intervention were excluded. The final sample included 12 studies.

Results: Multiple theories were utilized to explain/predict physical activity during pregnancy; however, the majority of these studies focused on intrapersonal level determinants. Seven studies aimed to predict physical activity based on theoretical constructs (i.e., intention, perceived behavioral control, self-efficacy). Five studies aimed to explain the behavior, identifying attitudes, beliefs, barriers, and benefits associated with physical activity.

Conclusion: This review found that previous research examining physical activity during pregnancy has focused primarily on intrapersonal theoretical determinants. Research examining factors at the interpersonal, community, and societal levels remain understudied. Future research should employ theory-driven multi-level determinants of physical activity to reflect the interacting factors during this critical period in the lifecourse.

Abstract #: 252

Presented by: Susan Tyler, BA, Graduate Student

"You Can't Get A Side Of Willpower:" Nutritional Supports And Barriers In The Villages, FI

<u>Susan Tyler, BA,</u> Department of Community and Family Health; Department of Anthropology, <u>Jaime Corvin, PHD,</u> Department of Global Health, <u>Philip Mcnab, MA, MPH,</u> Department of Community and Family Health; Department of Anthropology, <u>Sarah Fishleder, BA,</u> Department of Epidemiology and Biostatistics; Department of Anthropology, <u>Heather</u> <u>Blunt, PHD,</u> Department of Community and Family Health, <u>Carla VandeWeerd, PHD,</u> Department of Community and Family Health University of South Florida College of Public Health

Keywords: social eating, older adults, nutrition education, food assistance

Objective: Good nutrition in late life is key to the health of older adults and demands the attention of health promoters. In order to contribute to a better understand of nutrition and healthy aging we aim (1) to understand how the social lives of older adults in an active retirement community affect their nutritional health and 2) assess what environmental supports and barriers influence the diets of older adults.

Methods: Data is taken from 29 focus groups with 144 residents of The Villages, Florida. The focus groups were conducted as part of the third phase of a mixed-methods multiphase health assessment. Focus groups were transcribed and analyzed using Nvivo 10 software. Codes related to nutrition were reviewed for thematic content.

Results: Analysis revealed that the high social connectedness of residents confers both positive and negative influences on the nutritional lives of residents. Neighbors and friends are essential to a resident's ability to access foods in times of need. Conversely, many social functions in the community revolve around the consumption of nutrient deficient foods.

Conclusion: Friends and neighbors may provide the best point of entry for nutritional interventions, such as food assistance strategies, and health promotion and education. As more older adults choose to age in planned retirement communities, we need to prepare to address the unique challenges to nutritional health for older adults so they have the resources and tools to successfully age in place. Further policy and practice implications are also discussed.

Students with Diabetes: Meeting Unmet Needs of Young Adults with Type 1 Diabetes

<u>Paige Wagner, BA, MPH, Ashley Wingert, MPH</u> Bringing Science Home, College of Public Health, University of South Florida Dept. of Community & Family Health

Keywords: Young Adults, Type 1 Diabetes, Access to Care

Objective: The primary objectives of the Students with Diabetes program are (1) to identify health barriers for diabetes management; (2) to identify the barriers of accessing healthcare; (3) to create a social safety net for young adults with diabetes; and (4) to meet the unmet need for convenient, relevant, socially acceptable diabetes education.

Methods: In this study, the quality of clinical healthcare for diabetes management is assessed and compared to the education and support provided by the Students with Diabetes (SWD) program. Surveys and Hemoglobin A1c (HbA1c) glucose measures were collected. N=31

Results: Findings from the surveys collected show that 93% of the sample had access to healthcare services including 1 or more diabetes specialists, but 46.7% said healthcare visits make them feel worse, 40% said they don't "click" with their doctor(s), another 40% explained they couldn't afford the management tools they need. Another 55% reported having >1 distressing diabetes related social interaction in last month. The lack of support and discomfort with their medical providers is somewhat compensated by the support and education offered through the SWD program. 91% of the participants reported feeling more confident managing their diabetes since joining SWD. Similarly, again 91% reported that SWD has helped them feel more positive about their future.

Conclusion: The results indicate improved support of young adults with diabetes can positively impact an individual's ability to manage lifestyle and diabetes needs. Further research will be completed in Spring 2014 to see how SWD involvement impacts diabetes management. This model for health communication is useful for health and chronic disease education on college campuses and in transition health clinics.

Abstract #: 254

Presented by: Heather Williamson, OTR, MBA, Graduate Student

Is Being a Caregiver Related to Health and Well-Being: A Secondary Data Analysis of BRFSS 2010 Caregiver Module

<u>Heather J. Williamson, OTR, MBA¹, Russell S. Kirby, PhD, MS²</u> ¹University of South Florida College of Public Health, Department of Community and Family Health, ²Professor and Marrell Endowed Chair, University of South Florida, College of Public Health, Department of Community and Family Health

Keywords: Family caregiver, caregiver burden, caregiver mental health, caregiver physical health, secondary data analysis

Objective: Family caregivers fulfill a key role in health care and long-term care systems. The aging demographics of the U.S. population will result in a growing reliance on family caregivers. Caregiver health and well-being is important to maintain the caregiving role. The purpose of this study was to explore the impact caregiving has on self-reported health status, health related quality of life, emotional support, and life satisfaction.

Methods: The Behavioral Risk Factor Surveillance System (BRFSS) included an optional Caregiver Module completed by Connecticut and New Hampshire in 2010, which was used in this secondary data analysis. Bivariate and multivariable logistic regressions assessed if being a caregiver was predictive of reporting fair to poor health, physical health concern, mental health concern, activity limitations, minimal to no emotional support, and life dissatisfaction.

Results: Bivariate logistic regression results indicated that caregivers were more likely to report fair or poor health OR=1.33 (95% C.I. 1.10-1.61), physical health concerns OR=1.21 (1.04-1.41), and mental health concerns OR=1.59 (1.37-1.87). Controlling for age, gender, and race, caregivers were more likely to report fair or poor health, OR=1.38 (1.13-1.68) and mental health concerns, OR=1.53 (1.30-1.79).

Conclusion: The caregiving role is associated with mental and physical health outcomes. Caregivers will continue to play an important role in our medical and long-term care systems and more needs to be done to help them maintain their caregiving role including: monitoring caregiver health and wellness through surveillance, implementing and evaluating caregiver health and wellness programs.

Research supported by: No funding support. Project completed for PHC 6197 Secondary Data Analysis course.

Presented by: Ashley Wingert, MPH, Graduate Student

Experiences of Young Adults with Type 1 Diabetes: School, Work, and Relationships

Ashley Wingert, MPH, CPH Bringing Science Home, College of Public Health, Department of Community and Family Health, University of South Florida

Keywords: type 1 diabetes; young adults

Objective: The unique life challenges faced by young adults with type 1 diabetes (T1D) greatly impacts the health of this population, but is rarely discussed in current literature. The purpose of this study was to explore the specific challenges that young adults with T1D experience in regards to academics, work, and relationships.

Methods: Interviews were conducted with 41 participants, ages 18-34, attending the 2013 Students with Diabetes National Conference. The open-ended question design allowed participants to openly share their experiences as desired.

Results: Results indicate that accommodations, support (or lack thereof) from both management and co-workers, physical symptoms of diabetes (e.g. low blood sugar), and discrimination greatly affect the ability of young adult T1Ds to succeed in the workplace. Likewise, the physical symptoms of T1D, academic accommodations, support from professors, issues with transitioning into college, and personal characteristics (e.g. time management) impact the level of academic success. Relationships were largely affected by lack of understanding, support (or lack of) from friends, family, and/or significant other, as well as the presence of a T1D community. Additionally, several themes emerged that were found to be relevant across all areas addressed. These include the decision to disclose one's T1D, feelings of being different, fear of judgment, positive perspectives, finding opportunities to educate others, and psychological impact.

Conclusion: Findings from this study offer information regarding the most salient topics to discuss with young adult T1Ds in both clinical settings and support groups in order to enhance health outcomes and quality of life for this population.

Research supported by: The Patterson Foundation

Abstract #: 256

Presented by: Jacob Bourgeois, BS, Graduate Student

The Characterization of the Neuropathological Consequences of Plac1 Ablation in the Developing Mouse Embryo Jacob Bourgeois¹ (Presenting author), Xiaoyuan Kong¹, Juan Fuentes¹, Ray Harbison², Giffe Johnson², Gary Martinez³, Jose Rey³, <u>Michael Fant¹</u> ¹University of South Florida Morsani College of Medicine, Department of Pediatrics, ²USF College of Public Health, Department of Environmental and Occupational Health, ³Moffit Cancer Center

Keywords: Plac1, Fetal Development, Brain Development, Birth Defects

Objective: Placenta-specific 1 (Plac1) is a paternally-imprinted, X-linked gene that is essential for normal placental development. Interestingly, Plac1 ablation predisposes KO males and Xm-X Hets to an increased risk of lethal postnatal hydrocephalus, suggesting a role for Plac1 for fetal development. The objective of this study was to characterize the effect of Plac1 on brain development.

Methods: A mutant Plac1 mouse model, established on the C57BL/6J background, was studied. Formalin-fixed, paraffinembedded whole mount embryos and brain sections were obtained at various stages of development. Plac1 expression was assessed by qRT-PCR, IHC, and ISH. Brain structure was assessed by histopathological and MRI analysis.

Results: Plac1 expression throughout the fetal brain when assessed by qRT-PCR, IHC, and ISH at E14.5-E18.5. ISH revealed heavier expression in the hindbrain and periventricular regions. MRI analysis of an adult KO brain revealed microcephaly, a dysmorphic cerebellum, and increased heterogeneity of the medulla. H&E staining of the KO brain revealed a smaller cortical mantle and dysmorphia in both cerebellum and hippocampus. IHC analyses using anti-NF-M and anti-NeuN antibodies showed developmental disruptions and reduced neuronal cell numbers. Similarly, anti-NeuN staining of an Xm-X Het revealed decreased neuronal cell numbers.

Conclusion: Plac1 is an X-linked gene that is essential for normal brain development. Plac1 ablation is associated with the disruption of axonal development and decreased neuronal cell number. Plac1 promoters are in part under the control of RxR. Therefore, Plac1-mediated signaling pathways are likely relevant to neuropathies associated with retinoic acid signaling disruptions.

Research supported by: USF inter-departmental resources.

Presented by: Jayme Coyle, MS, Graduate Student

The Assessment of an In-vitro Model for Evaluating the Role of PARP in Ethanol-mediated Hepatotoxicity Jayme Coyle¹, Amora Mayo-Perez¹, Marie Bourgeois, Ph.D.¹, Giffe Johnson, Ph.D.¹, Steve Morris, M.D.², Raymond D. <u>Harbison, Ph.D.</u> ¹Department of Environmental and Occupational Health, College of Public Health, University of South Florida, Tampa, FI; Department of Pathology and Cell Biology, USF Morsani College of Medicine, ²USF College of Nursing

Keywords: In-vitro, Ethanol Toxicosis, HepG2, Poly(ADP-Ribose) Polymerase-1, Hepatotoxicity

Objective: To validate the consistency of the toxicological model, the HepG2 cell line, in ethanol toxicity and to assess the model for investigating PARP-1-mediated cellular death resultant of acute doses of ethanol.

Methods: HepG2 cells were dosed with ethanol at concentrations between 100 mM and 800 mM, and assessed for markers of cytotoxicity; a 50 µM etoposide treatment provided a positive control for apoptotic induction. After a 24 hour incubation period, cell culture medium isolates were quantified for aspartate aminotransferase (AST) activity while cellular viability was quantified via MTT. Additionally, PARP-1 activity in total cell protein lysates was quantified to as a proxy of apoptotic induction at six hours in a simultaneous experiment. All assays were conducted utilizing prepared kits per manufacturer's instructions.

Results: Exposure to graded concentrations of ethanol demonstrated a weak dose-response in cellular viability where only the positive control met statistical significance. AST, a biomarker of hepatotoxicity, revealed a significant response to ethanol toxicosis at 800 mM, equal to that of the positive control. A decreasing trend in PARP-1 activity was detected over dose, though the positive control did not decrease significantly as expected. A time-trend analysis revealed a systematic error which predominantly explained the apparent ethanol-PARP-1 correlation.

Conclusion: The HepG2 model has demonstrated significant insensitivity to ethanol toxicosis while PARP-1 activity did not reveal a dose-dependent influence by ethanol exposure. Therefore, the role of PARP-1 in ethanol toxicosis remains inconclusive.

Research supported by: USF Foundation

Abstract #: 258

Presented by: Kambria Haire, PhD, Graduate Student

Characterizing Pollutant Disparities through Air Monitor Locations Utilizing Geographic Information Systems (GIS) Kambria Haire, Raymond Harbison, Giffe Johnson University of South Florida College of Public Health, Department of Environmental & Occupational Health

Keywords: Pollution, GIS, Air Monitoring, Respiratory

Objective: Conduct a descriptive study to determine if the presence of air monitors can help characterize areas within Florida with pollutant disparities that may impact adverse health outcomes through the use of Geographic Information Systems (GIS).

Methods: Geographic data on air monitor locations for Florida, and county data for Florida, from 2011 was gathered from the Florida Geographic Data Library (FGDL) with the Metadata Explorer. Health outcomes for age-adjusted lung cancer mortalities and chronic lower respiratory disease for each county counts and rates information were gathered based on population from 2010-2012 from FloridaCHARTS. Geographic data on air monitors and county data were used to create a map overlay, and were merged with data on health outcomes.

Results: A total of 36 counties monitor air contaminant concentrations, and 31 counties did not contain any air monitors. For lung cancer death rates, Miami-Dade County had the lowest rate with 30.00 per 100,000, while Union County had the highest rate with 93.5 per 100,000. For chronic lower respiratory disease, hospitalization rates for Flagler County had the lowest rate with 179.7 per 100,000, while Okeechobee County had the highest rate with 892.8 per 100,000. Both Union and Flagler counties did not contain any air monitors.

Conclusion: Map configurations show urban counties have more air monitor sites, and these air monitor sites are located within close proximity to one another. The presence of air monitors in Florida helps to identify insufficient data in rural areas. Data gaps in rural areas hinder the ability to evaluate the role of air pollutants in the development of adverse health outcomes in these areas, despite per capita increases in some respiratory outcomes.

Presented by: Vikas Jindal, MD, Graduate Student

Hospital Visits and Cost in the U.S. for Firearm-Related Injuries, Over the Last Decade

V.JIndal,M.D.,H.Salihu,M.D.,Ph.D T.Truncale,D.O.,M.P.H., E.Naik,M.D.,PhD., A.Muktar, M.D.,DrPH., University of South Florida, College of Public Health, Dept. of Environmental & Occupational Health

Keywords: Gunshot, Firearm injuries related cost, Homicidal, Suicidal, firearm-related hospitalization

Objective: To evaluate hospitalization and cost burden of firearm-related injuries in the United States over the last decade. We explored the following research questions: (1) Is there any increase in prevalence of firearm injuries over the last decade? (2) What is the cost associated with firearm-related hospitalization in the United States? (3) Finally, are their racial/ethnic variations related to these injuries and their costs?

Methods: This is a descriptive cross-sectional study. A stratified sample of 54,875 hospital discharges were extracted from the National Inpatient Sample Database (NIS-HCUP) using E Codes for firearm related injuries. We performed trend analyses to determine the cost and prevalence of the firearm related injuries.

Results: An estimated 268,639 firearm-related hospital discharges were observed from 2001-2009. Homicidal intent was the leading cause of firearm related injuries, followed by accident. Hispanic and blacks are more likely to injure by firearms as compared to white population. Young adults aged 18-34 were more prone to get injured than children and the elderly. Male sex, urban residence and being black or Hispanic were the main risk factors for firearm-related hospitalizations. The average hospitalization cost for firearm-related injuries was \$ 17,700 totaling \$528 million/year. The trend had remained constant over the past decade.

Conclusion: Firearm-related injuries and associated costs remain a major source of hospital-related expenditures in the United States

Research supported by: This research is supported by NIOSH SERC-COPH-USF Department of Environmental & Occupational, and Department Epidemiology & Biostatistics.

Abstract #: 260

Presented by: Erin Pulster, PhD, Graduate Student

Spatial Distribution and Sources of Atmospheric Polycyclic Aromatic Hydrocarbons Surrounding an Active Oil Refinery in Curaçao

<u>E.L. Pulster¹, F.M. Jaward², R.D. Harbison², D.L. Wetzel¹</u> ¹Mote Marine Laboratory, Sarasota, FL; ²University of South Florida College of Public Health, Department of Environmental and Occupational Health, Tampa, FL

Keywords: Polycylcic aromatic hydrocarbons, oil refinery; Curacao

Objective: Limited information is available on polycyclic aromatic hydrocarbons PAH contributions from active oil refineries to ambient air. As such, efforts have been made to assess PAH contributions from the Isla Refineria located in Schottegat Harbor, Willemstad, Curaçao.

Methods: Passive air samplers containing polyurethane foam (PUF) disks were deployed in triplicate at 15 sites around the circumference of the Schottegat Harbor for ~9 weeks in the spring of 2011 (28 February - 6 May). PUF disk samples were extracted using methylene chloride by PLE and cleaned up using silica column chromatography and GPC. Sixty one PAHs were quantified and confirmed on an Agilent 7890A gas chromatograph coupled with a 5975C mass selective detector.

Results: Calculated atmospheric PAHs ranged from 0.30 to 178.62 ng/m3. As expected, concentrations decreased with increasing distance from the active refinery. In addition, concentrations increased from the east side of the refinery to the west side due to the prevailing trade winds. These concentrations are generally consistent with levels found in other urban areas globally. However, locations closest to the refinery and downwind were relatively high (103-179 ng/m3) and among some of the highest reported air concentrations worldwide.

Conclusion: One site (Habaai) downwind from the refinery approached the recommended guidelines for B[a]P and exceeded the fluoranthene guidelines with calculated concentrations ranging from non-detect to 0.1 ng/m3 and 3.5 ng/m3, respectively.

Research supported by: MINA Fonds Nederlandse Antillen, Dir of Public Health, Dept of Environment, Curaçao and Mote Marine Laboratory, Sarasota, FL

Analysis of Risk Factors in Food Facilities in the City of Minneapolis

<u>Davinderjit Singh</u> Department of Environmental and Occupational Health, College of Public Health, University of South Florida, Tampa, Fl

Keywords: Risk based inspection, violations, food facilities, hand washing

Objective: To analyze violations in food facilities in the City of Minneapolis to inform risk management on sources of potential food contamination.

Methods: Risk-based inspection reports from January 2008 to December 2011 were used to create and evaluate risk categories. Each inspection report has 58 factors on which violations can be marked. Analyzing the violations required categorization of various risk factors in sub categories of Employee health, Food safety, Active managerial control, Facility operation, Chemical handling, Licensing and Compliance.

Results: The most common facilities inspected were restaurants, restaurants with liquor for sale and food manufacturers. Food safety and protection had the highest number of codes under which a violation was cited (25). When compared for each outcome variable, facility operation had the highest number of absolute violations (29401), licensing and compliance had least number of violations (676), and violations per code were most common for active managerial control (375 per code).

Conclusion: Improper hand washing was the most common violation cited. Behavioral change regarding proper hand washing would result in an estimated 11 percent decrease in total violations. Even though there was an increase in out of compliance reports, absolute number of violations cited in individual reports decreased. Inspectors marked more violations for managerial control even though absolute number was higher for food safety and protection. Risk 1 facilities had a higher number of violations while Risk 2 had more violations per inspection suggesting that higher risk category does not lead to more total violations. The restaurants which serve liquor had a higher number of violations per inspection than restaurants without liquor.

Abstract #: 262

Presented by: Kyle Vogel, MS, Graduate Student

Characterization of waste anesthetic gas exposures to veterinary workers in the Tampa Bay area <u>Presenting Author: Kyle Vogel Affiliation:</u> SERC Invitee, University of South Florida, College of Public Health Dept. of Environmental & Occupational Health

Keywords: Isoflurane, veterinarians, anesthetic gas exposure

Objective: Characterize waste anesthetic gas exposures that veterinarians and veterinary technicians receive when conducting surgery in clinics.

Methods: A survey will be administered to the lead veterinarian at 5 different facilities to determine background information on the clinic, including frequency of surgical operations, type of anesthetic gas used, and control methods used to collect waste gases. Area sampling will then be conducted during surgery with a Miran SapphIRe XL to determine which worker at the facility receives the highest exposure to isoflurane during surgery. Finally, OSHA Method 103 will be used to sample in the breathing zone of this worker believed to have the highest exposure.

Results: Isoflurane exposures are expected to exceed the 2 ppm limit for halogenated anesthetic agents with exposures higher in facilities that do not perform as many surgeries. The individual with the highest exposure is expected to be the veterinary technician.

Conclusion: Conclusions will be reached concerning differences in high versus low volume surgery clinics. Exposures to the veterinary personnel will be characterized based off the data.

Research supported by: The University of South Florida's Department of Environmental and Occupational Health, The National Institute of Occupational Safety and Health

Presented by: Omonigho Bubu, PhD, Graduate Student

Predictors, Prevalence and Incidence of Sleep Complaints in Hispanic vs. Non-Hispanic Elders: Findings from the Health and Retirement Study

<u>Omonigho Michael Bubu, Lindsay Womack, Skai W. Schwartz</u>. College of Public Health, Department of Epidemiology and Biostatistics, University of South Florida, Tampa, FL

Keywords: insomnia in older adults; epidemiology; aging; Hispanic

Objective: To determine predictors, prevalence and incidence of sleep complaints in Hispanic vs. Non-Hispanic elders

Methods: Data on 1645 Hispanic and 14848 non-Hispanic elders aged 55-109 were extracted from the 2006 and 2010 waves of the Health and Retirement Study (HRS). Prevalence of sleep complaints (trouble falling asleep, waking during the night, waking up early or un-refreshing sleep) was obtained from 2006 wave. Incidence of new sleep complaints was obtained from 2010 wave for participants (N=3,850) with no sleep complaints in 2006 who were followed until 2010. Multivariate logistic regression determined Hispanic association with presence of sleep complaints, development of new sleep complaints and other potential predictors of incidence.

Results: In 2006 the prevalence of 3 or more sleep complaints was 30.9 vs. 27.3 for Hispanic and non-Hispanic respectively (p<0.001). Hispanics were more likely to develop new sleep complaints over the next 4-years after adjusting for age, sex, race and education (OR=1.60; p<0.001). Similar associations were seen for every 10-year age group, both gender and by strata of race or education (p<0.001). Other predictors of incident sleep complaints included having less than high school diploma, reduced self-rated health, recent unemployment (other than retirement), and not losing weight (p<0.01 for all). Recent retirement was protective (p<0.05), but was muted when adjusted for other factors.

Conclusion: Older Hispanics are more likely to develop incident sleep complaints with increasing age. These results may reflect differing lifestyle (e.g. being caretakers) or ethnic differences in risk factors (e.g. Diabetes) associated with sleep complaints. Understanding these factors may aid interventions to improve sleep problems.

Abstract #: 264

Presented by: Pengfei Li, MPH, Graduate Student

Hillsborough County Mosquito Larvae Data Analysis for Selected Months of 2011 and 2012

Pengfei Li¹, Jose Hasemann², Brian Trang², Aurora Sanchez-Anguiano², Azliyati Azizan² and Yangxin Huang¹ ¹Department of Epidemiology and Biostatistics, ²Department of Global Health. College of Public Health, University of South Florida, Tampa, FL

Keywords: dengue, mosquito, mixed model

Objective: This study examined the association of dengue -mosquito vectorAedes aegypti larvae number with environmental factors in Hillsborough County at Florida. Ten sampling sites were longitudinally surveyed from October 2011 to May 2012. Mosquito Ae.s aegypti number at each site was measured three times per month using standard ovi position traps. The environmental factors data including vegetation cover, visual_shade, and site_trap distance to residence were obtained for each site.

Methods: The raw data were examined and manipulated using SAS software, data distribution and descriptive analysis of number of larvae were performed. To predict the number of larvae, SAS mixed procedure was used in this study to establish a linear mixed-effects model. The model's flexibility enables the mixed procedure to analyze more types of repeated longitudinal data.

Results: The results showed that the number of Ae. aegypti larvae was highly associated with the sample collection time points, indicating time or season play an important role. However, the Ae. aegypti larve presence was not significantly associated with vegetation cover, visual_shade and site_trap distance to residence.

Conclusion: As there is no licensed vaccine available, vector control is the first line of defense against dengue. Our analysis demonstrates the importance of season climate in predicting Ae. aegypti larvae number and will help enhance the efficacy of mosquito control activities whenever possible.

Presented by: Patricia Medina-Ramirez, BS, Graduate Student

Exploring Type 2 Diabetes Management Beliefs and Practices in a Mexican Farmworker Community

Patricia Medina-Ramirez, BS^{1,2}, Nora Brickhouse Arriola, BA^{3,4}, Chrystal Smith, MPH, PhD⁵, Dinorah Martinez Tyson, MPH, PhD³ ¹University of South Florida College of Public Health, Department of Epidemiology and Biostatistics, and, ²Department of Global Health, and, ³Department of Community & Family Health, ⁴USF Department of Anthropology ⁵USF Department of Sociology

Keywords: diabetes, tertiary prevention, chronic disease self-management, cultural belief models, community-based research

Objective: Latino farmworkers carry a disproportionate burden of type 2 diabetes and face numerous challenges to accessing healthcare. The objective of this study is to explore knowledge and beliefs about type 2 diabetes, self-management practices, and barriers to care among Mexicans in a Florida farmworker community.

Methods: This study uses a mixed methods approach. A total of 30 in-depth ethnographic interviews were conducted in a community clinic with diagnosed diabetes patients. Interviews utilized free list elicitation and open-ended questions, as well as demographic questions. Participants' most recent A1C results were obtained from medical records, and the weight and height were measured to calculate participants' BMI.

Results: Most participants are knowledgeable about recommended lifestyle modifications for diabetic patients and attempt to incorporate them into their daily routine; however, only 25% show recommended glycemic control (A1C ≤7%), and 86.7% are overweight (BMI ≥25). Participants hold conflicting cultural belief models about diabetes and use a wide range of complementary and alternative medicines (CAM) to manage their glucose levels and symptoms. Barriers to self-management include limited income to pay for high cost of glucometer test strips and other diabetic supplies, as well as difficulty adhering to the recommended diabetic diet and exercise regimen.

Conclusion: In order for Latino farmworkers, an underserved subpopulation, to improve their diabetes self-management, barriers to diabetic care such as limited income, and the high cost of diabetic supplies must be addressed.

Research supported by: New Researcher Grant, USF System Internal Awards Program, PI: Martinez Tyson

Presented by: Malinee Neelamegam, BS, Graduate Student

Quality of Stroke Care in Malaysia: Understanding Key Performance Indexes from The National Stroke Registry of Malaysia

<u>Malinee Neelamegam, Sharad Malavade, Irene Looi</u> University of South Florida College of Public Health, Department of Epidemiology and Biostatistics

Keywords: Stroke, Stroke Unit, Key Performance Index

Objective: Key performance index based stroke care has been shown to improve functional outcomes in stroke victims. We aim to describe and assess the performance of two community hospitals in Malaysia and establish the association between stroke care performance and patient outcome in these sites.

Methods: Patient data from January 2010 to December 2011 was retrieved from the National Stroke Registry of Malaysia. Eight standard practices indexes were assessed. Patient outcome was assessed based on the composite outcome of mortality and length of hospital stay; and Modified Rankin Scale (MRS) score at discharge. All eight indexes were tested towards the outcome. However indexes for deep vein thrombosis prophylaxis and anticoagulation therapy for atrial fibrillation patients were excluded from the multivariate analysis due to the small sample size of these subgroups.

Results: Of the 1273 patients, majority were of Malay ethnicity with mean (SD) age of 63.6 (11.6). Two performance indexes, anti-thrombotic therapy upon discharge and statin upon discharge showed no improvement over the 2 years in these hospitals. In this period, significant improvement was observed in two performance indexes, deep vein thrombosis prophylaxis (p value= <0.001) and dysphagia screening (p value=<0.001). Multivariate analysis showed that only anti thrombotic therapy contributed significantly to patient outcome.

Conclusion: Patients discharged on anti-thrombotic therapy were 2.7 times more likely to be stroke survivors discharged from hospital care within 5 days. They were also 2.2 times more likely to have an MRS score between 0 and 2 at discharge compared to patients not receiving anti-thrombotic therapy at discharge.

Research supported by: National Stroke Registry, Malaysia

5-HTTPLR and COMT Genes are Predicitve of Intimate Partner Violence

<u>Presenting Author: Andrew Oustimov</u> University of South Florida College of Public Health, Department of Epidemiology & Biostatistics

Keywords: 5-HTTLPR, COMT, IPV, aggression, genetic marker

Objective: The objectives of this study were to assess the relationship between the following two genes, the serotonin transporter gene (5-HTTLPR) and the Catechol-O-methyltransferase gene (COMT), and intimate partner violence (IPV), as well as to investigate the possibility of a genetic overlap among its victims and perpetrators, utilizing data from a population-based community cohort.

Methods: Subjects, drawn from a community based longitudinal study (n = 320), were assessed for intimate partner violence in 1999 (mean age 31), and genotyped for 5-HTTLPR and COMT in 2010. Our analysis compared the likelihood of being involved in IPV, across genotypic variants of the two genes.

Results: Among males, carriers of the "low expressing" genotypes (S/S, S/Lg, Lg/Lg) were more likely to find themselves as both, a victim (P < 0.001, OR = 4.49 (95% CI: 1.70 – 11.87)) and a perpetrator (P = 0.033, OR = 2.63 (95% CI: 1.02 – 6.77)) of IPV. Also, female carriers of the high activity genotype (Val/Val) exhibited significantly greater odds of perpetrating intimate partner violence in the 12 months prior to assessment (OR=2.29, 95% CI: 1.10-4.74, p=.026).

Conclusion: Results suggest, that among males, the "low expressing" variants of the 5-HTTLPR polymorphism are significantly associated with an increased risk for perpetrating, as well as for becoming a victim of IPV. While female carriers of the "high activity" (Val/Val)variant of COMT gene are at an increased risk of perpetrating IPV. This is the first study to link the 5-HTTLPR to both sides of this dangerous phenomenon, providing evidence of a shared genetic etiology of the victim-offender overlap, while confirming previous associations between the risk for general aggression and intragenic variation in the COMT gene.

Abstract #: 268

Presented by: Shitaldas Pamnani, MPH, Graduate Student

Amount and Duration of Alcohol Consumption and Risk of Adult Glioma: Results from Southeastern Regional Study of Adult Brain Tumors

Shitaldas J. Pamnani^{1,2}, Kathleen M. Egan², Zachary J. Thompson², Gabriella M. Anik² ¹College of Public Health, Department of Epidemiology and Biostatistics, University of South Florida, ²Department of Cancer Epidemiology, H. Lee Moffitt Cancer Center & Research Institute

Keywords: alcohol consumption, brain tumors, glioma, case-control study, risk factors

Objective: Southeastern Regional Study of Adult Brain Tumors is one the largest case-control studies carried out to understand etiologic risk factors of adult brain tumors in U.S. and we tried to explore the association between alcohol consumption and risk of adult brain glioma.

Methods: A total of 1249 glioma cases and 1369 controls were included in the study. Glioma cases were obtained from five leading cancer centers in Southeastern US. Cases diagnosed within previous 3 months were enrolled in the study for the enrollment period of December 2004 to June 2012. Community controls were identified by SDR- Sampling Services. Demographic information and alcohol consumption were recorded through telephone interview into machine readable forms.

Results: Alcohol consumption of \geq 24 grams/day (>2 bottles/day) was positively associated with increased risk of glioma in unadjusted model, with OR 1.70, 95% CI (1.28, 2.28), p value of 0.003 and in adjusted model, with OR 1.45, 95% CI (1.06, 1.97), p value 0.018. A separate analysis for Non-glioblastoma tumors indicated stronger adjusted OR of 2.36, 95% CI (1.56, 3.58), p < 0.001; while glioblastoma (GBM) tumors (Grade IV gliomas) did not have statistically significant results. Analysis for beverage specific alcohol consumption indicated higher risk associated with beer consumption for glioma and Non- GBM, while reduced risk associated with wine consumption for glioma and GBM tumor.

Conclusion: Alcohol consumption, especially use of beer, is associated with increased risk of adult brain glioma and lower grades non-GBM tumors.

Research supported by: Department of Cancer Epidemiology, H. Lee Moffitt Cancer Center & Research Institute

Maternal Diabetes Mellitus and the Risk of Childhood Mortality among Children with Birth Defects: a Large Retrospective Cohort Study

<u>Shams Rahman¹, Wendy N. Nembhard¹, Alfred Mbah¹, Mary K. Ethen²</u> ¹University of South Florida, College of Public Health, Department of Epidemiology and Bio-statistics, ²Birth Defects Epidemiology and Surveillance Branch, Texas Department of State Health Services

Keywords: Maternal diabetes; birth defects; childhood mortality

Objective: To examine the association between maternal diabetes mellitus (DM) and the risk of childhood mortality among children with birth defects, and to assess whether this association varies by race/ethnicity.

Methods: This was a retrospective cohort study of mothers who gave birth to children with birth defects between Jan 01, 1999 and Dec 31, 2008 in Texas. All cases were ascertained from the Texas Birth Defect Registry. Maternal DM was ascertained from hospital, medical, and vital records.

Results: No significant difference for childhood mortality was observed among birth defect children of ever-diabetic mothers compared to children of non-diabetic mothers Hazard Ratio Adjusted (HRa)=0.97; 95% confidence interval (CI) [0.87–1.08]. Maternal DM Type1 was associated with decreased risk of childhood mortality HRa=0.69[95%CI:0.47–1.01]. Maternal DM Type2 and DM unspecified was associated with insignificant elevated risk of childhood mortality among children with birth defects HRa=1.11 [95%CI: 0.72–1.71] and HRa=1.14; [95%CI: 0.88–1.46] respectively. We noticed a pattern of elevated risk for children with birth defects born to NH-black mothers in all groups of DM. Ever DM: HRa=1.05 [95%CI: 0.79–1.39]; DM Pre-pregnancy: HRa=1.50 [95%CI:0.21–10.73]; DM during Pregnancy: HRa=1.74 [95%CI: 1.00–3.03]; DM Type2: HRa=1.24 [95%CI: 0.31–4.96]; and DM Unspecified: HRa=1.67 [95%CI: 0.94–2.97]. Birth defects count, maternal age, maternal education, infant sex and gestational age were significant predictors for childhood mortality among children with birth defects in our cohort.

Conclusion: Maternal DM (gestational and pre-gestational) did not significantly increase the risk of childhood mortality in our cohort. However, racial disparity may exist for this association.

Abstract #: 270

Presented by: Yuri Sebastião, MPH, Graduate Student

Self-Reported Hypertension in The Villages: Prevalence and Associated Factors in a Retirement Community of Central Florida

<u>Yuri V. Sebastião¹, Carla VandeWeerd², Sarah Fishleder^{1,3}, Jaime Corvin⁴</u> ¹Department of Epidemiology & Biostatistics, College of Public Health, University of South Florida, Tampa, FL, ²Department of Community & Family Health, USF College of Public Health ³Department of Anthropology, USF College of Arts & Sciences, ⁴Department of Global Health, USF College of Public Health

Keywords: Blood pressure; Aging; Elderly; Middle Aged; Chronic disease

Objective: Although the majority of older Americans are affected by hypertension, the leading risk factor for heart disease and stroke, few studies have described the occurrence of this condition in the increasingly popular age-restricted retirement communities. We assessed the prevalence of hypertension and associated factors in The Villages, a planned retirement community in Florida.

Methods: The study utilized data from 31,577 respondents of The Villages health survey, which was conducted in 2012 among residents aged 55 and older. Logistic models were used to identify lifestyle factors and conditions independently associated with self-reported hypertension in men and women.

Results: Just over a quarter (28.4%) of respondents reported to have hypertension. No difference in the overall prevalence of hypertension between men and women was observed, although an increasing trend with age was observed in women only. Race other than white, higher BMI, daily consumption of 3 or more alcoholic beverages, presence of diabetes and heart problems, minimal physical activity in either gender, in addition to older age in women, were independently associated with hypertension.

Conclusion: These findings indicate that hypertension is an important public health problem in The Villages. Preventive efforts should promote excess weight loss and physical activity. The observed prevalence, although a likely underestimate, could be an indication that Villagers have lower hypertension-related risk of cardiovascular disease (CVD) than older Americans. Future prospective follow-up of this population and utilization of blood pressure measurements to assess hypertension control rates and risk of developing CVD are needed to confirm this hypothesis.

Presented by: Matthew Strohhacker, BA, Graduate Student

Prevalence and Associated Factors of Dementia in an Active Retirement Community

<u>Matthew A. Strohhacker¹, Carla VandeWeerd², Heather Blunt², Yuri Sebastiao¹, Ngozi Agu², Jaime Corvin² ¹Department of Epidemiology and Biostatistics, College of Public Health, University of South Florida, Tampa, FL, ²Department of Community and Family Health, USF College of Public Health</u>

Keywords: dementia, cross-sectional, psychological, behavioral, aging

Objective: As the percentage of older adults in the US continues to increase, prevalence of dementia is drastically increasing. Evaluation of socio-demographic, psychological and behavioral factors associated with dementia in large populations is limited. This study aims to examine associated factors of dementia using data from the USF Health in The Villages study, a sample of older adults living in an active retirement community in central Florida (N>89,000).

Methods: Cross-sectional data from the USF Health in The Villages study was utilized for the current study (N=31,119). Bivariate analyses were completed across socio-demographic, psychological and behavioral variables from a comprehensive health questionnaire sent to all residents of The Villages in 2012. Multiple logistic regression was used to identify independent associated factors of dementia.

Results: Results from the multiple logistic regression indicate strong associations between dementia and gender (males), increasing age (76+ years), minimal physical activity, depressive symptoms, high nutritional risk, alcohol consumption frequency (never) and alcohol-related illness (alcoholism).

Conclusion: Findings suggest that individuals diagnosed with dementia are at increased nutritional, physical, and psychological risk, reinforcing the importance of these factors for healthy aging. We recommend annual depression screening at regular clinical visits for patients with dementia. We suggest nutritional and physical activity education for older adults with dementia. Additionally, we recommend implementation of community-based programs in retirement communities to target individuals with dementia that may be at increased risk for nutritional, physical and psychological health.

Abstract #: 272

Presented by: Lindsay Womack, MPH, Graduate Student

Very Premature Live Births in Florida: Does Birth Place Still Matter?

Lindsay S. Womack¹, William M. Sappenfield, MD, MPH¹, John S. Curran, MD², Judette Louis, MD, MPH^{2,3} Linda A. Detman, PhD¹ ¹Lawton & Rhea Chiles Center for Healthy Mothers and Babies at the University of South Florida, ²USF Morsani College of Medicine, ³University of South Florida College of Public Health, Department of Community and Family Health

Keywords: Maternal and Child Health, neonatal intensive care, infant mortality

Objective: Perinatal guidelines, based on studies in the 1990s, recommend that very premature infants be delivered at specialized perinatal hospitals with neonatal intensive care units. This study's purpose is to examine whether this recommendation is associated with higher mortality rates among these infants in Florida's de-regionalized perinatal care system: Level 3 hospitals compared to Level 1 and 2.

Methods: The study includes 10,453 infants born at 24-29 weeks gestation, using Florida's 1998-2007 vital records linked to hospital inpatient records. Risk ratios (ARR) and 95% confidence intervals (CI) for mortality rates <90 days were calculated using generalized estimating equations for multinomial logistic regression, adjusting for medical risk factors and hospital, maternal, and infant characteristics.

Results: Nearly 17% of infants died during the first 90 days. Mortality risk was higher at Level 2 hospitals with 25 or more very premature births per year, compared with Level 3 hospitals with neonatal fellowship training programs (ARR: 1.31; CI: 1.01, 1.72). Although higher, mortality risks were not significantly higher in Level 1 hospitals or Level 2 hospitals with <25 very premature patients per year. Higher mortality risk was also associated with low birth weights, low gestational ages, no prenatal care (ARR: 1.32; CI: 1.07, 1.63), and hospitals with >30% Medicaid births (ARR: 1.22; CI: 1.02, 1.47).

Conclusion: These findings are supportive of current perinatal guidelines. Very premature births have a survival advantage in hospitals with higher perinatal care capabilities. In Florida, birth place does still matter.

Presented by: Andrea Bingham, PhD, Graduate Student

Host Feeding Patterns of Potential Vectors of Eastern Equine Encephalitis Virus from an Endemic Focus in Florida During the Winter Months

Andrea M. Bingham, USF Nathan D. Burkett-Cadena, UF Hassan K. Hassan, Thomas R. Unnasch, University of South Florida, College of Public Health, Department of Global Health

Keywords: arbovirus, host preference, wading birds, winter

Objective: Florida is the only state in the USA in which transmission of Eastern Equine Encephalitis virus (EEEV) occurs throughout the winter months. The dynamics of winter transmission of Eastern equine encephalitis virus (EEEV) in Florida were examined to elucidate potential vectors and associated vector-host interactions.

Methods: Mosquito pool testing for viral RNA, blood meal analysis of blood-engorged mosquitoes, and avian point counts were used in this study.

Results: EEEV was detected in two species of mosquitoes, Culieta melanura and Anopheles quadrimaculatus, both in the month of February. Culex erraticus was the most abundant mosquito captured in the study. The host feeding patterns of eight mosquito species were identified. Mammalophilic mosquito species fed upon nine different hosts, feeding primarily upon white tailed deer and humans. Cs. melanura, thought to be the primary enzootic vector for EEEV also fed occasionally on mammalian hosts somewhat, primarily humans. All blood-fed mosquito species fed upon avian hosts to some extent, with a total of 35 avian species being identified as hosts. The majority of these avian species were water/wading birds belonging to the order Ciconiiformes or Suliformes (formerly Pelecaniformes). Cs. melanura fed on a large proportion of water birds (39.6%) during the winter months. The four most prominently fed upon avian hosts were the black-crowned night heron, yellow-crowned night heron, anhinga, and great blue heron. The white ibis and whistling duck were underutilized.

Conclusion: These findings suggest that vector species for EEEV may preferentially feed upon wading birds during the winter months and these species should be investigated to further elucidate their role in the transmission cycle.

Research supported by: NIH

Abstract #: 274

Presented by: Shanna Bolcen, BS, Graduate Student

Parasite and Vector Identification from Canine Ocular Lesions

Shanna Bolce, Hassan Hassan, Thomas Unnasch USF Global Health Research, University of South Florida College of Public Health, Department of Global Health

Keywords: Onchocerca, parasite, vector, identification

Objective: Onchocerca is a genus of roundworm most commonly associated with the human infection onchocerciasis, or river blindness. While typically a zoonotic infection of ungulate populations, canine cases (Onchocerca lupi) have been identified in the United States and Greece. In 2012, Los Angeles County, Veterinary Public Health Program identified 3 cases of Onchocerca sp infections in domestic canines. Samples from the ensuing blackfly collections were sent to the Global Health Infectious Disease Research Unnasch Laboratory for parasite isolation and vector species identification.

Methods: Species-specific primers were designed and optimized for O. lupi using a non- specific cytochrome oxidase (COI) gene target (689bp) previously utilized in Onchocerca identification as a base. A secondary, nested PCR primer set (115bp) was additionally designed to aid in the screening process. Extracted DNA samples from the collected blackflies were screened for the presence of the parasite and positive samples were further tested against the larger fragment for confirmation.

Results: The primers designed for the study were determined to be specific to O. lupi and not cross-reactive with other Onchocerca species or Dirofilaria immitis. Of the 213 blackflies screened, 6 samples tested positive for parasite presence. The blackfly species was identified as Simulium spp.

Conclusion: The presence of the O. lupi parasite in the blackfly population implicates the likely vector in the LA County cases. While the blackfly identification was unable to be determined to the species level, the identification of Simulium spp. confirms the typically suspected vector in Onchocerca infections. Concerns of cross-species transmission make O. lupi an important parasite for public health study.

Presented by: Miriam George, MPH, Graduate Student

Identifying Minimal Reactive Epitopes On The Surface Of Plasmodium Vivax Duffy Binding Protein Reactive With Neutralizing Monoclonal Antibodies

<u>Miriam T. George¹, Jesse L. Schloegel³, Francis B. Ntumngia¹, Samantha J. Barnes¹, Christopher L. King², Joanne L. <u>Casey³, Michael Foley³, John H. Adams¹</u> ¹Department of Global Health, University of South Florida College of Public Health, Tampa Florida, ²Center for Global Health & Diseases, Case Western Reserve University, Cleveland, Ohio, ³Department of Biochemistry, La Trobe University, Victoria, Australia.</u>

Keywords: Malaria, Vaccine, Plasmodium vivax, Duffy Binding Protein, Epitope mapping

Objective: Plasmodium vivax Duffy Binding protein region II (PvDBPII) is an essential ligand for reticulocyte invasion, thereby making this molecule an attractive vaccine candidate to protect against asexual blood-stage P. vivax. Similar to other blood-stage vaccine candidates, DBP allelic variation eliciting a strain-specific immunity may be a major challenge for development of a broadly effective vaccine against vivax malaria. This study aims to identify conserved epitopes of anti-DBP neutralizing monoclonal antibodies (mAbs) by phage display technology to help design a strain-transcending vaccine.

Methods: Crystal structure of PvDBPII consists of 2 α -helical bundles with an antiparallel β -hairpin near the N-terminus and may be assigned into three subdomains delineated by six disulphide bonds. Using a phage display approach, we expressed the various subdomains and combination of subdomains in their correctly refolded and disulphide bonded conformation on the surface of the M13 filamentous phage. Biopanning was used to screen phage clones reactive with anti-DBP mAbs. In a second strategy, the anti-DBP mAbs were also used to screen against a DBPII gene fragment and a random peptide library to identify the minimal epitopes bound by these mAbs.

Results: All inhibitory mAbs (3C9, 2H2, 2D10, 2C6) bound to subdomain 3 containing fragments of DBPII, while mAb3D10, a non-inhibitory antibody bound to subdomain 1. Using the gene fragment and random peptide libraries, we have defined the minimal epitopes for mAbs 3C9 and 3D10.

Conclusion: Information derived from this study will contribute to our understanding of the specific targets of neutralizing antibodies on DBPII for inclusion in a vaccine designed to protect against Plasmodium vivax malaria.

Research supported by: NIH grant 2R01Al064478-07

Abstract #: 276	Presented by: Emily Lupton, BS, Graduate
	Student

Comparison of Gliding Activity Over Time of Plasmodium sporozoites incubated in Multiple Dissection Medias <u>Emily Lupton¹, Alison Roth¹, Jetsumon Prachumsri², John Adams¹</u> ¹University of South Florida College of Public Health, Department of Global Health, Tampa Fl, ²Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Keywords: malaria sporozoite gliding

Objective: Many unknowns still exist regarding the liver stage forms of malaria causing Plasmodium species. To investigate the liver stage invasion and development, malaria parasites need to be preserved in the infectious sporozoite form to prevent maturation during mosquito dissection. Our goal is to create a dissection buffer that keeps sporozoites alive and infectious to allow for longer dissection times and sporozoite transport.

Methods: Plasmodium sporozoites, isolated from Anopholene mosquitoes, were added to 4 experimental and 1 control buffers. Gliding assays were performed on sporozoites from each buffer at time 0, 4, 8, and 24 hours post dissection. Buffers consist of different variations of Hanks Balanced Salt Solution (HBSS), RPMI 1640, and Grace's Insect Media (GIM). Gliding percentages were calculated for 15-20 fields of vision per buffer and time point.

Results: At time 0, RPMI/3% BSA had the highest average gliding percentage (65%) compared to other buffers, then dramatically decreased to a gliding percentage lower than all other buffers at 4-hours (28%). Both variations of HBSS/3% BSA (with and without glucose) had comparable initial gliding percentages at time 0 (53%, 58%), and decreased similarly over time. GIM/3% BSA had the lowest 0 hour experimental buffer gliding percentage (44%), but had a significant increase to 56% by 4 hours, and remained at 56% through 8 hours. GIM also had a similarly high gliding percentage by the 24-hour time point (22%) compared to HBSS/3% BSA/glucose.

Conclusion: Our variation of GIM/3% BSA best preserved sporozoites over time based on gliding percentages.

Research supported by: Bill and Melinda Gates Foundation (Grant # OPP1023643)

Presented by: Steven Maher, BS, Graduate Student

A Liver Sinusoid Device for Stable Primary Hepatocyte Culture and Plasmodium Liver Stage Development Steven P. Maher^{1,} Richard B. Crouse¹, Amy J. Conway¹, Naresh Singh², Emilee C. Bannister¹, Anil Kumar H Achuta¹, Joseph D. Cuiffi¹, John H. Adams², Dennis E. Kyle², Wajeeh M. Saadi¹ ¹Bioengineering Center at USF, Charles Stark Draper Laboratory, Tampa, FI, ²Department of Global Health, University of South Florida, College of Public Health, Tampa, FI

Keywords: microfluidic liver culture Plasmodium liver stages Primary human hepatocytes

Objective: Malaria remains one of the world's most resilient public health problems, fighting the spread of this disease has been hampered due to inadequate in vitro culture protocols for the liver stages of Plasmodium falciparum and P. vivax, two causative agents of malaria. Here we describe a novel dual-chambered microfluidic device designed to serve as an improved liver-stage culture platform.

Methods: Devices are fabricated in poly(dimethylsiloxane) and incorporate a PDMS membrane with 10 µm pores separating two microfluidic channels. Primary hepatocytes are concentrated to 10,000 cells per µl and are injected into a collagen-coated channel to initiate culture. Time course experiments include analysis by microscopy, quantification of hepatic metabolites by ELISA, or infection of hepatocytes with freshly isolated Plasmodium sporozoites.

Results: This device incorporates key elements of the in vivo microenvironment such as spatial cell organization, media flow, and cell co-culture. Individual analysis of these factors reveals that spatial confinement of the channel helps to promote hepatocyte architecture and stable primary phenotype expression. Optimized infection conditions with as few as 10,000 parasites yield several developing liver forms within each device.

Conclusion: This culture system is essential for studies of complete development of Plasmodium, as hepatocytes alone do not retain their architecture or phenotypes long enough to allow for 7-10 days of parasite development within their host cells. Serving as a functional Plasmodium liver-stage model, we aim to use this culture system to test prospective parasite invasion inhibitors and anti-development drugs.

Research supported by: The Bill and Melinda Gates Foundation and a Draper Laboratory Fellowship awarded to SPM

Abstract #: 278

Presented by: Samuel Matos-Bastidas, MPH, Graduate Student

Breaking the Cycle of Maternal-Child Health Disparities: Evaluating a Conception Care Program Samuel Matos-Bastidas¹, Fayez Alshehri² ¹University of South Florida College of Public Health, Department of Global Health, ²University of South Florida College of Education

Keywords: Collaborative Evaluation, Health Programs, Maternal-Child Health, Program Evaluation

Objective: Infant mortality rates are higher among some minorities such as Latinos and African-Americans. This presentation will describe the collaborative evaluation process of an educational program targeting young women and their partners aimed to promote healthy reproductive choices such as adequate baby spacing and parenting skills, as well as family health literacy. The Interconception peer support education intervention is one of five components in the Central Hillsborough Healthy Start (CHHS) program, and it is delivered through monthly sessions in either English or Spanish language.

Methods: We assessed both strengths and weaknesses of this community intervention by conducting closed-ended question structured surveys with program users, and in-depth individual interviews of program staff providers, both in English and Spanish-speaking groups. The Model for Collaborative Evaluations (MCE) (Rodríguez-Campos & Rinconez-Gomez, 2013) was applied throughout the evaluation process, allowing the active involvement of both program providers and beneficiaries at each stage such as evaluation design, data collection and analysis.

Results: We determined several benefits from the program not only for participants but also for their families, as well as some operational constraints in terms of scheduling, transportation and childcare services availability.

Conclusion: The collaborative evaluation approach proved to be a good match to this community-based health education intervention. There was a sense of program ownership, but at the same time a perceived need for improving both contents and implementation. Recommendations to increase both program attendance and adherence are discussed.

Research supported by: REACHUP Inc.

Presented by: Tommy McGaha Jr., MS, Graduate Student

Identification of Attractive Odorant Compounds to Vectors of Onchocerciasis

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Keywords: onchocerciasis, river blindness, black flies, Simulium damnosum, Simulium ochraceum, insect behavior

Objective: Onchocerciasis, also known as river blindness, is a neglected tropical disease caused by a parasitic nematode, Onchocerca volvulus. The parasite is transmitted from an infected human to a naïve human by black flies of the genus Simulium. With proper monitoring and surveillance this disease could potentially be eliminated by 2025, but monitoring for the disease currently uses humans as bait for collecting the flies needed for testing. In an effort to eliminate humans as bait for collecting the flies, this study was conducted to identify odorant attractants that could be used to bait a trap.

Methods: Odorant compounds in human sweat were identified by gas chromatography coupled with mass spectrometry were exposed to collected vectors, Simulium ochraceum and Simulium damnosum/sirbanum, from Mexico and Burkina Faso, respectively, using an electroantennograph to assess the physiological response. Compounds eliciting a significant physiological response were tested in a Y-tube olfactometer to assess attractive behavior.

Results: Three of the compounds identified from human sweat, acetophenone, decanal, and octanoic acid, were found to be significantly attractive to the African vector, S. damnosum/sirbanum. The Mexican vector, S. ochraceum, was attracted to 1-octen-3-ol, acetophenone, and hexadecanoic acid to attractive to the host-seeking females.

Conclusion: This study has successfully identified attractive odorant compounds for the onchocerciasis vectors, S. damnosum/sirbanum and S. ochraceum. In the next step of the study, the attractive compounds will be incorporated into a lure and evaluated on traps in the field.

Research supported by: Bill and Melinda Gates Foundation (grant # 101787).

Abstract #: 280

Presented by: Amruta Mhashilkar, MD, Graduate Student

Development of an In-vitro Assay to Screen for Agonist and Antagonist Compounds for the Ecdysone Receptor of Brugia malayi

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Keywords: ecdysone, transactivation assay, filariasis

Objective: Elephantiasis is a debilitating parasitic disease caused by filarial nematodes. Recent studies suggest that the ecdysone receptor in B.malayi (BmEcR) can be targeted to develop new drugs against filariasis. The B.malayi ecdysone receptor controls genes involved in molting and embryogenesis, and represent an attractive chemotherapeutic target

Methods: Mammalian two hybrid system was used to create BmEcR Gal4 and RXR VP16 fusion constructs. This constructs heterodimerize and, when bound to the cognate ligand, activates transcription of a luciferase reporter gene. A ligand that can activate the ecdysone response element is an agonist whereas any ligand suppressing the response is an antagonist. A 96 well plate seeded with NIH3T3 cells were transfected with the constructs and the reporter. Half the wells are exposed to 20-OH ecdysone and other half exposed to solvent alone.

Results: On induction with 20-OH ecdysone, transactivation of the luciferase gene with a signal to noise ratio of roughly 6. The Z' of the assay is between 0.6 and 0.7.

Conclusion: The results confirm that this assay exhibits characteristics that make a viable screen for agonists and antagonists of the Bm EcR. This assay will be employed to screen natural product libraries and a collection of ecdysone analogs in the near future

Presented by: Asmita Mhaskar, MPH, Graduate Student

An Overview of Systematic Reviews Addressing Efficacy And Effectiveness of Homeopathic Medicines.

Asmita Mhaskar¹, Azliyati Azizan¹, Yashwant Pathak² ¹University of South Florida, College of Public Health, Department of Global Health, ²USF College of Pharmacy

Keywords: Homeopathy, efficacy, effectiveness, review

Objective: To investigate efficacy and effectiveness of Homeopathy by reviewing systematic reviews (SRs).

Methods: PubMed, Web of Knowledge, and Cochrane library were searched using a combination of free text and Mesh terms to identify SRs addressing efficacy and effectiveness of Homeopathy. Google and Google scholar were also searched. Duplicate citations were removed to populate a single EndNote library.

Results: Thirty-four SRs studying 25 conditions were identified. Almost all SRs concluded that evidence to support the use of homeopathic medicines was insufficient and limited. There was heterogeneity among the included SRs in terms of methodological quality. Overall, these SRs concluded that the included studies had low sample size, low quality of reporting and suffered from selection and other biases.

Conclusion: Although SRs conclude that evidence is limited and of low quality to support efficacy and effectiveness of Homeopathic medicines, the methodological quality of these SRs needs to be comprehensively assessed. In order to conclude on effectiveness and efficacy of Homeopathic medicines assessment metrics should include the individualized selection of medicine, the basic principle of Homeopathy.

Abstract #: 282

Presented by: Karlette Peck, BS, Graduate Student

Dengue Seroprevalence Study in Martin County, Florida

Karlette J. Peck, MPH, PA^{1,2}, Stephanie Moody-Geissler³, Melinda Thomas³, Katrina Kintzinger³, Grethel Clark¹, Dr. Karen A. Thomas¹

¹Florida Department of Health in Martin County, ²University of South Florida, College of Public Health, Department of Global Health, ³Florida Department of Health

Keywords: Dengue; Local transmission; Florida

Objective: To Identify the size and scope of the dengue outbreak; to determine the incidence and prevalence of dengue in Martin County; to identify risk factors for acquisition of dengue among Martin County residents and to describe the dengue strain by comparing Martin samples with other isolates currently in laboratory archives.

Methods: Business and household Seroprevalence surveys were randomly administered to residents in the Rio and Jensen Beach area of Martin County. Six teams consisting of an interviewer and a phlebotomist were deployed to the randomly selected residences. After informed consent, those that agreed to participate were interviewed and a specimen was collected. Specimens were tested for Dengue by the FDOH laboratory in partnership with the CDC using standard laboratory protocols. Survey data was collected and entered into an Access database and will be analyzed using SAS.

Results: Over 2,000 residences were visited by FDOH teams and three hundred and sixty (360) samples were obtained for testing. One additional symptomatic case was identified. Forty-four (44) samples are pending RT-PCR and PRNT results. All other samples were negative for dengue.

Conclusion: This is the second episode of local transmission of dengue in Florida, but the first time that the Florida Department of Health conducted a Dengue Seroprevalence survey in Florida; the previous survey was conducted by the Centers for Disease Control. In this outbreak, dengue cases were clustered around businesses in addition to households. Other laboratory tests and survey data analyses are pending (may have results by poster presentation date).

Research supported by: Florida Department of Health

Presented by: Arturo Rebollon, MD, MPH, Graduate Student

Cancer Epidemiology in Panama: Morbidity and Mortality Trends 2002-2010

<u>Arturo Rebollon¹, David Sultan²</u> ¹University of South Florida College of Public Health, Department of Global Health, USF Health, ²University of South Florida College of Public Health, Department of Health Policy and Management, USF Health, Tampa Fl

Keywords: Cancer, Epidemiology, Panama

Objective: To analyze the trend of the morbidity and mortality of all cancers in Panama between 2002 and 2010

Methods: De-identified data was obtained from the National Cancer Registry of Panama public records. SAS 9.3 was used to estimate gender-standardized incidence and mortality rates for all cancers in Panama between 2002 and 2010, and annual percentage change (APC) by these rates.

Results: Between 2002 and 2010, a total of 37,682 cancers were diagnosed and 21,146 cancer deaths occurred in Panama. The annual incidence rate (APC=1.1%), and mortality rate (APC=0.5%) for all cancers combined increased across the study period. Over the study period, an increase in incidence rates were observed in prostate (APC=2.2%), breast (APC=4.1%), corpus uteri (APC=5.3), skin (APC=9.0), thyroid (APC=5.1%), liver (APC =8.4%), pancreas (APC=8.4%), larynx (APC=4.1%), brain (APC=2.8%), vulva (APC= 0.2%), hematopoietic and reticuloendothelial system (APC=0.2%), lymphatic (APC=10.9%), other types of cancers (APC 8.1%). Mortality rates increases were found in Prostate (APC=1.3%), stomach (APC=0.5%), colon (APC=1.0%), breast (APC=4.0%), leukemia (APC=1.4%), liver (APC=2.2%), pancreas (APC=3.6%), non-hodgkin lymphoma (APC=0.3%), ovarian (APC=5.6%), larynx (APC=5.0%), urinary bladder (APC=1.0%), melanoma (APC=1.7%), other types of cancer (APC=2.2%).

Conclusion: The standardized incidence and mortality rates have increased in the majority of the cancers in Panama. Further trend analysis will serve as a baseline study for future cancer prevention interventions, especially for those with the most prominent increase.

Abstract #: 284

Presented by: Jennifer Sedillo, MS, Graduate Student

Identification of a Novel Type II MAPK-like Phosphatase in Plasmodium falciparum

<u>Jennifer L. Sedillo¹, Shulin Xu¹, Christopher O. Campbell¹, Negin Taghizadehasl¹, Bharath Balu¹, Steve Maher¹, Julian <u>Rayner², John H. Adams¹</u> ¹Department of Global Health, College of Public Health, University of South Florida, Tampa, FI, ² Malaria Programme, The Wellcome Trust Sanger Institute, The Wellcome Trust Genome Campus, Hinxton, Cambridge CB10 1SA, UK</u>

Keywords: malaria, MAPK, phosphatase, signaling pathways

Objective: Signaling pathways in Plasmodium falciparum are of great interest in drug discovery. Recently, parasite kinases and phosphatases have been implicated in invasion and cell cycle replication within the host erythrocyte. However, much remains unknown about signaling pathways. The MAPK pathway is vital in cell growth and differentiation within eukaryotic cells such as yeast and human, but the existence of this pathway in the P. falciparum is unclear. MAPK homologues in the parasite have been identified and studied but homologues to other enzymes in this pathway have yet to be described. Through the piggyBac mutagenesis project, we identified a putative phosphatase as important in cell growth.

Methods: In order to further characterize this gene, we produced recombinant protein of the two domains present in the gene, an inactive rhodanese domain and a dual-specificity phosphatase (DUSP) domain.

Results: Using recombinant proteins, we found that the domains within the gene interact with both Pfmap1 and Pfmap2. We also were able to show activity of the DUSP domain in a phosphatase assay.

Conclusion: Further work will focus on site-directed mutagenesis of putative critical residues for binding and activity. In this work, we have identified a novel Type II MAPK-like phosphatase that is involved in cell cycle regulation and growth of the parasite.

Research supported by: NIH, USF Presidential Doctoral Fellowship

Phenotypic Characterization of the Plasmodium falciparum NOT1 (PF3D7_1103800) Gene Knockout and Heat Shock Analysis of the piggyBac Mutant Library

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Keywords: malaria, CCR4-NOT complex, mRNA transcription, immunofluorescence, phenotype

Objective: The objective of this work is to characterize PF3D7_1103800 and identify other genetic factors in the piggyBac mutant library affected by heat shock. The Not1 gene is a part of a gene regulatory system in eukaryotes known as the CCR4-NOT complex, which is involved in mRNA transcription and degradation. Our research on the asexual stages of the major malaria parasite uses the phenotypic analysis of genetic mutants. The primary phenotypic screens are growth attenuation and changes in virulence factors. My dissertation focuses on the screening for genes involved with stress responses to increased temperature.

Methods: In the process of a whole genome random transposon mutagenesis of P. falciparum, a knockout of Not1 was isolated. Characterization of protein extracts from mutant and wild type parasites were analyzed by immunoblots with antibodies to EBA-175 and GAP45. The IFA localization of these proteins in the Not1 mutant was compared with wild type patterns. NOT1 and other piggyBac mutants were analyzed for altered sensitivity to febrile temperatures.

Results: The immunoblots display altered expression at mid to late trophozoite stages in the mutant when compared to the wild type. The IFAs for the Not1 mutant reveal patterns similar to that of the Caf1 mutant, which is also in the CCR4-NOT complex and important for parasite egress. Of the 32 parasites tested, 15 were significantly decreased in growth compared to the wild type, including the Not1 knockout.

Conclusion: Validation of the Not1 mutant phenotype should result in delayed growth and invasion of the parasite. Exposure of the piggyBac mutant library to increases in heat may reveal genetic factors involved with the intraerythrocytic cycle that lead to new drug targets.

Research supported by: NIH grant R01 Al094973

Abstract #: 286

Presented by: Zachary Pruitt, PhD, Graduate Student

Relationship of Healthcare Expenditures to Adherence among Florida Medicaid-insured Patients Diagnosed with HIV or AIDS

Zachary Pruitt, PhD¹, Barbara Langland Orban, PhD¹, Robert Brooks, MD¹, John Robst, PhD² ¹University of South Florida College of Public Health, Department of Health Policy & Management, ²University of South Florida, College of Behavioral and Community Sciences, Department of Mental Health Law and Policy

Keywords: retrospective study, managed care, health, quality, care management

Objective: Research supports the benefits of antiretroviral treatment (ART) for people living with HIV or AIDS (PLWHA). However, the relationship of ART adherence to total healthcare expenditures is not well understood. The objective was to analyze the association of ART adherence to expenditures for Medicaid-insured PLWHA in a 24 month period.

Methods: Data included Florida Medicaid claims from July 2006 through June 2011. All subjects (n=502) were HIVpositive, adults ages 18 to 64, non-pregnant, and ART naïve for at least 12 months prior to the measurement period. Each subject was categorized, based upon medication possession ratios (MPR), as adherent (>90%) or non-adherent (<90%). Expenditures were payments from Medicaid to providers. For HIV-positive (n=232) and the AIDS-diagnosed (n=270) groups, generalized linear models predicted the mean monthly total expenditures for the non-adherence group versus the adherence group, controlling for covariates.

Results: For the HIV-positive group, the adjusted mean expenditures for the non-adherent group was \$1,291 (95% CL \$840-\$2,004); the adherent group was \$1,926 (95% CL \$1,157-\$3,231). The non-adherent group mean was significantly less than the adherent group (-40%, p<.001). However, for the AIDS-diagnosed group, no statistical difference existed between the non-adherent \$2,279 (95% CL \$1,572-\$3,322) and adherent \$2,005 (95% CL \$1,387-\$2,913) groups. Also, no statistical difference existed between the HIV adherent group and the AIDS non-adherent group.

Conclusion: The results of the present study underscore the necessity for appropriate financial incentives for organizations paid through capitation that will support and reward ART adherence interventions, especially among asymptomatic HIV-positive patients.

Presented by: Joseph Smith, MPH, Graduate Student

Characteristics of Local Health Departments Providing HIV/AIDS Services

<u>Joseph L. Smith, MPH¹, Willie H. Oglesby, PhD, MSPH, FACHE²</u> ¹University of South Florida College of Public Health, Department of Health Policy & Management, Tampa Florida, ²Kent State University College of Public Health, Department of Health Policy & Management, Kent, Ohio

Keywords: HIV Services Local Health Departments Organizational Capacity Secondary Data Analysis

Objective: In order to better understand the delivery of HIV screening and treatment by local health departments (LHDs) in the US, we examined the characteristics of LHDs that do and do not provide these services.

Methods: This study analyzed cross-sectional survey data from the 2010 NACCHO National Profile of Local Health Departments. Using bivariate logistic regression models, we examined the relationship between the provision of HIV screening and treatment and various characteristics of LHDs.

Results: Just over two-thirds of the LHDs responding to the survey reported providing HIV screening services, while under one-third provided HIV treatment. LHDs providing HIV screening and/or treatment were significantly more likely to a board of health and a full-time CEO. Additionally, LHDs that provide HIV screening and/or treatment are more likely to employ a range of public health practitioners. Finally, LHDs providing HIV screening and/ or treatment are more likely to provide other services. Likelihood of providing HIV services was also related to population served. Conversely, LHDs providing HIV services were no more likely to provide school-based clinical services, compared to those not providing HIV services.

Conclusion: LHDs play an important role in reducing health care expenditures and new infections through the provision of HIV screening and treatment. LHDs that provide HIV screening and treatment services tend to have greater organizational capacity to provide a range of services. Thus, LHDs should maintain or expand organization capacity to provide HIV services in order to maximize the health of communities.

Abstract #: 288

Presented by: Sara VanWyk, MPH, Graduate Student

Screening for Type 2 Diabetes and Diabetes Risk in a Physician-Supervised Weight Loss Program

<u>Sara VanWyk¹ Macklin Guzman², Eva Imperial³, Jennifer Nguyen¹, Elise Schram⁴, Christine K. Holub⁵ Edward Zbella³, Segal Shah Alvarez³ ¹University of South Florida College of Public Health, Department of Health Policy and Management, ²Nova Southeastern University, ³Medi-Weightloss, ⁴University of South Florida College of Public Health, Department of Community and Family Health, ⁵San Diego State University</u>

Keywords: Insulin resistance, Intervention, Glucose metabolism.

Objective: To assess the HgA1c level changes of patients that attend a physician-supervised weight loss program.

Methods: Investigators performed an observational study of new and restart patients at four physician-supervised weight loss sites. The primary outcome, HgA1c, was assessed at baseline (n=3482) and post-treatment (n=151).

Results: 52% of new patients (n=1188) and 60% of restart patients (n=725) had HgA1c levels in the normal range. 42% of new patients (n=952) and 37% of restart patients (n=452) were in the prediabetic range. 6% of new patients (n=136) and 2% of restart patients (n=29) had levels in the diabetic range. 71% of patients in the prediabetic or diabetic range had a BMI > 40. After an average participation time of 14 weeks and a weight loss of 25-35 pounds, there was a significant improvement of HgA1c levels in both groups (<0.005). 59% of prediabetic patients were reclassified as having normal HgA1c levels, and 82% of diabetic patients were reclassified as prediabetic as a result of having achieved a 17% improvement in HgA1c levels.

Conclusion: Individuals who experienced weight loss saw a decrease in their risk of developing type 2 diabetes. Results indicate that implementing HgA1c testing within physician-supervised weight loss programs can help patients realize the full benefits of weight loss.

Research supported by: Medi-Weightloss

Presented by: Firas Abuqalbeen, Undergraduate

L-Arginine Metabolism Impacts Tau Biology

Firas Abuqalbeen, Devon Placides, Etee Patel, Jerry B. Hunt Jr, Daniel C. Lee, PhD University of South Florida College of Arts and Sciences, Department of Chemistry

Keywords: Tauopathy, Autophagy, L-Arginine metabolism, Arginase

Objective: Tau is a microtubule stabilizing protein that can become phosphorylated and form neurofibrillary tangles, leading to cell death and Alzheimer's disease. Recent data from our lab suggests L-arginine metabolism impacts tau biology. We aimed to identify the role with L-arginine metabolism in cells that stably overexpress tau. Data suggests that arginase-1 (Arg1), an L-arginine metabolizing enzyme, reduces pathology in tau transgenic mice. Herein, we aimed to determine how L-arginine metabolism impacts tau biology.

Methods: Stably transfected HeLa cells (C3 Hela) were used to test the role of L-arginine. Varying concentrations of L-arginine were added to the C3 cells and incubated for 72 hours. Arg1 was then transfected and overexpressed in C3 cells for 72hrs. Western blot analysis was used to determine the levels of total tau and several phospho tau species. Western blot analysis was also performed on tau transgenic mice (rTg4510) to determine the levels of Arg1 during tau pathology.

Results: Tau transgenic mice showed increased levels of Arg1 in the brain compared to the wild type literates. The addition of L-arginine in C3 cells showed a concentration dependent total tau, and phospho tau Ser 199/202, and ser 396. L-arginine supplementation increased the autophagy inhibitor mammalian target of rapamycin (mTOR). Furthermore Arg1 overexpression significantly reduced phospho and total tau levels in C3 cells. Finally, Arg1 overexpression also decreased mTOR expression suggesting activation of autophagy.

Conclusion: These data suggest L-arginine accumulation may significantly affect tau biology by inhibiting autophagy. In addition, L-arginine metabolizing enzymes such as Arg1 may serve as a therapeutic target to reduce tau pathology.

Abstract #: 290

Presented by: Stephen Bell, BS, Undergraduate

Melatonin Rescue of Age and AD Associated Changes in Mitochondrial Cytochrome c Oxidase (COX) Activity is Partially Dependent on Melatonin Receptors

Stephen Bell & Crupa Kurien, Anh Phan, Sandra Živković, Vedad Delić, Patrick Bradshaw Department of Cell Biology, Microbiology and Molecular Biology, University of South Florida College of Arts and Sciences

Keywords: melatonin receptors, MT1, MT2, Alzheimer's, mitochondria

Objective: To determine if the protective effects of melatonin are achieved by restoring function to mitochondrial electron transport chain (ETC) complex IV cytochrome c oxidase (COX). We also wished to determine if the restorative effects are achieved through a receptor-mediated pathway.

Methods: Transgenic mice modeling amyloid-beta mediated AD were used. Double melatonin receptor (MT1 and MT2) knockout mice and transgenic APPSWE mice were bred. With melatonin treated and untreated groups.

Results: Cytochrome c oxidase activity decreases with age in the absence or presence of melatonin receptors. Melatonin prevented the decreased COX activity in 16 month WT-WT mice. In AD mice cytochrome c oxidase activity increased between 13 and 16 months of age and melatonin treatment prevented the increased COX activity in 16 month AD-WT mice.

Conclusion: There is a progressive decline in COX activity in both WT-WT and WT-KO untreated mice as a function of age. Melatonin treatment completely restored COX activity to 6-month levels in 16-month WT-WT mice COX activity was increased in 16 month mice in both AD-WT and AD-KO groups suggesting a compensatory mechanism resulting from amyloid-beta mediated mitochondrial dysfunction and increased ROS production. Melatonin prevented the increased COX activity in the 16 month AD-WT mice

Research supported by: This study was supported by University of South Florida (College of Arts and Sciences) startup funds awarded to Dr. Bradshaw.

Presented by: Sonya Bhaskar, Undergraduate

Mild Traumatic Brain Injury and Dendritic Neuroplasticity in the Mouse Neocortex

Sonya Bhaskar¹, Jessica N. Chang^{2,3}, Stephanie K. Foley^{1,4}, Nikhil Bhatia¹, Gurtej Walha⁵, Noah Peeri¹, Bruce A. Citron^{2,3}, Ronald F. <u>Mervis^{4,6}</u> ¹The Honors College, University of South Florida, ²Laboratory of Molecular Biology, Bay Pines VA, ³Dept of Molecular Medicine, USF Morsani College of Medicine, ⁴ Neurostructural Research Labs, Inc., Tampa, FL, ⁵The Graduate School, USF Morsani College of Medicine, ⁶Center for Aging & Brain Repair, Dept Neurosurgery & Brain Repair, USF Morsani College of Medicine

Keywords: brain injury, golgi staining, dendritic branching, neuroplasticity

Objective: Mild traumatic brain injury (TBI) is a widespread occurrence. Sports-related head injuries are currently particularly concerning. TBI often results in cognitive impairment, memory loss, and deficits in executive functioning. In this study our objective was to evaluate the effect of TBI on alterations in the dendritic arbors of neocortical layer V pyramids in the mouse parietal cortex.

Methods: The experimental protocol utilized a closed head system. Anesthetized adult mice were exposed to a single weight drop-induced impact directed at the right temporal cortex. Brains were harvested 30 days following TBI. The Golgi method was used to stain neurons for quantification of the dendritic arbor. From coded slides, camera lucida drawings of the basilar trees of randomly selected layer V pyramids from the damaged region of sham controls and experimental brains were evaluated.

Results: Layer V pyramids from the TBI-damaged region showed a 17% increase in the amount of total dendritic length compared to sham controls (p = 0.0003) Branch point analysis – a measure of dendritic complexity - indicated there was a 10% increase in the neurons from the damaged region (p = 0.06).

Conclusion: Our findings suggest that the neurons from the damaged cortex showed a compensatory dendritic hypertrophy. We hypothesize that the TBI resulted in neuronal damage which – over a 30 day time frame – resulted in loss of the most heavily damaged neurons. The less damaged, surviving neurons then expanded their dendritic domains to fill the space vacated by the now-dead neighboring neurons – e.g., compensatory neuroplastic dendritic hypertrophy.

Research supported by: Dept of Veterans Affairs, Bay Pines Foundation, Florida DOH JEKing Program

Abstract #: 292

Presented by: Sumir Desai, BS, Undergraduate

Targeting the Brain with Glutathione-Coated Docetaxel Nanoparticles

Sumir Desai, Aditya Grover, Anjali Hirani, Yashwant Pathak, Vijaykumar Sutariya University of South Florida College of Pharmacy, Department of Pharmaceutical Sciences

Keywords: Nanoparticle, glutathione, docetaxel, brain cancer, blood-brain barrier

Objective: Docetaxel is used against a number of cancers but has not been able to target brain cancers because of the blood-brain barrier (BBB). In the presents study we coat a PEG-PLGA nanoparticle (NP) with glutathione to propose a brain-targeting mechanism and test its toxicity and in vitro BBB permeability for its potential use as an anti-brain cancer agent.

Methods: Glutathione was added to 1 mL of the NP suspension to yield a 2% w/v coating. MTT assay and Transwell based in vitro BBB permeability assay were performed by comparing the free docetaxel drug solution, uncoated PEG-PLGA docetaxel NPs, and 2% gluatathione coated PEG-PLGA NPs. RG2 (rat glioma) and C6 (rat astrocytoma) cell lines were used for the MTT assay and the RBE4 (rat brain endothelial) and C6 cell lines were used for the Transwell in vitro BBB model.

Results: Paired t-test analyses of the MTT assays in RG2 and C6 cell lines of 5 and 10 uM treatments showed that both NP treatments were significantly less toxic in both concentrations to both cell lines when compared to the free drug solution. The Transwell in vitro BBB model revealed that the glutathione-coated NPs have trans-BBB endocytosis properties.

Conclusion: The toxicity of tissues affected by docetaxel drug solution when administered intravenously has been a concern to clinicians. We show that the NP-based docetaxel vector is significantly less toxic than the free drug solution. We show that coating NPs with glutathione can induce its transport across the BBB. In the case of docetaxel, the glutathione-coated NP vector may be used in clinical settings against brain tumors.

Research supported by: Research was supported by startup grant provided to Dr. V. Sutariya by USF College of Pharmacy.

Abstract #: 293 withdrawn 2 10 14

Presented by: Amanda Duke, Undergraduate

The Role Of L-arginine Decarboxylase in Polyamine Synthesis and Tau Pathology

Byrd Alzheimer Institute, University of South Florida⁽²⁾ Department of Pharmaceutical Sciences; College of Pharmacy, Byrd Alzheimer Institute, University of South Florida

Keywords: tauopathy, L-arginine decarboxylase, polyamines

Withdrawn

Methods: . In order to achieve this we started by cloning the ADC from mRNA extracted from mouse brain tissue. The mRNA was reverse transcribed to generate cDNA for PCR. Primers for ADC were designed for the 5' ATG to the 3' termination signal. A hemagglutinin (HA) tag sequence was added to the 3' primer in frame with the ADC sequence for detection of the ADC protein. The cDNA was cloned into a recombinant adeno-associated viral expression vector. ADC sequence was confirmed by DNA sequencing analysis. Protein expression was confirmed by transfection into HEK293 cells followed by western analysis using an anti-HA tag antibody.

Results: We are currently examining the effects of over expression of ADC in a number of cell lines that model microglia and neurons.

Conclusion: Future experiments will examine the effects of ADC in vivo using viral gene delivery

Abstract #: 294

Presented by: Kai Greene, Undergraduate

Neurotoxic Impact of in Utero and Early Postnatal Exposure to Benzyl Butyl Phthalate (BBP) on Dendritic Development in the Rat.

Kai Greene¹, Khalid Shakfeh¹, Puja Solanki^{1,2}, Mouwafak Moureiden¹, Jensen Le¹, Stephen DiGiacomo¹, Mark Maresco¹, Stephanie K. Foley^{1,2}, Peter Hanna^{1,3}, Dianna Pham¹, Danielle DeBartolo⁴, Adrienne Betz⁴, Ronald F. Mervis^{2,5} ¹The Honors College, University of South Florida; ²Neurostructural Research Labs, Inc., Tampa, FL; ³USF Morsani COM; ⁴Dept Psychology, Quinnipiac Univ, Hamden, CT; ⁵Center for Aging and Brain Repair, Dept of Neurosurgery & Brain Repair, USF Morsani College of Medicine

Keywords: Brain Development, Neurotoxicology, Golgi staining, Dendrites, Cortex

Objective: Benzyl butyl phthalate (BBP) is a widely used industrial plasticizer. Phthalates appear to have endocrine disrupting properties, but their effect on the developing CNS is poorly understood. The purpose of the present study was to evaluate the effects of gestational and lactational exposure to BBP on the development of dendritic branching and spines of cortical pyramidal cells.

Methods: Pregnant S-D rats were fed pellets containing 10um/ml of BBP throughout pregnancy and up to postnatal day 23 when the pups were sacrificed. Control pups received no BBP. Formalin-fixed brains were stained with the Golgi method and all slides were coded. Analysis of dendritic branching and spines was carried out on randomly selected parietal layer V pyramids and granule cells of the dentate gyrus in the hippocampus.

Results: The morphology of hippocampal granule cell branching and spines was largely unaffected by the in utero and pre-weaning exposure to BBP. In contrast, analysis of dendritic branching of cortical layer V pyramids showed a highly significant increase in dendritic branching throughout the basilar dendritic tree (+26%,Wilxocon test, p = 0.0001). Dendritic branch complexity was also significantly increased in the BBP-exposed rats (+24%, t-test, p=0.03). Dendritic spine density however was not significantly affected.

Conclusion: Cortical pyramidal neurons from BBP-exposed 28 do pups had significantly larger and more complex dendritic arbors. BBP exposure may contribute to either additional cortical dendritic growth or diminished dendritic pruning during the course of normal maturation of cortical circuitry. Early environmental BBP exposure is therefore shown to influence neuronal development.

Research supported by: Quinnipiac University Research Foundation

Presented by: Rinko Grewal, Undergraduate

Pharmacological Inhibition of CCR2/CCL2 Pathway Affects Tauopathy in a Cellular Model

<u>Rinko Grewal¹, Daniel Lee PhD¹, Dave Morgan, PhD, ²Marcia N. Gordon, PhD², Maj-Linda B. Selenica, PhD¹ ¹College of Pharmacy, Dept. of Pharmaceutical Sciences, University of South Florida, ²Dept. of Molecular Pharmacology and Physiology, Morsani College of Medicine, University of South Florida</u>

Keywords: p-mTOR (phosphorylated mammalian target of rapamycin), p-tau (phosphorylated tau), t-tau (total tau). **Objective:** The binding of chemokine (C-C motif) ligand 2 (CCL2) chemokine to its main receptor CCR2, regulates monocyte infiltration into tissue and both proteins are regarded as therapeutic targets of inflammation (Prinz et al, 2011).

However, studies have shown that binding of CCL2 to CCR2 receptors also results in declined autophagy activity in cancer cells.

Methods: To study the effect of pharmacological antagonism of CCR2, two well-characterized receptor antagonists, INCB-3344 (IC50= 9.5nM, Brodmerkel et al, 2005) and sc-202525 (IC50 = 18nM, Cherney et al, 2008) were used to treat the human cancer cell line (Hela). These cells were genetically modified to stably express human tau (4R0N). The downstream effects of both antagonists were investigated by biochemical approaches (western blot). Cells were treated with 50nM CCL2 and incubated for 24 hours with various concentrations of each antagonist. Levels of total tau and phosphorylated human tau were measured (H150 and pS396 antibodies), while p-mTOR and p62 were used as autophagy markers.

Results: Our data demonstrates that INCB-3344 significantly decreases t-tau levels (H150) at 10nM (p=.0359), meanwhile pS396 tau levels were decreased at both 3nM and 10nM concentrations. We found that INCB-3344 compound efficiently reduced p62 levels (3nM and 10nM). Analysis also demonstrated dose-dependent increases in p-mTOR levels (3nM-100nM). In addition, sc-202525 compound demonstrated slight efficacy in decreasing levels of t-tau (H150) while significantly increased levels of p-mTOR at 3nM (p=.0255) and 10nM (p=.0335).

Conclusion: This study will attest to the hypothesis that the aggregation of tau can be altered through the inhibition of the CCL2-CCR2 pathway in the pathology of Alzheimer's Disease.

Abstract #: 296

Presented by: Ian Heller, BS, Undergraduate

Repositioning of the FDA-approved Anti-Cancer Tyrosine Kinase Inhibitors to Treat Metabolic Diseases Ian E. Heller¹, Lun Yang², Minghua Li¹, Isaac Raplee¹, Steven Guzman¹, John P. Pasciak¹, Kevin B. Sneed³, Lin He², Shu-Feng Zhou¹ and Jiazhi Sun¹ ¹Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida; ²Bio-X Center, Shanghai Jiao Tong University, Shanghai, China; and ³Department of Pharmacotherapeutics and Clinical Research, College of Pharmacy, USF

Keywords: TKI, drug repositioning, CPI, metabolic diseases, cancer

Objective: Drug repositioning is a unique way to identify and extend new indications for approved drugs in drug discovery. We hypothesize that these TKIs act on other molecular targets in addition to tyrosine kinases and may manage metabolic diseases given that there is a complex network of kinases that work together to regulate a number of important cellular processes.

Methods: Employing a comprehensive docking method with our established chemical-protein interactome (CPI) and 11 FDA-approved TKIs, we have discovered 301 PDB-deposited proteins corresponding to 353 ligand binding pockets among a total of 1,780 PDB-deposited human protein entries. Systemic pharmacology approach also applied including validation the molecular target(s) of TKIs in vitro and efficacy study in vivo.

Results: Notably, sorafenib, dasatinib and crizotinib had a CPI binding score (ZZ_score) against HDAC, B-Raf, PPAR and VDR, suggesting a high binding affinity of those TKIs with these target proteins. Our preliminary studies have showed that oncogenic Akt signaling was inhibited in human multiple melanoma cells by these TKIs. Interestingly, dasatinib increased VDRE and HDLR luciferase reporter activity in A-549 cells, and dasatinib and crizotinib induced autophagy activated LC3 and apoptosis by in vitro.

Conclusion: FDA-approved TKIs may be switched to become a "magic bullet" concurrently targeting tyrosine kinase, HDAC, PPAR and VDR, shedding a light for future anti-metabolic disorder drug discovery & development. Further validation of additional "hot targets" besides tyrosine kinase such as HDAC, B-Raf, PPAR, Sirt1, Akt and VDR, and in vivo evaluation of anti-metabolic disorder by TKIs are undergoing at our laboratory.

Research supported by: State funding

Presented by: Jerry Hunt Jr., Undergraduate

Overexpression of Arginase-1 in the CNS Mitigates tau Pathology in rTg4510 tau Transgenic Mice

Jerry B. Hunt Jr., Kevin Nash Ph.D, Devon Placides, Peter Moran, Santiago Rodrigez-Ospina, Miloni Savlia, Clement G.Y. Yang, Maj-Linda B. Selenica Ph.D, Marcia Gordon Ph.D, Dave Morgan Ph.D, Daniel C. Lee Ph.D. University of South Florida, College of Arts and Sciences, Department of Integrative Biology

Keywords: Tau, Arginase, transgenic mice, virus

Objective: Tau pathology is associated with many neurodegenerative diseases collectively referred to as tauopathies. Tauopathies associate with cognitive impairment, parkinsonian features, motor impairment, and behavioral imbalances. No therapies exist to contest these phenotypes. In some inflammatory events, Arginase (Arg1) and nitric oxide synthase (iNOS) levels increase and compete for production of either polyamines or nitric oxide via L-Arginine metabolism. Polyamines modulate cellular growth and division, contingent upon microenvironment and cell type. We detected dysregulation of the polyamine pathway in rTg4510 tau transgenic mice compared to non-transgenic littermates. We suggest increased Arg1 expression in the CNS influences tau pathology.

Methods: Four month old rTg4510 tau transgenic mice received intracranial injections of either adeno-associated viral constructs containing arginase-1 (rAAV-Arg1) or green fluorescent protein (rAAV-GFP) into the hippocampus. Four months post injection; brains were harvested for histology, immunohistochemistry, western blotting and ELISA.

Results: Arg1 overexpression reduced several phospho-tau epitopes (i.e. AT8, AT180, AT270, Ser262, Ser396, nY18), tangle pathology designated by Gallyas silver positive staining, and several kinases associated with phosphorylating tau including GSK3 and CDK5 as compared to rAAV-GFP. Additionally, Arg1 overexpression also decreased several cytokines including IL-1beta, TNF-alpha, and IL-12 along with microglial activation measured by CD45 and significantly moderated hippocampal atrophy.

Conclusion: This data suggests that Arg1 and the polyamine pathway may provide new and potential therapeutic targets for AD and tauopathies.

Research supported by: AG 15490 & AG 04418 to DM & MG, Alzheimer's Assoc. DL

Abstract #: 298

Presented by: Radim Jacob, BS, Undergraduate

A Socioeconomic Predictive Model for Access and Survival of Liver Transplant Patients: The Effects of Distance, Race, Insurance, Income, Work Status

Radim Jacob and Michael Katzen, Dr. Angel Alsina, Dr. Alexia Makris University of South Florida Honors College

Keywords: Retrospective Chart Review, Hepatocellular carcinoma (HCC), Hepatitis C (HCV), Post-Transplant survival, Socioeconomic Predictive Model, Survival Analysis

Objective: This study will comprehensively examine the effect of Socio-Economic Status (SES) and distance of patient's residence to transplant center on outcomes using single center's retrospective data. A Socioeconomic Predictive Model (SPM) will be developed to quantify the impact of SES on survival post-transplant.

Methods: We identified 821 patients who were transplanted at Tampa General Hospital from multiple medical databases (EPIC, Chartview, OTTR). Those with acute liver failure, who relocated temporarily and multiple organ transplants were excluded. Kaplan Meier curves were used to screen variables for significance and a Cox Proportional Hazards model was used to develop a preliminary SPM.

Results: The results show that the etiology plays a role in survival, specifically those with both hepatocellular carcinoma and hepatitis C (hazard ratio 2.5, p-value=0.0001). Patients living beyond 180 miles had a HR of 2.85 (p-value=0.0024) compared to those within 180 miles. In the model, adjustments were made for insurance status, gender and age. Patients on Medicare have a better survival (HR=0.75) compared to other insurance. An improved survival was noted in females compared to males (HR=0.82) and patients under the age of 65 (HR=0.80).

Conclusion: Currently, our data shows a trend in SES variables that can predict survival post-transplant. Etiology, gender, insurance type, and distance from the transplant center all had an effect. We will continue to refine outcomes models by collecting additional data, incorporate SPM into medical models of outcomes. We anticipate having the opportunity to improve outcomes for transplant patients nationally by disseminating our research to transplant societies, the transplant community and UNOS.

Research supported by: Angel E. Alsina Alexia Makris

Presented by: Avery Johnson, BS, Undergraduate

Effect of Atp8b1 Deficiency on Bleomycin-Induced Pneumopathy

Avery Johnson, Jutaro Fukumoto, Young Cho, Itsuko Fukumoto, Ruan R.Cox Jr, Richard F Lockey and Narasaiah Kolliputi Division of Allergy and Immunology, Department of Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa Fl, University of South Florida, Honors College

Keywords: Atp8b1 bleomycin penumopathy

Objective: To characterize the influence of Atp8b1 deficiency on bleomycin-induced pneumopathy.

Methods: Seven to nine-week-old wild type C57BL/6 mice and age-matched Atp8b1-deficient mice with the same genetic background were administered 1 or 1.5 U bleomycin (BLM) or saline into the trachea. Mice were sacrificed at two weeks to collect lung tissues for histological evaluation. The pathological scores of inflammation and fibrosis in the area of midsagittal sections were evaluated under 40 x magnifications using a semi-quantitative scoring method.

Results: Bleomycin-treated Atp8b1-deficient mice exhibit lower survival rates and larger weight loss compared to WT controls. However, no significant difference was found between Atp8b1-deficient and WT mice in lung pathological scores.

Conclusion: The results suggest that the lower survival rate observed in bleomycin-treated Atp8b1-deficient mice is due to enhanced inflammation rather than enhanced fibrosis.

Abstract #: 300

Presented by: Nicholas Johnson, Undergraduate

TDP-43 Pathology in Neurodegenerative Disorders

<u>Nicholas Johnson¹, Jerry Hunt^{2,3}, Joseph Liu¹, Blake Housley¹, Kevin Nash PhD^{1,3}, Daniel Lee PhD^{1,3}, Maj-Linda Selenica PhD^{1,3} ¹Byrd Alzheimer's Institute, University of South Florida, Tampa, FL; ²Department of Molecular Pharmacology and Physiology, USF Morsani College of Medicine, ³USF College of Pharmacy, Department of Pharmaceutical Sciences, Tampa, FL.</u>

Keywords: TDP-43, a-synuclein, frontotemporal lobar degeneration

Objective: TAR DNA-binding protein-43 kDa (TDP-43) has been found in neuronal inclusion of frontotemporal lobar degeneration (FTLD), mainly in the cortex and hippocampus (Sen, et al 2014). α-synuclein is the main component in neuronal inclusion of Parkinson's Disease. This study aimed to investigate induction of TDP-43 or _____synuclein pathology via recombinant adeno associated virus serotype 9 expression (AAV9) in the brain of CAMKII mice. We also investigated the effect of TDP-43 pathology on induction of inflammation.

Methods: 12-20 month old CAMKII mice were injected with AAV9-CBA-GFP (8.0*1012 vg/ml), AAV9-CBA-GFP-TetO-TDP43 (8.3*1012vg/ml), or AAV9-CBA-GFP-TetO-αsyn (7.2*1012vg/ml); viral expression was allowed for four months. TDP-43/ synuclein pathology was analyzed in the brain tissue of mice by immunohistochemistry (IHC). Markers of microglia activation (Iba1, CD45) and levels of TDP43/a-synuclein expression were measured by using human monoclonal rat Mab anti-TAP DNA binding protein (Millipore) and Alpha-Synuclein Rabbit Mab (Epitomics) antibodies.

Results: IHC analysis Iba-1 stain indicated a slight increase in microglial levels near the injection site in TDP-43 but not in α -synuclein injected mice compared to the GFP control group. The levels of microglial activation investigated by CD45 marker showed no changes in either of the injected groups. Ongoing IHC analysises are determining the extent of TDP-43 and α -synuclein pathology in these mice.

Conclusion: Ongoing studies will determine the effect on TDP-43 pathology/accumulation and inflammation on normal function and survival of glial and neuronal cells.

The Development of Dexamethasone Encapsulated Nanoparticles for Treatment of Ocular Inflammation

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Sciences, Tampa, FL

Keywords: Nanoparticle, dexamethasone, ocular inflammation

Objective: To develop a non-toxic, nanoparticle-encapsulated form of dexamethasone for a sustained release treatment of ocular inflammation.



salt (MTT) assay was used to asses cytotoxicity in vitro in ARPE-19 (human retinal epithelial) cells

Results: The average size of the particles was found to be less than 200 nm. By using UV spectroscopy at 239 nm, the NP yielded 46.28% encapsulation of dexamethasone drug. Dexamethasone encapsulated NPs showed no cytotoxic effect on ARPE-19 cells.

Conclusion: The present study describes the development of dexamethasone encapsulated PLGA-PEG nanoparticles for the potential treatment of ocular inflammation. Initial characterization and cytotoxicity studies show the proposed targeting system for dexamethasone could be an effective sustained release treatment for ocular dysfunction.

Research supported by: Research was supported by startup grant given to Dr. V. Sutariya by USF College of Pharmacy.

Abstract #: 302

Presented by: Daniel T. Lee, Undergraduate

Soy Isoflavone Daidzein Induces Arginase 1 and Curtails Tau levels in Vitro

Daniel T. Lee, Devon Placides, Firas Abuqalbeen, Etee Patel, Umesh Jinwal, PhD, Daniel C. Lee, PhD University of South Florida, College of Arts and Sciences, Department of Chemistry

Keywords: tau, arginase, daidzein

Objective: Neurodegenerative diseases associated with tauopathies are pathologically characterized by accumulation of aberrant protein aggregates such as tau. Tau is a microtubule-associated protein (MAP) that stabilizes microtubules in neurons, however can become hyperphosphorylated and lead to neuronal death. Currently no therapies exist that curtail tau pathology, however our recent data suggest that arginase 1 (Arg1) an enzyme that initiates the polyamine pathway might impact tau pathology. Herein, we aimed to identify agents that increase protein expression of Arg1 in cells in an attempt to modify tau.

Methods: A mouse hippocampal cell line (HT22 cells) was created to stablely express full-length human tau (subclone HTDL11). Using semi-high throughput screening methods, previous results identified several drugs that increase Arg1 expression, one of which was a soy isoflavone (daidzien). HTDL11 cells were treated with daidzein for 72 hours at 1 μ M, 10 μ M, 50 μ M and 100 μ M. Western blot analysis was performed, to measure the levels of total tau and Arg1.

Results: Daidzein at 50 µM and 100 µM significantly reduce total tau levels in HDTL11 cells and significantly increase Arg1 expression when compared to the control. Several additional agents are currently being investigated for Arg1 and tau expression.

Conclusion: These data suggest that daidzein modifies tau levels and increases Arg1 expression in a hippocampal cell line that overexpresses full-length human tau. Furthermore, these data supports our previous work and hypothesis demonstrating that Arg1 overexpression reduces tau pathology in tau transgenic mice and cells. For proof of principle, we have identified agents that increase Arg1 promoter expression and reduce tau levels at the cellular level.

Presented by: Mackenzie Lee, Undergraduate

Uncoupling Akt and FoxO1 by aPKC in Obesity

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Keywords: Atypical Protein Kinase C, Insulin, Liver, Gluconeogenesis, FoxO1, Propeller/Fyve, Lipogenesis, High Fat Diet, Obesity, Hyperlipidemia, Metabolic Syndrome, Type 2 Diabetes

Objective: The aim of this project was to ascertain the initiating and sustaining mechanisms that impair gluconeogenic enzymes and spare lipogenic enzymes in diet-induced obesity (DIO).

Methods: Here, we examined insulin signaling to Akt and atypical PKC (aPKC) in liver and muscle, and hepatic enzyme expression in two diet-dependent obesity models: (a) mice fed a moderate (40% of calories) high-fat (HF) diet over 10 weeks, and (b) 5 month-old obese non-diabetic ob/ob mice.

Results: In HF and ob/ob mice, hepatic Akt and aPKC activities were increased. Despite elevated Akt activity, FoxO1 phosphorylation, which diminishes gluconeogenic enzyme expression, was impaired. Diminished Akt-dependent FoxO1 phosphorylation was traceable to reduced Akt activity associated with a scaffold protein, ProF, which facilitates Akt-dependent FoxO1 phosphorylation. In contrast to Akt, levels and activity of aPKC associated with ProF was markedly increased. Selective but partial inhibition of hepatic aPKC with small molecule agents during the 10 week period reduced aPKC association with ProF, restored ProF-associated Akt activity and FoxO1 phosphorylation, and diminished expression of gluconeogenic enzymes. With inhibition of hepatic aPKC, hepatic lipogenic enzyme expression also diminished, as did glucose intolerance, weight gain, hepatosteatosis and hyperlipidemia.

Conclusion: Our findings show that in liver, Akt-dependent FoxO1 phosphorylation occurs on the ProF scaffold and is selectively inhibited in both initial and later phases of DIO by increases in activity of co-compartmentalized aPKC.

Research supported by: Research supported by funds from the Department of Veterans Affairs Merit Review Program and the National Institutes of Health Grants [7R01DK 065969-09] to R.V. Farese.

Abstract #: 304

Presented by: Joseph Leung, BS, Undergraduate

Atp8b1, an Approach toward Protective Treatment of Acute Lung Injury.

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Keywords: lung, hyperoxia, inflammation, apoptosis, mitochondria

Objective: To characterize the influence of ATPase, Aminophospholipid Transporter, Class I, Type 8B, Member 1 (Atp8b1) deficiency on hyperoxia-induced lung injury.

Methods: Wild type C57BL/6 mice and 7-9-week-old age-matched Atp8b1 deficient mice with the same genetic background were exposed to 100% oxygen. After 48 hours exposure, mice were sacrificed to collect bronchoalveolar lavage fluid (BAL fluid) for cell count and cytokine measurement. Concurrently, lung tissue was collected for H&E staining, Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) staining, and immunohistochemical staining.

Results: BAL fluid analysis revealed IL-6 concentration to be significantly higher in Atp8b1 deficient mice while protein concentration showed almost no difference. Diff-Quik staining using BAL fluid cells showed that the numbers of neutrophils was greater in Atp8b1 deficient mice. Histological evaluation using H&E stained lung tissue sections revealed that there is no apparent difference in alveolar congestion and interstitial thickening, which is compatible. Meanwhile, CCSP-positive Clara cells exhibit more exfoliation in Atp8b1 deficient mice compared to age-matched WT littermates. These exfoliating cells were negative for TUNEL, suggesting that Atp8b1 deficiency induce loosened contact between Clara cells and adjacent extracellular matrix (ECM) in the setting of hyperoxic injury.

Conclusion: Atp8b1 plays a protective role against hyperoxia-induced lung injury. The mechanism could be through suppressed inflammation including blunted IL-6, neutrophil activity in the lung, and anchoring Clara cells to keep lung homeostasis. Atp8b1 enhancers could be novel pharmaceutical therapies for the treatment of acute lung injury.

Presented by: Joseph Liu, Undergraduate

CCL2-CCR2 Dysregulation and Its Implication in Clearing Phosphorylated Tau Aggregates

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Keywords: CCR2 tau CCL2 autophagy neurotoxicity

Objective: Chemokine receptor type 2 (CCR2) and its ligand CCL2, are markers of myeloid derived cells, involved in regulating monocyte infiltration into tissue. CCR2 expression is shown in various cell types, and the receptor has been shown to play a functional role in neurological diseases. We aim to investigate the impact of CCR2 signaling in the autophagy machinery of neurons with direct impact on tau pathology.

Methods: We investigated the role of CCR2 receptor by utilizing two cell lines: human cancer cell line (HeLa) and the mouse hippocampal cell line (HT22). Both cell lines stably express full length human tau (4R0N, 441aa). To demonstrate the CCR2 expression in the transmembrane of both cell lines, we used biochemical and immunocytochemical (ICC) approaches. We performed transfection of Hela-tau expressing cells (C3 cells) and HT22 cells with shRNA-/siRNA- CCR2 to silence the receptor's expression. Transfection efficiency was observed by microscopy utilizing the GFP tag in these constructs. We extracted the membrane-bound proteins from cell homogenates, and probed for CCR2 levels by western blotting.

Results: We observed 95% transfection efficiency in C3 cell by fluorescence microscopy. Biochemical analyses showed 75% downregulation in CCR2 expression in C3 cells and 65% in HT22 cells compared to untreated or scramble-shRNA treated cells. Further, ICC staining displays expression of CCR2 and total human tau levels in both cell lines.

Conclusion: By genetically silencing the expression levels of CCR2, we will investigate whether the inhibition of CCR2/CCL2 pathway stimulates the degradation of human tau by inducing autophagy machinery. These findings will suggest that CCR2 signaling can be targeted in the brain to prevent neurotoxicity.

Abstract #: 306

Presented by: Jomar Lopez, BA, Undergraduate

Genotype Demonstrates a Stronger Association in Contextual and Cued Fear Conditioning than Stress Paradigms or Immune System Activation

Jomar Lopez, Trish Dinh, B.S., Joshua Gamsby, Ph.D., Danielle Gulick, Ph.D. University of South Florida Morsani College of Medicine, Dept. of Molecular Medicine

Keywords: Schizophrenia, Fear Conditioning, Mice, Hippocampus

Objective: In this experiment, we investigate the role of Reelin (RELN) and Disrupted-in-Schizophrenia 1 (DISC1) genes on contextual and cued learning in the fear conditioning paradigm. This is important because these genes convey susceptibility to schizophrenia, and learning is often impaired in this disease.

Methods: Twenty-five male and 11 female mice (8-14 weeks old) of wild-type, RELN, and DISC1 genotypes, were grouphoused. Fear conditioning is a measure of associative learning, in which an auditory conditioned stimulus is associated with an unconditioned stimulus, a foot shock. The response measured was freezing. In contextual fear conditioning, the animal learns to associate a chamber with the shock; although not for cued fear conditioning, in which the animal associates a tone with the shock. Fear conditioned training lasted 7min. At 3min, a 70 dB tone played for 30s. During the final 2s of the tone the mice were given a 50 mA electric shock. The process was repeated at 5 minutes. The next day, the context test was 3min. No tone was presented. During the cue test, mice were placed in an altered context for 3min, then the tone was played for 3min. The scores were recorded in five second intervals.

Results: RELN +/- male and female mice froze less than all other mice in both context and cued tests, but only RELN +/- female mice were impaired in cued testing. DISC1 mutant females froze less than all other mice.

Conclusion: Preliminary data suggests that contextual learning, which is hippocampus-dependent, is affected by genotype regardless of sex, although cued learning is only affected in mutant females. RELN gene mutation may affect hippocampal development more than development of other learning-related brain regions.

Presented by: Jonathan Low, BS, Undergraduate

Schizophrenic Social Trends in Dual Transgenic Disc1 and Reelin Mutant Mice

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Keywords: Schizophrenia, animal model, social behavior, DISC1, Reelin

Objective: Schizophrenia is a devastating disorder for which needs more valid animal models. Two current animal models of SCZ include mice with DISC1 or Reelin mutations. These models are inadequate because each lacks enough of the anatomical and behavioral abnormalities seen in SCZ. Taking into account the possibility of prenatal risk factors for SCZ, the aim of this study is to combine DISC1 transgenic with Reelin transgenic mice, this cross yielding 4 different variants of mice. Prenatal stressors will be introduced via Poly I:C viral mimetic injections. Social interaction and social novelty tests are then used to quantify social behavior and social memory.

Methods: Subjects: The mice (males and females, 8-14 weeks old at testing) are group housed with a 12/12 light cycle. Poly I:C injections are introduced embryonically at 9/17 days or postnatal at 2/6 days. Social Interaction is a 10 minute test with two mice placed on opposite ends of an open field, scoring nose to nose and following interactions. Social novelty is a 10 minute, two-step test. An open field is divided into left, center and right sections. In part 1, one control mouse is caged on one side, in part 2, a second mouse is added to the far chamber. Nose to cage interactions and circling the zones containing each control mouse are scored.

Results: In SN, control mice showed greater preference for the mouse chamber than the empty chamber in the first part of the test and greater preference for the new mouse in the second part. These behaviors were attenuated in the Disc1 and Reelin mutant mice. There were no differences in social interaction, however.

Conclusion: DISC 1, and to a lesser extent TTA/Reelin mutations, reduce normal social preference and memory without reducing general social behavior.

Abstract #: 308

Presented by: Diego Lozano, Undergraduate

Splenic Expression of CD-36 in a Rat Model of Traumatic Brain Injury

<u>Diego Lozano^{1,} Diana G Hernandez-Ontiveros^{1,} Cyrus Tamboli¹, Sarosh Tamboli^{1,} Daniela Aguirre^{1,} Naoki Tajiri^{1,2,} Mibel M Pabon^{1,2}, Sandra Acosta^{1,2,} Yuji Kaneko^{1,2}, Paula C. Bickford^{1,2,} Cesario V Borlongan^{1,2, 1}Center of Excellence for Aging and Brain Repair, ²Department of Neurosurgery and Brain Repair, University of South Florida, College of Medicine, Tampa, Fl</u>

Keywords: Traumatic brain injury (TBI), Fatty acid translocase (FAT,CD-36), monocyte chemoattractant protein-1 (MCP-1), oxidized/modified low density lipoprotein (ox-LDL,mLDL), controlled cortical impact (CCI)

Objective: Morbidity and mortality of TBI continues to increase steadily due to sports related concussions, traffic accidents, and armed military conflict worldwide. Primary injury due to war related head injury may result in direct neuronal cell loss, followed by a secondary wave of events such as neurodegeneration, inflammation, and cell death. In recent studies, FAT/CD-36, found in B cells and macrophages in the spleen, is a multifunctional scavenger receptor of mLDL linked to lipid breakdown, atherogenesis, cardiomyopathy, the inflammatory response after cerebral ischemia, and Alzheimer's disease. Our study will focus in the characterization of CD-36 in the spleen of a murine TBI model to determine a pathological connection between CD-36 and inflammation in TBI.

Methods: TBI was inflicted to adult male Sprague-Dawley rats using CCI. Different cohorts of TBI rats were euthanized at twenty-four and forty-eight hours after TBI. Their spleens were removed and processed accordingly for immunohistochemical (IHC) staining against CD-36, and MCP-1. Sham animals were processed similarly and served as controls.

Results: Spleen is a big reservoir of monocytes/macrophages. Preliminary data revealed major co-localization of CD-36 and MCP-1 in the red pulp of spleen of TBI animals when compared to sham.

Conclusion: Ongoing ischemic and hyperlipidemic rodent models suggest that infiltrating monocytes/macrophages from the periphery are the major source of CD-36 in the post-ischemic brain. Likewise, CD-36 expressing monocytes in the spleen after TBI may suggest its role in peripheral immune response, which may exacerbates the inflammatory response after TBI.

Research supported by: Dept. of Defense, USF-VA Reintegration Funds

Developing a Line of More Severe Schizophrenic Mice Via Multiple SCZ-linked Gene Mutations and Environmental Stressors

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Keywords: Forced swim test, elevated plus maze, reelin, locomotion, depression, anxiety

Objective: Developing drug therapies for schizophrenia (SCZ) has been challenge as there are no ideal animal models. Testing models display varying severity of the disorder compared with real patients. We propose developing a mouse line that more closely mimics full-scale SCZ by modulating SCZ-linked genes and environmental stressors.

Methods: To test the behavioral effects of a gene mutation, both wild-type (RLN +/+) and mutant heterozygous (RLN +/-) Reelin mice were tested for locomotor ability, depression, and anxiety using forced swimming test (FS) and elevated plus maze (EPM). FS measures the subject's willingness to swim for 6 minutes to measure depressive behavior. Mice that are more depressive will give up easily. EPM tests the subject's activity and preference for open or walled arms of the maze (a measure of anxiety) for 5 minutes. A mouse that spends more time in the open arms of the EPM is less anxious.

Results: Preliminary data from EPM trials show both the RLN+/+ and RLN+/- mice covered the same distance and moved between arms an equal number of times, but the RELN+/- mice spent more time freezing and less time in the open arms, indicative of greater anxiety in these mice. In addition, male mice spent more time in the open arms than female mice across genotype, suggesting greater anxiety in female mice. Finally, females had a greater latency to their first immobile episode on Day 1 of FS but greater overall immobility on Day 2 than males, suggesting less reactivity to acute despair but a higher degree of learned helplessness.

Conclusion: These results will serve as a foundation for breeding more ideal animal models used in developing schizophrenia drug treatments.

Research supported by: Molecular Medicine

Abstract #: 310

Presented by: Preya Patel, Undergraduate

The Development of Docetaxel Nanoparticles for Potential in Vivo Use

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Keywords: Nanoparticle, docetaxel, brain cancer

Objective: To develop an organic, non-toxic, nanoparticle-encapsulated form of the drug, docetaxel, in an attempt to make its use safer.

Methods: The poly(ethylene glycol)ylated (PEGylated) poly-(lactide-co-glycolide) (PLGA) nanoparticles were formulated to encapsulate the free docetaxel drug by using the nanoprecipitation method. After the formation of the nanoparticles, dynamic light scattering (DLS) was used to investigate the size of the particles, a methanol-based method was used to determine its encapsulation efficiency of the drug, and the nanoparticle's in vitro release of the drug was tested.

Results: The average size of the particles was found to be 83.76 nm +/- 7.66 nm. By using UV spectroscopy at 231 nm, the nanoparticle yielded 42.79% +/- 17.12% encapsulation of the docetaxel drug. The nanoparticle's in vitro release of the drug revealed a sustained release over 72 hours in which 5.5% of the drug was released. The lack of an initial burst release reveals that the drug was well encapsulated by the nanoparticle and did not exist at the surface of the nanoparticle.

Conclusion: The present study describes the development of a nanoparticle-based delivery system for docetaxel that is encapsulated, therefore far less toxic than the free drug solution that is administered today against a number of different cancers. The nanoparticle's surface can be coated with a number of different compounds to induce its targeting of specific tissues against specific types of cancers.

Research supported by: Research was supported by startup grant offered to Dr. V. Sutariya through the USF College of Pharmacy.

Presented by: Diego Peralta, Undergraduate

Screening and Identification of a Novel Drug Targeting TDP-43 for the Treatment of ALS

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Keywords: Amyotrophic Lateral Sclerosis, TDP-43, Drug discovery, In-Cell Western technique, C. elegans

Objective: Our goal is to discover novel drugs either to cure or delay Amyotrophic Lateral Sclerosis (ALS) disease progression. Abnormal accumulation of the RNA-binding protein trans-active response DNA-binding protein 43 (TDP-43) in neurons has been shown to be a critical factor for ALS progression. Using a newly developed TDP-43 protein based In-Cell Western (ICW) technique, we have screened ~300 drugs to identify a novel drug for TDP-43 regulation. The newly identified drug is being characterized in vitro and in vivo using TDP-43 expressing cellular and C. elegans based models.

Methods: N9 cells expressing endogenous TDP-43 were treated with drugs for 24 hours and processed for ICW. Any drug/s that altered TDP-43 levels was tested by western blotting to confirm its effect. Subsequently, TDP-43 targeting drug was tested in the TDP-43 expressing C. elegans animal model of ALS. Animals were treated with the drug for 24 hours and then analyzed for behavioral and biochemical changes.

Results: ICW screening of over 300 drugs particularly revealed a drug (B10) that dramatically reduced TDP-43 levels by ~50% compared to the vehicle-treated (DMSO) control. Validation of ICW data on B10 by western blot analysis also showed similar reduction in TDP-43 levels. Preliminary data from in vivo analysis of a TDP-43 expressing C. elegans animal model showed improvement in motility upon B10 treatment.

Conclusion: We have found that treatment with B10 reduced TDP-43 levels in cellular models. Additionally, preliminary analysis of B10 treatment of the in vivo C. elegans TDP-43 expressing model of ALS showed promising improvement in motility. Overall, our data suggest that B10 could serve as a potential drug molecule for the treatment of ALS.

Abstract #: 312

Presented by: Ryan Putney, BS, Undergraduate

Methylation Signal Comparison using Illumina Arrays

<u>Ryan Putney¹, Anders Berglund², Erin Siegel², David Shibata², Steven Eschrich² ¹Department of Computer Science and Engineering, University of South Florida College of Engineering, ²Moffitt Cancer Center</u>

Keywords: methylation, bioinformatics, statistics, microarray

Objective: DNA methylation is an epigenetic factor that plays an important role in cancer, including tumorigenesis. Technical advances in high-throughput microarrays allow for extensive, parallel evaluation of methylation status throughout the genome, however analysis remains challenging. The objective of this research is to gain a deeper understanding of methylation estimates from microarray data.

Methods: Methylation data was replicated on successive generations of Illumina Beadchips (the 450k and 27k) and used to study methylation signal. Raw methylation data was downloaded from TCGA (The Cancer Genome Atlas). Beta values (ratio of methylated signal to the sum of methylated and unmethylated signals) and raw signal intensity were used for comparisons using the R/Bioconductor statistical software

Results: Replicate methylation data from 6 lung adenocarcinomas were analyzed on both the 450k and 27k platforms. Many probes on the older 27k were converted to a different chemical assay on the 450k, while some remained unaltered. Comparisons across platforms were performed to investigate methylation signal. As expected, high correlations were observed in beta values between probes common to both platforms (R2>0.9). However, lower correlation in intensities was observed and the intensity distribution differed between the platforms despite similarity in beta values. This suggests wider variability between platforms than the ratio data (beta values) describe.

Conclusion: Although beta values are frequently used to determine differential methylation, our results suggest that beta values may not accurately reflect the desired underlying biological methylation state. This indicates alternate methods for interpreting high-dimensional methylation data need to be explored.

Presented by: Kevin Ratnasamy, BS, Undergraduate

Analysis of Efficiency of Promoter-Driven Expression in rAAV in Mouse Brains

<u>Kevin Ratnasamy¹, Peter Moran², Kevin Nash², ¹University of South Florida College of Arts and Sciences, Dept. of Cell Biology, Microbiology & Molecular Biology, ²USF Morsani College of Medicine, Dept.of Molecular Pharmacology and Physiology</u>

Keywords: rAAV, gene therapy, cell targeting

Objective: To examine a variety of cell-type-specific promoters in recombinant adeno-associated virus (rAAV) to establish highly efficient cell-specific expression within the various cell types found in the mouse brain.

Methods: Different cell-type-specific promoters were generated by PCR from mouse gDNA and cloned into rAAV plasmids driving green fluorescent protein (GFP) expression. Stereotaxic surgeries were performed following an IACUC-approved protocol. Viral constructs were delivered directly into the right hippocampus and left anterior cortex of the mouse brain. Following a month long incubation, the mice were euthanized, brains collected, fixed, and subsequently sectioned on a microtome. Sections were then used for fluorescent immunohistochemistry (IHC) to stain for cell-specific markers such as GFAP, Iba1, Neu-N, and OSP. Stained sections were then mounted, coverslipped, and analyzed using fluorescence microscopy to determine colocalization of GFP with the cell specific markers.

Results: We have identified several promoters that give cell-specific expression and some that do not. Further analysis is underway on other remaining promoter sequences.

Conclusion: The characterization of new cell-specific promoters will be an invaluable tool in the study of individual cell types within the complex cell structure of the brain. Cell-type-specific expression will also be critical in understanding specific cell type contributions to neurological disorders. Expression in specific cells within the brain will also have a more targeted therapeutic approach in neurological disorders and hopefully reduce negative off-target effects of any therapeutic delivered genes.

Abstract #: 314

Presented by: Andrea Rivero, Undergraduate

Molecular Basis of Extreme Resistance in Plasmodium Falciparum to Atovaquone and Other Mitochondrial Inhibitors

<u>Andrea Rivero¹, Sasha Siegel², and Dennis E. Kyle³</u> ¹Department of Chemistry, College of Arts and Sciences, University of South Florida; ²USF Morsani College of Medicine; Dept. of Global Health, USF College of Public Health

Keywords: Malaria, drug resistance, Plasmodium falciparum

Objective: Atovaquone is a safe, effective antimalarial drug that inhibits the mtETC of P. falciparum. Clinical resistance is conferred by SNPs in cyt b. We are investigating additional mechanisms by which some isolates of P. falciparum became extremely resistant to atovaquone and other mtETC inhibitors by selecting for in vitro resistance to the DHODH inhibitor DSM-1.

Methods: We characterized isolates from patients that failed treatment in atovaquone phase II studies by using a series of chemotypes that target mitochondrial function. We defined their structure-activity relationships and observed broad resistance (5-10,000 fold in atovaquone), suggesting that cyt b mutations alone are not sufficient. We tested this by selecting for DSM-1 resistance in atovaquone susceptible and resistant parasites (paired patient admission and recrudescent isolates). Following selection, the parasites were sequenced for mutations in cyt b, DHODH and others.

Results: The extreme atovaquone resistance phenotype accompanies high-grade resistance to all mtETC inhibitors tested including DSM-1. Selection studies of atovaquone susceptible parasites rapidly generated resistance in vitro to both atovaquone and DSM-1 alone (10x IC50 concentration) yet atovaquone resistant parasites could only generate low resistance to DSM-1 (2x IC50).

Conclusion: Cyt b mutations are not sufficient to explain extreme mtETC resistance, and selective pressure on the DHODH enzyme revealed that the cyt b mutation incurs a fitness cost on the parasite that cannot be overcome at high concentrations of DSM-1, yet resistance was easily obtained in atovaquone susceptible parasites. Further studies are required to determine the impact of this phenotype on the development of new mitochondria targeted drugs.

Presented by: Awa Sanneh, Undergraduate

Pathology and Propagation of C-terminal Truncated Tau and Full Length Tau in Wild Type Mice

<u>Awa Sanneh^(1,), Kevin Nash⁽¹⁾, Steven B. Housley⁽³⁾, Barbara Manchec⁽³⁾, Joseph Liu⁽¹⁾, Marcia N. Gordon⁽¹⁾, Dave Morgan⁽¹⁾, Maj-Linda Selenica^{(1,2), 1}Byrd Alzheimer's Institute and Dept. of Molecular Pharmacology and Physiology, Morsani College of Medicine, University of South Florida, Tampa, FL; ²Dept. of Pharmaceutical Sciences, USF College of Pharmacy; ³USF Morsani College of Medicine</u>

Keywords: tau, aggregation, Alzheimer's disease, truncated tau, p-tau

Objective: Tau exists in hyperphosphorylated and truncated isoforms which induce aggregation and have been recognized as components of neurofibrillary tangles which elicit neurodegeneration in Alzheimer's Disease (AD). A study was designed to ascertain the neurodegenerative effects of full length (FL-tau) and C-terminal truncated tau (C-tau) so as to characterize the structural changes associated with tau polymerization. Also of interest was to investigate the mechanism of tau propagation.

Methods: FL and C-tau proteins were delivered via adeno associated virus technology (AAV9). These viruses were injected bilaterally in the hippocampus and cortex of 15 month old wild type mice and incubated for 4 months. Immunohistochemistry (IHC) was used to analyze the tau pathology (H150, AT8, Ser396, Ser199-202, Gallyas) within brain tissue.

Results: IHC analyses showed a consistent spread of the virus from the injection sites into the striatum, corpus collosum, and subiculum of the mice brains. Levels of total tau, measured by H150 stain revealed no significant differences between tau levels in the FL-tau and C-tau mice. Levels of phosphorylated tau detected by AT8 antibody were significantly higher in the hippocampus of C-tau injected mice than in FL-tau injected animals. Meanwhile, significantly higher levels of Ser396 p-tau were measured in the cortex in FL-tau injected mice. No changes in Ser199-202 p-tau were observed between groups.

Conclusion: Further analyses of tau pathological markers, neuronal loss and synaptic markers are in progress; however the preliminary results show great promise in a renewed understanding of structural influences on tau propagation and pathology

Research supported by: Funding provided by Byrd Alzheimer's institute, University of South Florida

Abstract #:316

Presented by: Tanya Sehgal, Undergraduate

Functional Role of ADAM10 in Ovarian Cancer

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Keywords: Ovarian Cancer, secretases, ADAM10, APP, secreted APP

Objective: The goal of this project is to determine the role of alpha secretase, ADAM10, in proliferation, metastasis and growth of ovarian cancer cells.

Methods: Four different ovarian cell lines were used in this study: two normal and two cancerous cell lines. These cells were treated with or without 5µM Gl254023X, a specific inhibitor of ADAM10 (A Disintegrin and metalloproteinase domaincontaining protein), and cell lysates and tissue culture supernatant were analyzed by SDS polyacrylamide gel electrophoresis (SDS-PAGE) and Western blot. Cellular distribution of the proteins were analyzed by immunocytochemistry; the cells were cultured in 8-chamber slides, treated with Gl254023X, fixed with 4% PFA, incubated with primary and secondary antibodies and staining was analyzed under a fluorescent microscope.

Results: Ovarian cancer cells express higher levels of both ADAM10 and its substrate, APP. The cells treated with Gl254023X showed an inhibition of ADAM10 activity, as evident by the decreased generation of secreted APP (sAPPalpha). Additionally, Gl254023X treated cells showed an increase in the levels of an ~80 kDa ADAM10 fragment, indicative of its altered processing upon treatment with the inhibitor. The appearance of the ~80 kDa band correlated with decreased generation of sAPPalpha, suggesting that this could be an inactive fragment of ADAM10.

Conclusion: The increased expression of ADAM10 and its substrates in ovarian cancer cells suggests that it may play a role in the growth and proliferation of the cells. Inhibition of ADAM10 led to a decrease in the generation of the growth-promoting fragment of APP. Our findings suggest that targeting ADAM10 may serve as a means for prevention of growth and metastasis of ovarian cancer.

Research supported by: USF-COM

Presented by: Nina Slouha, Undergraduate

Inflammation Induced by IL-1beta Impacts Tau Pathology in tetO-MAPT P301L Mice

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Keywords: Inflammation Induced by IL-1B

Objective: Tau(MAPT) is a microtubule-associated protein that stabilizes microtubules, however it can accumulate and become hyperphosphorylated, which lead to neurodegeneration. Data suggest that neuroinflammation impacts neurodegenerative disorders. We aim to test if interleukin-1beta(a proinflammatory cytokine) impacts tau pathology in a model that expresses human tau mutation on a tetracycline operator(tetO-MAPT P301L) and driven by tetracycline activator protein(tet).

Methods: Using adeno-associated virus(AAV)to express the tet protein in tetO-MAPT P301L mice, we stereotaxically injected the AAV constructs that express tet and green fluorescent protein(GFP)into the hippocampus and anterior cortex. Three groups of mice were used consisting of: Group1 tet-AAV-GFP only; Group2 tet-AAV-GFP+CBA-AAV-IL-1beta; and a naive group(group3)that received no injections to establish basal levels of tau expression in tetO-MAPT P301L mice. Groups 1 and 2 received unilateral injections of the tet-AAV-GFP construct. Group 2 also received the CBA-AAV-IL1beta construct on the opposite hemisphere to identify if inflammation throughout the brain impacts the tau pathology. Immunohistochemistry and unbiased image analysis measured tau and GFP expression.

Results: The model demonstrated that local injection tet-AAV-GFP greatly increased tau expression in the hippocampus and cortex of tetO-MAPT P301L mice compared to the naïve mice. Also, mice that received the IL-1beta construct showed greater tau expression on the ipsilateral and contralateral hemisphere.

Conclusion: These data suggest that inflammation provoked by IL-1beta impacts tau pathology. These data also suggest that tetO-MAPT P301L mice and tet-AAV-GFP may serve as a model for pathological tau spreading induced by inflammation.

Abstract #:318

Presented by: Meaghan Staples, BS, Undergraduate

Repair of the Blood Brain Barrier for Attenuation of Metastatic Brain Cancers of Melanoma

Meaghan Staples, Naoki Tajiri, Sandra Acosta, Mibel Pabon, Yuji Kaneko, Thomas B. Freeman, Harry van Loveren, Seung U. Kim, Cesar V. Borlongan University of South Florida Morsani College of Medicine, Department of Neurosurgery and Brain Repair

Keywords: Blood Brain Barrier, Cancer, Endothelial Progenitor Cells, Bone Marrow-Derived Stem Cells

Objective: To date, there is scarce data on treatment strategies targeting repair of the blood brain barrier (BBB) in brain cancer. In fact, reparation of the BBB through angiogenesis or vasculogenesis is thought to exacerbate the formation of metastatic brain cancers. Here we will show that continued neglect of BBB contributes to the formation of brain metastatic cancers of melanoma. Subsequently, we will demonstrate that bone marrow-derived endothelial progenitor cell (BMEPC) therapy can repair the BBB by augmenting angiogenesis and vasculogenesis, resulting in the attenuation of developing metastatic brain cancers.

Methods: B16F10 mice are evaluated at three time points (day 3, 7, and 21) and compared to controls. Western immunoblotting, immunohistochemistry, and PCR, are used to examine metastatic brain cancer growth, BBB leakage, and inflammation. Secondly, we evaluated the efficacy of grafted BMEPCs to repair BBB damage and ameliorate brain inflammation. Cell transplantation occurred at acute and delayed time points to represent varying stages of metastasis and determine optimal timing.

Results: Preliminary data showed that transplantation of BMEPCs repaired the damaged BBB associated with metastatic brain cancers of melanoma. Such BBB restoration appeared to prevent the entrance of inflammatory factors from systemic circulation, thereby attenuating brain inflammation and suppressing brain tumor growth.

Conclusion: This study characterizes the immunological and inflammatory responses associated with a leaky BBB that may contribute to the development of brain metastatic cancers of melanoma. This impacts our understanding of the pathology of metastatic brain cancers and represents a novel therapeutic approach.

Research supported by: USF Department of Neurosurgery and Brain Repair

Presented by: Cyrus Tamboli, Undergraduate

The Battle of the Sexes for Stroke Therapy: Female- Versus Male-Derived Stem Cells Cyrus Tamboli¹, Yuji Kaneko^{1*}, Travis Dailey^{1*}, Nathan L. Weinbren^{1*}, Jessica Rizzi¹, Julie Vasconcellos², Nicole Kuzmin-Nichols^{3,} Paul R. Sanberg¹, David J. Eve¹, Naoki Tajiri¹, and Cesar V. Borlongan¹ Department of Neurosurgery and Brain Repair, University of South Florida College of Medicine, Tampa, FL²Cryo-Cell International, Inc., Tampa, FL³Saneron-CCEL Therapeutics Inc., Tampa, FL

Keywords: menstrual blood, Sertoli cells, autologous, ischemic stroke, regenerative

Objective: We evaluate the experimental and clinical application of menstrual blood cells and Sertoli cells to treat stroke. Also, we describe menstrual blood and Sertoli cells, discuss their mechanisms of repair in ischemic stroke, and depict transplantable features of menstrual blood cells and Sertoli cells as autologous cell donors for personalized medicine.

Methods: The assessment of menstrual blood cells and Sertoli cells as viable therapy for stroke was conducted by analyzing previous studies related to menstrual blood cells and Sertoli cells to understand the principal mechanisms of the different cells and how they may aid in the process of recovery from ischemic stroke.

Results: Menstrual blood and Sertoli cells are two gender-specific sources of viable transplantable cells for stroke therapy. The use of autologous cells for the subacute phase of stroke offers practical clinical application. Menstrual blood cells are readily available, display proliferative capacity, pluripotency and angiogenic features. Additionally, menstrual blood cells, post-transplantation in stroke models, display the ability to migrate to the infarct site, regulate the inflammatory response, secrete neurotrophic factors, and potential differentiate into neural lineage. Also, the testis-derived Sertoli cells secrete many growth and trophic factors, are highly immunosuppressive, and exert neuroprotective effects in animal models of neurological disorders.

Conclusion: Menstrual blood and Sertoli cells are novel therapeutic options for stroke therapy. Stem cells may be linked to repairing stroke brain by a modulated immune system and trophic factors. Cryopreservation of autologous cells may be wise for stroke patients.

Research supported by: USF Department of Neurosurgery and Brain Repair Funds

Abstract #: 320

Presented by: Nick Torelli, Undergraduate, Undergraduate

Structure Based Inhibitor Discovery Against Beta-lactamase in Countering Bacterial Resistance Nick Torelli, Dr. Yu Chen University of South Florida, Morsani College of Medicine, Department of Molecular Medicine

Keywords: beta-lactamase, antibiotic resistance, penicillin, drug discovery, protein structures

Objective: Antibiotic resistance is a world-wide epidemic that is growing in magnitude. One of the main resistance mechanisms against β -lactam antibiotics, the primary antibacterial chemotherapeutic agents, is the production of serine β lactamases in Gram-negative bacterial pathogens. These enzymes hydrolyze β-lactam antibiotics such as penicillins and thereby render them unreactive with their original targets. There is an urgent need for inhibitors that can restore susceptibility to β-lactam antibiotics in multi-drug-resistant Gram-negative pathogens. The goal of my research is to discover novel inhibitors against TEM-1 β-lactamase.

Methods: My research project has consisted of cloning TEM-1, a β -lactamase commonly observed in clinic, crystallization of TEM-1 to aid in future complex structure determination, and using virtual screening to identify novel, non-covalent inhibitors against this protein.

Results: I have crystalized the apo protein of TEM-1 and solved the 3-D structure. I have also identified top ranking compounds that have high potential for binding and inhibition. These compounds will be tested using a biochemical enzyme assay. True inhibitors can potentially be developed into new antibiotics in the future to counter drug resistance caused by β-lactamases.

Conclusion: My docking results suggest that novel compounds complementing the active site can be identified and some compounds may turn out to be true inhibitors when tested. My future work will consist of co-crystalizing an inhibitor and protein structure to help understand how the inhibitor binds in the active site. This will aid in designing future inhibitors with better efficiency for both TEM-1 and other β-lactamases.

Research supported by: NIH

Presented by: Rodrigo Urcia, Undergraduate

Arginase 1 Deficiency in Myeloid Cells Promotes Tau Pathology

Rodrigo Urcia, Jerry B. Hunt Jr., Marcia Gordon, PhD, Dave Morgan, PhD, Daniel C. Lee, PhD, Kevin Nash, PhD. University of South Florida, College of Arts and Sciences, Dept. of Chemistry, USF Morsani College of Medicine, Dept. of Molecular Pharmacology and Physiology

Keywords: Arginase deficiency in myeloid cells

Objective: Tau (MAPT) pathology remains one of the closest corollaries to neurodegeneration. Hyperphosphorylation remains a hallmark of tau pathology however mechanisms of these events remain less defined. Arginase1 (Arg1) is a key enzyme activated during inflammation and shown to be involved in Alzheimer's disease. Previous data showed that overexpression of Arg1 in tau transgenic mice decreased tau pathology and reduced inflammation. Herein, we aim to identify the impact of tau pathology in mice with an Arg1 deletion in myeloid (immune) cells.

Methods: We bilaterally injected an adeno-associated viral construct (rAAV) consisting of a C-terminally truncated tau construct in mice with an Arg1 conditional-knockout allele (using loxP-flanked(floxed)Arg1(Arg1 flox/flox)and the deleter strain(Lyz2 tm(cre);LysMcre promoter),which generates mice that lack Arg1 in cells of myeloid lineage and (Arg1 wt/wt)littermates. Mice received four months of the rAAV-Tau-CT construct. Immunohistochemistry for tau (total) and phospho tau (AT8) was performed using unbiased image analysis.

Results: Three different genotypes (Arg1wt/wt/ Cre -/-);(Arg1Flox/Flox/ Cre +/-);(Arg1Flox/Flox/ Cre +/+)received the rAAV-Tau-CT construct. All three groups showed comparable levels of total tau suggesting that all mice expressed the same levels tau following viral expression. However, mice lacking Arg1 in myeloid cells(Arg1Flox/Flox/ Cre +/+) showed higher expression levels of AT8 suggesting that the lack of Arg1 promotes tau pathology.

Conclusion: Consistent with previous data in our lab showing that Arg1 overexpression reduces tau pathology, these data suggest that lack of Arg1 promotes tau pathology. Overall, the Arg1 pathway may serve as a therapeutic target for tauopathies.

Abstract #:322

Presented by: Selwin Varghese, Undergraduate

Characterization of a Semi-High Throughput Method for Reducing Tau Expression

<u>Selwin Varghese, Devon Placides, Daniel C. Lee, PhD</u> University of South Florida, College of Engineering Dept. of Chemical & Biomedical Engineering

Keywords: Semi-high throughput screening

Objective: Tau is a microtubule-stabilizing protein that aggregates and promotes neurodegeneration. More than 15 different tauopathies exist with no disease modifying drugs to date. Herein we aimed to identify drugs and pathways that reduce tau expression using a semi-high throughput drug screening method. We tested 13 drugs with various pharmacological targets and pathways. Several included or targeted pathways such as histone deacetylase, histone demethylase, histone methyl transferase, isoflavones, polyamines, and hypusination.

Methods: A hippocampal cell line(HT22) was transfected with a fusion tau protein appended to enhanced-green fluorescent protein(eGFP-Tau). Cells were seeded in black clear bottom 96 well plates at a 5000 cells/well density. After 24 hrs, cells were treated in triplicate with various drugs at 10µM and 100 µM along with four groups of controls. 48 hours post drug-treatment the plate was measured for eGFP-tau fluorescence in a fluorescent microplate reader. A fluorescent nuclear stain(Hoescht) was added to cells to evaluate toxicity, and fixed in 2% paraformaldehyde for microscopy validation.

Results: Compared to controls, several drugs caused significant reductions in relative fluorescence, suggesting that these agents reduce tau levels even at lower concentrations. Of note,specific drugs targeting histone demethylase and hypusination caused 40-50% reduction of eGFP tau fluorescence. Likewise,several soy isoflavones also showed significant reductions in eGFP tau.

Conclusion: These data validate a semi-high throughput method for measuring drugs that reduce or increase eGFP tau fluorescence. Several pathways and drugs have also been identified that may modify tau biology. Future experiments will validate these candidates to a greater extent.

Presented by: Katherine Woo , BS, Undergraduate

Role of the Circadian Per1 and Per2 Genes in Attention, Learning and Memory Across the Lifespan.

Katherine Woo, Trish Dinh, Josh Gamsby, Danielle Gulick Affiliations (for all): USF Health, University of South Florida, Honors College

Keywords: memory, attention, sensory gating, locomotion, Period gene

Objective: Recent studies have demonstrated relationships between circadian rhythmicity, aging and cognitive function. This study determines the role of mutations in the circadian Period 1 (Per1) and Period 2 (Per2) genes as well as age on attention, learning and memory.

Methods: Animals: young Per1Per2 mutant (2-3 months), old Per1Per2 mutant (7-8 months) as well as young and old wild-type (C57BL/6J) mice. Mutant mice were bred in the Byrd Institute and wild-type mice were purchased from Jackson Laboratories. After genotyping, three different behavioral tests were run and scored for each group: Fear Conditioning (FC), Pre-Pulse Inhibition (PPI) and Elevated Plus Maze (EPM).

Results: Per1Per2 mutant mice displayed impaired fear conditioning in relation to the control mice. Young mutant mice froze significantly less compared to their wild-type counterparts during contextual and cued fear conditioning. Old control mice had lower percent freezing times than young mice in contextual fear conditioning, but there was no affect of age in the mutant mice. In pre-pulse inhibition, mutant mice had a slightly higher degree of response inhibition, indicating that the mice did not have impairments in sensory gating. In addition, during elevated plus maze, all mice groups traveled similar distances in total, showing that the mutant mice did not have impaired locomotor activity.

Conclusion: The results show reduced contextual and cued learning in Per1Per2 mutant mice, and reduced context learning in older control mice, suggesting dissociable impairments in learning and memory by genotype and age. This suggests that mutations of both Per1 and Per2 genes negatively impact learning and memory.

Abstract #:324

Presented by: Redjon Zhuleku, BS, Undergraduate

Tau & α-Synuclein expressing Caenorhabiditis elegans: Generation and Characterization for Neurodegenerative Diseases

<u>Redjon Zhuleku, Kaitlyn Braswell, Malathi Narayan, Enzo A. Nicosia, Diego A. Peralta, Ekta Sood, Umesh K. Jinwal</u> Department of Pharmaceutical Sciences, College of Pharmacy, Byrd Alzheimer's Institute, USF Health, University of South Florida, Tampa

Keywords: tau, α-synuclein, C. elegans, Alzheimer's disease, Parkinson's disease

Objective: Accumulation of tau and α -synuclein proteins is considered a marker for neurodegenerative diseases such as Alzheimer's and Parkinson's disease. Worms of the genus Caenorhabditis such as C. elegans serve as an elegant model to understand the complex mechanism of diseases and for drug discovery. Our main goal is to generate and characterize a novel C. elegans model that stably co-expresses tau and α -synuclein proteins in the same animal. We have utilized existing models for these two proteins and generated a hybrid model.

Methods: To generate hybrids of tau and α -synuclein, male worms from α -synuclein-YFP (pkls2386 [unc-54p::alpha synuclein::YFP + unc-119(+)]) transgenic lines were crossed with L4 hermaphrodites from tau (hdEx81 [F25B3.3::tau352(PHP) + pha-1(+)]) transgenic lines. YFP positive worms were selected and used for western blot and behavioral analysis such as liquid thrashing assays.

Results: Screening of α -Synuclein/Tau crossed lines resulted in one hybrid line that stably co-expressed tau and α -synuclein. Western blot analysis of this newly created hybrid line showed co-expression of tau and α -synuclein proteins as expected. Furthermore, preliminary behavioral analysis data suggests reduced liquid thrashing activity in the hybrid model compared to tau and α -synuclein models.

Conclusion: We have successfully generated a hybrid C. elegans model stably co-expressing tau and α -synuclein to study mechanisms of neurodegenerative diseases. Our data clearly indicates that the newly generated model has dramatic reduction in motility compared to wild type, tau, and α -synuclein worm lines. Overall this model could be useful for understanding disease mechanisms and for drug discovery.

Extraversion as a Predictor of Workplace Accidents

Stephanie A. Andel, USF Sunshine ERC Occupational Health Psychology Program

Keywords: Occupational Safety Accidents Personality Extraversion

Objective: The prevalence of occupational accidents and injuries is high, and therefore much work has gone into examining potential antecedents to such incidences. However, while some research has examined personality as a potential antecedent, work has mostly centered upon personality at the factor level. This study takes a finer grained approach by examining extraversion at the FACET level in order to investigate extraversion facets as predictors of occupational safety.

Methods: I surveyed 114 employees taking classes at a large southeastern university. All employees worked at least 20 hours per week. Most of the sample was female (N = 101) and the average age of participants was 22.8. Each employee completed a battery of self-report scales that measured extraversion (at both the factor and facet level) and workplace accidents.

Results: Factor level extraversion was not significantly related to occupational accidents. However, the extraversion facets of warmth (r = -.20, p < .05) and positive emotions (r = -.23, p < .05) were each significantly and negatively related to occupational accidents. The remaining extraversion facets (i.e., gregariousness, assertiveness, activity, excitement seeking) were not significantly related to occupational accidents.

Conclusion: Overall, these results suggest that taking a facet-level approach when studying the relationships between personality and occupational safety may be beneficial. Specifically, results demonstrated that extraversion at the factor level was not a significant predictor of workplace accidents. However, when analyzed at the facet level, results demonstrated that a couple of the extraversion facets (i.e., positive emotions and warmth) were in fact significantly related to workplace accidents.

Research supported by: USF Sunshine ERC

Abstract #: 326

Presented by: Maryana Arvan, BA, Graduate Student

Customer Mistreatment and Musculoskeletal Disorder Symptoms <u>Maryana Arvan, Paul Spector</u>, USF Sunshine ERC Occupational Health Psychology Program

Keywords: customer verbal aggression, customer incivility, musculoskeletal disorder symptoms

Objective: To examine whether exposure to low-intensity and high-intensity customer mistreatment relates to musculoskeletal disorder symptoms among customer service employees.

Methods: Participants were 134 individuals who worked at least 20 hours per week in a customer service occupation. Participants were recruited via snowball sampling and from the USF Department of Psychology human subjects pool. Each participant completed an anonymous, web-based survey with a number of measures, including overall perceptions of customer verbal aggression and customer incivility, exposure to an incident of customer verbal aggression over the past year and/or month, and musculoskeletal disorder symptoms over the past six months.

Results: Overall perceptions of customer verbal aggression and customer incivility positively related to pain in the low back, upper limb, upper body, and lower extremity areas. Exposure to an incident of customer verbal aggression over the past year positively related to upper body pain.

Conclusion: The results of this study suggest that both high-intensity (i.e., verbal aggression) and low-intensity (i.e., incivility) customer mistreatment are positively related to musculoskeletal disorder symptoms among customer service employees.

Research supported by: USF Sunshine ERC

High Heat: Risk and Related Illnesses for Florida Delivery Drivers

Leah E. Brown, RN, BSN, USF Sunshine ERC Occupational Health Nursing Program

Keywords: Heat Vulnerability Exertion Preventable

Objective: Prevention of heat stress amongst Florida delivery drivers.

Methods: Review and summary of occupational safety and health research literature.

Results: Exposure to high heat and humidity, when coupled with intense physical activity multiplies vulnerability to heat related illnesses. Environmental heat; direct sunlight, radiant heat from the asphalt and concrete, and the internal metabolic heat generated by exertion, make delivery drivers in Florida extremely vulnerable.

Conclusion: Heat stress is preventable; with proper education and allocation of time for rest and hydration, delivery drivers can remain safe.

Research supported by: USF Sunshine ERC

Abstract #: 328

Presented by: Poulomy Chakraborty, MA, Graduate Student

Estimating the Impacts of Rotavirus Vaccination on Gender Disparities <u>Poulomy Chakraborty, Richard D Rheingans, John D Anderson IV</u>, University of Florida

Keywords: Rotavirus, gender, vaccination, India, disparities

Objective: This study aims to assess how temporal changes in gender disparities in routine vaccination coverage impact the estimated benefits of introducing rotavirus vaccination in various geographic and socioeconomic settings in India.

Methods: A Microsoft Excel based spreadsheet model is used to model the expected health and economic outcomes disaggregated by gender of the child, for one annual birth cohort of children during the first five years of life. Three survey datasets have been used in the model: National Family Health Survey-3 2005-6, District Level Health Survey-3 2007-8 and Coverage Evaluation Survey 2009 to estimate the changes overtime, in three high mortality states and six regions of India.

Results: There is an overall increase in vaccination coverage with reductions in the gap between boys and girls. Overall, it is estimated that girls would benefit more across all wealth quintiles, especially as per the CES survey. However, estimates from the three surveys indicate that girls in the second and third quintiles are at higher risk. Increases in gender parity are associates with increases in benefits and more favorable cost effectiveness of rotavirus vaccination introduction.

Conclusion: It is of immense importance to sustain the efforts of bridging the gender gap in health care utilization and create enabling conditions to further improve the impacts of rotavirus vaccination. Preferential treatment of boys increases the risk of mortality amongst girls and reduces cost effectiveness of implementation of vaccination programs. Hence more effort for targeted coverage of girls needs to be done.

Research supported by: PATH and Bill and Melinda Gates Foundation

Presented by: Héctor Claudio, BS, Graduate Student

Potential exposure to avian flu in poultry industries according to knowledge and prevention practices. Comparison of countries.

Héctor E. Claudio, University of Puerto Rico Industrial Hygiene Program

Keywords: influenza, poultry industries, knowledge and preventive practices, bird contact

Objective: Compare studies from around the world identifying poultry employees' knowledge about the potential exposure to avian flu in their work environments.

Methods: Five different studies were compared that surveyed the knowledge that employees in poultry plants had about the potential exposure to avian flu in their work environments. The countries included were Nepal, Italy, United States, Nigeria and Australia. Authors used questionnaires and face-to-face interviews for data collection. The variables studied included demographic information, knowledge about avian flu and prevention practices used to protect employees against avian flu.

Results: Seventy six percent of Italians workers reported having knowledge about the avian Flu and 62% reported using prevention practices. Thirty two percent of Nepal workers reported having adequate personal protective. Regarding specific prevention practices such washing hands, 88% of Nepal workers and 39% of Australian workers reported complying with this prevention practice.

Conclusion: The comparison of the studies had certain limitations, mainly because they did not have all the same variables. It shows that countries with the higher probability of employees catching influenza are those countries were regulations regarding worker protection are not very stringent. Different employers must supply the necessary protective personal equipment to their workers, so they can realize their jobs more effectively while being safer.

Abstract #: 330

Presented by: Brianna Clendenin, MSN/MPH, Graduate Student

Chemical Exposure in Nail Salon Technicians

Brianna Clendenin, RN, BSN, USF Sunshine ERC Occupational Health Nursing Program

Keywords: Nail Technician, Occupational Health, Chemical exposure

Objective: Nail salon technicians are exposed to toxic chemicals in the workplace. There is little regulation of cosmetics in the U.S. placing nail salon technicians at risk for developing both acute and chronic adverse health effects. Nail salon technicians face multiple cultural and educational barriers that can be addressed by educating both employers and employees regarding control mechanisms recommended by NIOSH to limit toxic chemical exposure.

Methods: A systematic review of published literature was conducted. Databases searched included CINAHL, PubMed, Google Scholar, CDC, NIOSH, and OSHA.

Results: Although studies have indicated chemical exposure below the Occupational Safety and Health Administrations Permissible Exposure Limits, technicians still commonly report respiratory symptoms and dermatitis. Workers who wear surgical type masks believe it will protect them from chemicals and dust. A National Institute of Safety and Health study indicates decreased lung functioning and increased airway inflammation in workers chronically exposed to acrylics. Evaluating air quality in 21 nail salons revealed carbon dioxide levels well above the Environmental Protection Agencies standards for indicating adequate ventilation. Carbon dioxide levels in 22 salons exceeded EPA standards. Sixty-four percent did not have any mechanical ventilation to provide fresh air or provide local exhaust.

Conclusion: The occupational health and safety nurse can educate and promote the use of local exhaust systems, appropriate use of respirators, gloves, and avoidance of products containing toluene, formaldehyde, or dibutyl phthalate.

Research supported by: Sunshine Education and Research Center

Presented by: Mayra De Jesus-Rivas, MS, Graduate Student

Pneumatic Nail Gun Injury

Mayra De Jesus-Rivas, USF Sunshine ERC Occupational Health Nursing Program

Keywords: nail gun, injuries, safety

Objective: Construction work using nail guns is highly dangerous. When construction workers are injured it is costly to the employee and employer. There are factors that contribute to the cause of injury incidents such as: Organizational stressors, emotional and physical stress and poor safety behaviors. It is important for the OHN to emphasize proper training in the use of any equipment, the regular checking or maintenance of the equipment, and the use of personal protective equipment.

Methods: Evidence-based nursing research.

Results: High numbers of pneumatic nail gun injuries.

Conclusion: Injuries can be preventable.

Research supported by: USF Sunshine ERC

Abstract #: 332

Presented by: Rebeca Delgado, BS, Graduate Student

Effects of excessive back loads from student's backpacks of the University of Puerto Rico Medical Sciences Campus.

Rebeca M. Delgado B.S., Lida Orta Anés, Ph.D., University of Puerto Rico Industrial Hygiene Program

Keywords: Musculo-skeletal Disorders, Occupational Health, Ergonomics

Objective: Backpacks are a tool used to transport personal materials These may be beneficial, but it also can be a risk factor for musculo-skeletal injuries. Improper use of this tool can cause musculo-skeletal problems. The American Occupational Therapy Association (AOTA) recommends that a healthy backpack should not exceed 10% of the user's body weight. This study analyzes the association between backpacks loads excess and musculo-skeletal pain among university students.

Methods: A survey was created and sent to the students by e-mail receiving 61 answered.

Results: The statistical analysis showed a relationship magnitude of 2.5 (OR = 2.5) between overloaded backpacks (more than 10% of body weight) and pain the back, an OR = 1.5 for pain in the neck and OR = 1.03 for pain in the shoulders.

Conclusion: Given these results it is recommended that the weight of student backpacks must be less or equal to 10% of their body weight. Results show that using overweight backpacks could increase risk of musculo-skeletal problems.

Presented by: Kimberly French, PhD, Graduate Student

Work-family conflict and job satisfaction: A meta-analysis of cultural differences

<u>Kimberly A. French, Soner Dumani, Tammy D. Allen,</u> USF Sunshine ERC Occupational Health Psychology Program and Kristen M. Shockley, Baruch College and The Graduate Center CUNY

Keywords: work-family conflict, meta-analysis, job satisfaction, culture

Objective: We investigate the moderating role of culture (individualism/collectivism and performance orientation) on the relationship between work-family conflict and job satisfaction.

Methods: Database keyword searches and a search of relevant review references yielded 407 possible studies; 36 studies including 73 effect sizes from 20 countries were included in the meta-analysis. Cultural dimension values found in the GLOBE study (House et al., 2004) were imputed for each study based study country. Random-effects meta analysis and meta-analytic regression were used to test the hypotheses.

Results: Both WIF and FIW are negatively related to job satisfaction (r = -.22, r = -.16). The relationship between WIF and job satisfaction is weaker for cultures high in both forms of collectivism (p < .01). The relationship between FIW and job satisfaction is weaker for cultures high in institutional collectivism (p < .01), but not in-group collectivism (p = .10). Performance orientation moderates the relationship between FIW and job satisfaction (p < .01); the relationship is weaker for cultures high in performance orientation. The moderation is marginally significant for WIF and job satisfaction (p = .05); follow-up analyses this may be due to an incorrectly reported effect size.

Conclusion: The relationship between WIF and FIW and job satisfaction is moderated by performance orientation and collectivism. Workers in cultures with low performance orientation and/or high collectivism (e.g., Latin America, Eastern Europe, Javidan et al., 2006) may be particularly susceptible to negative work affect due to WIF and FIW. Implications of this study therefore extend to both research and practice focused on alleviating work-family issues in work settings across the globe.

Abstract #: 334

Presented by: Lynn Henderson, MS, Graduate Student

Carpal Tunnel Syndrome: An Occupational Health Risk for Dental Hygienists Lynn A. Henderson, USF Sunshine ERC Occupational Health Nursing Program

Keywords: carpal tunnel syndrome, dental hygiene, musculoskeletal disorders, occupational illness

Objective: The repetitious hand and wrist movements of dental hygienists' daily work activities place them at extremely high risk for CTS. Occupational health goals for CTS management in dental hygienists should be teaching and emphasizing prevention with ergonomics, early diagnosis of the disease, and high-quality treatment with an occupational focus.

Methods: A literature review was completed that included systematic reviews of studies on the prevalence of CTS, occupational factors, dental ergonomics, and clinical management of the disease.

Results: Dental Hygienists must take preventive ergonomic measures to protect their most valuable asset, their hands. Some occupational health measures for CTS prevention include: identifying existing medical predispositions, causes, and exacerbating activities. Ergonomic interventions include using: lighter weight, larger diameter, padded instruments; interchanging tools during repetitious activities; ergonomic work station design; optimal seat and mirror positioning; frequent hand rest breaks; and adequate lighting. Some non-operative treatment recommendations include: minimizing forceful and repetitious activities; 6 weeks of wearing a neutral positioned splint; not exceeding 4 steroid injections; and avoiding the use of opioids, laser therapy, muscle relaxants, opioids, diuretics, and non-steroidal anti-inflammatory drugs (NSAIDS).

Conclusion: CTS is an extremely complex illness to manage, especially in a field like dental hygiene where hand activities are the dominate practice. Occupational health is essential in keeping this population healthy, keeping them working, and keeping them in their profession.

Research supported by: USF Sunshine ERC

Presented by: Derek Hutchinson, BA, Graduate Student

Development of a General Organizational Climate Scale

Derek Hutchinson, Stephanie Andel, Paul Spector, USF Sunshine ERC Occupational Health Psychology Program

Keywords: Scale Development, Organizational Climate, Workplace Wellbeing

Objective: A number of studies have shown a relationship between organizational climate perceptions (e.g., safety and violence prevention) and injuries, accidents, and acts of violence in the workplace. To date, the literature has treated safety climate and violence prevention climate as separate constructs that predict different workplace outcomes. Safety climate is concerned with exposure to workplace accidents and injuries, while violence prevention climate is concerned with workplace physical and/or verbal aggression. Emerging research indicates that injury and violence exposure are related. The purpose of this study was to create a generalized organizational climate scale that measures organizational safety and violence prevention climate without focusing on a particular facet.

Methods: The sample consists of 114 employed participants who were recruited online through an electronic participant pool at a large public university in the southeastern U.S. Students completed our measure of general workplace climate and measures of safety compliance, reported accidents, job satisfaction, experienced incivility, aggression, and interpersonal conflict.

Results: Our general climate scale was significantly related to one's compliance to safety procedures, job satisfaction, experienced incivility, experienced aggression, and experienced interpersonal conflict.

Conclusion: Overall, the results of this study suggest that a general organizational climate scale is suitable to measure both an organization's promotion of safety and prevention of violence in the workplace. The results of this study support the use of a single unified scale to measure both facets of workplace climate when differential predictions between constructs are not being investigated.

Research supported by: USF Sunshine ERC

Abstract #: 336

Presented by: Ivory Iheanacho, MS, Graduate Student

Can the NWS Heat Index Substitute for Wet Bulb Globe Temperature for Heat Stress Exposure Assessment Ivory Iheanacho, Dr. Thomas E. Bernard, USF Sunshine ERC Industrial Hygiene Program

Keywords: stress, heat index, WBGT; Index; Steadman; occupational exposure limit

Objective: There has been substantial research about the effects of heat stress on human health. Past findings have led to the creation of several heat stress indices and the development of occupational heat exposure limits. The established occupational heat exposure limits currently use the wet-bulb globe temperature index (WBGT). However, Steadman's Heat Index (HI) has high visibility because it is promoted by the National Weather Service. The objective of this study was to determine whether the Heat Index can substitute for the WBGT index.

Methods: Following the methods and data used to establish the WBGT exposure limits and subsequent studies that determined the upper sustainable exposure, WBGT and HI were compared.

Results: While there was a general linear correlation between WBGT and HI, there was a loss of agreement at high and low humidities.

Conclusion: In order to safely use HI in lieu of WBGT, the relationship between the two should be established for a particular workplace of geographical location.

Research supported by: USF Sunshine ERC

Presented by: Garrick Johnson, MS, Graduate Student

The Effects of Fungal Growth on Phthalate Ester Emissions from pPVC

Garrick K. Johnson, Yehia Y. Hammad, Sc.D, René R. Salazar, Ph.D., CIH, USF Sunshine ERC Industrial Hygiene Program

J. David Krause, Ph.D. - Geosyntec Consultants, Inc.,

Keywords: Phthalates, fungal growth, plasticized PVC, exposure assessment

Objective: The purpose of this research was to attempt to determine the effects of fungal growth on the phthalate ester constituents of the plasticized PVC (pPVC) film component of metal building insulation used in a large book warehouse. We also investigated the potential exposure implications on the workers in the building.

Methods: Individual 232 cm2 pieces of the pPVC film that were clear of fungal growth and pieces that had fungal growth were collected from the building being investigated. A chemical analysis of the phthalate ester content was then performed on the pieces by solvent extraction followed by analysis of the extract using a GC/MS technique. The mass of phthalate ester content in a sample set of 25 pieces each of the clean pPVC film and pPVC film with fungal growth collected was statistically compared. The results of the chemical analysis were then used to model the potential increased exposure the fungal growth may contribute to the occupants of the building by determining a worst case exposure scenario and comparing that to published exposure data in similar settings.

Results: The results of the chemical analysis showed that there is a statistically significant difference between the clean pPVC film and pPVC film with fungal growth for all four phthalate esters investigated. The results also showed that the mean content of all four phthalate esters was lower in the pieces that had fungal growth. The mean content will be used for exposure assessment modeling purposes, which is still being investigated.

Conclusion: The presence of fungal growth is related to lower phthalate content in the pPVC film. Our plan for future investigation of this problem is to use the collected data for exposure assessment modeling.

Research supported by: USF Sunshine ERC

Abstract #: 338

Presented by: Julie Lanz, MS, Graduate Student

Predictors of Resilience

Julie Lanz, Armando Falcon, April Schantz, Archana Manapragada, Valentina Bruk-Lee, Florida International University Department of Psychology

Keywords: Resilience, personal control, personality, coping skills

Objective: Resilience is defined as a characteristic of positive psychology (Wagnild & Young, 1993) that facilitates "positive adaptation in the context of significant risk or adversity" (Ong , Bergeman, & Boker, 2009, p. 1777). Interventions (e.g. the Comprehensive Soldier & Family Fitness Program by the Army) aimed at increasing resilience are valuable for individuals that have faced traumatic experiences. This study expands the research of resilience by integrating personal control and supervisor support into the resilience process to explain why individuals are able to overcome difficult situations.

Methods: Two hundred and twenty eight U.S. participants were recruited using mTurk (56.8% female). Participants worked between 20 and 80 (M=39.4, SD=9.76) hours per week. The constructs of resilience (Wagnild & Young, 1993), personality (Goldberg, 1999), coping skills (Carver, 1997), perceived supervisor support (Eisenberger et al., 2002) scale, and personal control (Paulhus, 1990) were measured.

Results: A hierarchical regression examined the impact of emotional stability, extraversion, conscientiousness (Step 1; R2 = .40), coping skills (Step 2; R2 = .47), and perceived supervisor support and personal control (Step 3; R2 = .56) on resilience. All variables significantly predicted resilience except for perceived supervisor support (β = .01, p = ns).

Conclusion: Exploring the impact of personal control (i.e. personal efficacy) and perceived supervisor support are novel contributions to research on resilience, and suggest that personal control is a significant predictor of resilience above and beyond other protective factors (personality and coping skills).

Presented by: Archana Manapragada, BS, Graduate Student

Uncovering Safety Silence

Archana Manapragada, Ramses Corzo & Valentina Bruk-Lee, Florida International University Department of Psychology

Keywords: safety silence, safety violations, accidents, injuries, justifiable violations

Objective: The objective of this exploratory study was to examine the construct of safety silence (SS), which is an employee's act of not addressing the occurrence of an unsafe event that he/she has witnessed in the workplace. SS can occur in relation to unsafe behaviors (e.g. safety violations & errors) or safety outcomes (e.g. accidents & injuries). SS can pose as a barrier to increase or maintain workplace safety by not giving employees and management the opportunity to take corrective and preventative measures against unsafe events.

Methods: Twenty six individuals employed in organizations required to follow OSHA standards participated in this study. Sixteen individuals participated in focus groups and ten were individually interviewed. Participants were asked a list of general discussion questions and were also asked to provide two or more critical incidents in which they chose not to speak up about unsafe events that they have witnessed.

Results: Findings suggest that SS does exist and the main safety issues that employees choose to stay silent about are safety violations, followed by safety hazards, injuries, and accidents. Several motives were also found behind SS behaviors. Justifiable violations, which are violations that are rationalized by coworkers witnessing the event, were found to be the main reason for why employees decided to engage in SS.

Conclusion: By exploring the construct of SS further, tools to measure, identify, and reduce SS can eventually be developed. However, there is much more to be researched in this area before such objectives can be met. Nonetheless, this study makes a significant contribution to the safety literature by uncovering the construct of SS and taking positive steps towards determining why it exists.

Abstract #: 340

Presented by: Adam Marty, MSPH, Graduate Student

Characterization of a Nano-Aerosol Using a Portable Scanning Mobility Particle Sizer and Electron Microscopy Adam Marty, MSPH, Dr. Yehia Hammad, D.Sc., USF Sunshine ERC Industrial Hygiene Program

Keywords: nanoparticle, aerosol, microscopy, SMPS, distribution

Objective: Portable scanning mobility particle sizers (SMPS) offer convenient means to collect information about nanosized aerosols because they provide real-time distributions. Electron microscopy (EM) applied to a filter sample has been considered the traditional method for the sizing and counting of small particles. However, the later method is time consuming. The objectives of this research are to generate a stable and reproducible sodium chloride aerosol and to compare the size distributions obtained from SMPS and EM.

Methods: A sodium chloride aerosol was generated and introduced into a sample chamber. The size of the generated particles ranged from 20 to 250 nm. The consistency of the aerosol concentration was monitored using a particle counter. A portable SMPS was used to determine the size distributions of the generated aerosols. Polycarbonate membrane filters were used to collect the aerosols for subsequent EM analysis. The particle size distributions were determined from photographs of the membrane filters. SMPS and membrane samples were collected simultaneously.

Results: Background counts were less than 0.3 particles/cc. Conditions during data collection showed that target particle size, particle concentration, and relative humidity were well controlled. SMPS data yielded log-normal size distributions with a geometric means between 65 to 80 nm. EM analysis of the particles collected yielded log-normal size distributions with a geometric means between 40 to 42 nm.

Conclusion: A well characterized aerosol could be generated and reproduced. Physical counting methods using EM were cumbersome and different than those obtained from SPMS. The differences in the results could be attributed to the sensitivities of the methods used in this study.

Research supported by: USF Sunshine ERC

Presented by: Rocio Melendez Lebron, MS, Graduate Student

Working in a clinical laboratory, why does it have to hurt?

Rocío Melendez Lebron, Lida Orta Anes, University of Puerto Rico Industrial Hygiene Program

Keywords: Ergonomic Clinical Laboratory

Objective: Workers from a clinical laboratory are professionals who have multiple tasks which include microscope reading and pipetting. These tasks are performed using awkward postures which may cause musculoskeletal disorders. This study wants to prove that using ergonomic workstations will reduce musculoskeletal injuries in employees.

Methods: Medical Technologists in a clinical laboratory in San Juan, Puerto Rico were asked to answer anonymously a checklist about their workstation, musculoskeletal injuries, sex and age. The checklist was made for yes or no answers and divided by tasks. Based on their no answers the workstations were evaluated and modifications were made. After the changes, the medical technologist were asked again to answer the same checklist about musculoskeletal injuries. Thirty medical technologists from the clinical laboratory participated.

Results: In the last sixteen months 51% of the medical technologists received medical treatment due to musculoskeletal injuries. Three employees had suffered from carpal tunnel syndrome, 90% of the employees have suffered from muscular spam and in the last twelve months 49% of the employees were absent from work. When they answer again the checklist three months later, the feedback was positive and the percent of muscular spam was reduced.

Conclusion: Medical Technologist are trained and educated to avoid blood-borne pathogens but they are not educated about work related musculoskeletal disorders and this was the major problem leading them to have these injuries. The results of this study suggest that the laboratory should move to working in an ergonomic clinical laboratory in order to get optimization and a reduction of work overload and injuries.

Abstract #: 342

Presented by: Raisa Nazario-Rodríguez, BS, Graduate Student

How the indoor air quality affects the development of occupational asthma among UPR-MSC workers? Raisa V. Nazario-Rodríguez, B.S., University of Puerto Rico Industrial Hygiene Program

Keywords: asthma, occupational asthma, indoor air quality, university workers

Objective: OSHA estimates that 11 million workers in a wide range of industries and occupations are exposed to at least one of the numerous agents known to be associated with occupational asthma (OA). This disease is very common among workers, especially in industrialized countries (Voelter-Mahlknecht, 2011).

Methods: The prevalence of OA was analyzed among 90 subjects working at Medical Sciences Campus (UPR-MSC). Data was collected through a link of the questionnaire in Survey Monkey Program; and was sent through the institutional email.

Results: The data collected shows of 38.9% of OA in UPR-MSC among workers. Also, prevalence for chronic allergies was calculated as well (55.6%). In comparison to others studies, this is a high prevalence of OA.

Conclusion: This high prevalence could be because of poor indoor air quality, since the Building was built in 1972 and because a high number of participants reported that their symptoms of asthma or allergies get better when they are out of work, on weekends or vacations.

Presented by: Marysel Pagán-Santana, BS, Graduate Student

Students Perception of Safety in the UPR-Medical Sciences Campus Educational Laboratories Marysel Pagán-Santana, Lida Orta Anés, University of Puerto Rico Industrial Hygiene Program

Keywords: Safety Culture, Educational Laboratory, Safety Perception, Students

Objective: Laboratory safety in universities is generally observed in terms of security measures in structures and law requirements, while safety components like safety management, safety knowledge and safety culture usually take a back seat in terms of regulations and policies. This study aims to evaluate the safety climate in teaching laboratories at the UPR-Medical Sciences Campus based in the student perception of safety.

Methods: The study asks a sample of UPR-Medical Sciences Campus' students to answer a series of pre-established questions that will measure their perceptions about their laboratory work site and its management. Study data is collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools. The survey questions are categorized into relevant safety culture areas to include Supervisor and Coordinator Execution, Student Execution, Safety Training and Reinforcement, and Organizational Factors.

Results: Responses for each of the statements are ranked using the Likert Scale, commonly known as an agreement scale. In the analysis of the survey's results, mean average Likert Scores are calculated for every statement, as well as percentages for favorable, unfavorable and neutral responses.

Conclusion: After the analysis and evaluation of the responses and their resulted ranking, the percentages obtained indicate the need for intervention in one or more of the areas investigated in the survey. A lower percentage in the score points to a higher need for attention. Understanding the safety culture of this kind of academic environment provides a pathway to improvement in safety education and awareness of students in the campus.

Research supported by: UPR Industrial Hygiene Program, NIH Minority Health and Health Disparities

Abstract #: 344

Presented by: Laura Riley, PhD, Graduate Student

Expansion of the Performance Capabilities of the USF Inhalation Challenge Chamber Laura Farina Riley, MSPH, Yehia Hammad ScD USF Sunshine ERC Industrial Hygiene Program

Keywords: aerosols, chamber, thoracic, impactor, inhalation

Objective: This study enhances the capabilities of a whole-body human exposure chamber and determines the largest particle size that can be generated consistently. Once this size is determined, the inhalable and thoracic fractions of the dust cloud are determined. This chamber is located in the Breath Laboratory of the Sunshine ERC at the University of South Florida, College of Public Health. The chamber is Plexiglass, has a volume of 75 ft3, and is operated at a flow rate of 33.8 ft3/min. Both makeup and exhaust air are HEPA filtered.

Methods: Previous work has been conducted with this chamber to generate respirable dust fractions only, using an elutriator to eliminate larger particles. A direct-reading instrument (TEOM) was used to determine particle concentration. In this work the generated thoracic dust fractions were sampled using gravimetric and direct-reading instruments.

Results: Total dust concentrations in μ g/m3 measured by the TEOM at various RPM settings of the Wright Dust Feeder were 110 + 2.8, 173 + 8.5, 398 + 20 and 550 + 17. Total dust concentrations as measured by gravimetric analysis, in μ g/m3, at various RPM settings of the Wright Dust Feeder were 135 + 21, 200 + 35, 333 + 18 and 891 + 27. Similar results were found for the inhalable fraction and lower concentrations were found for the respirable fraction. Dust concentrations measured at different points within the chamber showed uniform distribution with variability less than 10%. The particle size distributions were consistent across the different RPM settings.

Conclusion: By determining the largest particle size that can be consistently generated, future inhalation challenge studies using inhalable and thoracic-size particles will be possible with this chamber.

Research supported by: USF Sunshine ERC

Presented by: Enid Román, BS, Graduate Student

Correctional Officers: Duty or Illness?

Enid Román Arce B.S., Lida Orta Anés Ph.D, University of Puerto Rico Industrial Hygiene Program

Keywords: Chart Review Stress Musculoskeletal Psychosocial Factors Correctional Officers

Objective: The worker population in the prisons of Puerto Rico has a high exposure to job stress and violence, specifically correctional officers. High exposure to stress is associated with the development of musculoskeletal disorders. Psychosocial factors in the work area cause muscle tension generated musculoskeletal injuries. The main purpose of this study is to establish a relationship between the psychosocial work environment of correctional officers and the development of musculoskeletal disorders

Methods: The hypothesis was tested by a critical literature analysis, a comparison of previous studies and statistics of workers with anxiety, tension, aggression and irritability behaviors.

Results: We expect to establish a relationship between existing health conditions and working conditions.

Conclusion: The present study provides a framework to study the current status of Correctional Officers in prisons of Puerto Rico, their needs and provides information to prevent future health conditions and lost days of work.

Abstract #: 346

Presented by: Amanda Rowell , BS, Graduate Student

Going Green: Occupational Hazards in Renewable Energy

Amanda C. Rowell BSN, RN, USF Sunshine ERC Occupational Health Nursing Program

Keywords: Environmental/Economic Sustainability, Renewable Energy, Green Job(s), Occupational Risk/Hazard(s)

Objective: To educate the public and occupational health arena on the risk and hazards of renewable energies; to promote prevention through design and foster research in occupational health and safety that protects the public, communities and employees from the risks and hazards of renewable energy.

Methods: Literature review includes Cochrane Library, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Pub Med, Ovid MEDLINE, American Council on Renewable Energy (ACORE), American Wind Energy Association (AWEA), International Energy Agency (IEA), International Labor Organization (ILO), National Institute for Occupational Safety and Health (NIOSH), Occupational Safety and Health Administration (OSHA), Solar Energy Industries Association (SEIA), and U.S. Department of Energy.

Results: 137 results; after a comprehensive review of all the literature on renewable energy occupational risk and hazards, epidemiology, and prevention research and data pertaining to wind, solar, biomass, and hydro power were selected and presented

Conclusion: Going green is not without occupational risk. The renewable energy industry is growing rapidly, stimulating the economy and creating "green jobs". Investigations into the long-term occupational health outcomes of these emerging renewable energy industries—biomass, solar, hydro and wind are limited. Without prevent through design (PtD), incidences of occupational injuries, diseases and possible deaths are likely to increase as the renewable energy industry grows.

Research supported by: USF Sunshine ERC

Presented by: Frances Santiago Eliza, BS, Graduate Student

Lead exposure among workers from a battery recycling plant

Frances Santiago Eliza, BS; Lida Orta Anés, Ph.D., University of Puerto Rico Industrial Hygiene Program

Keywords: Lead exposure, battery recycling plant, personal protection equipment

Objective: Lead is a gray heavy metal and used in industry because it forms alloys with other metals. Lead poisoning does not happen very often, but the greatest effects occur when fumes are inhaled or dust contacts with skin (Lenntech, 2013). The objective of this literature review is to provide information related to the behavior of workers with increased risk of exposure to lead.

Methods: The studies selected used several methodologies, such as interviews and blood tests, to know about the health of the workers. Blood tests for ZZP and ALA-U were conducted. These parameters measure the lead exposure in a period of time. Interviews and blood samples were obtained from workers exposed both directly and indirectly to lead.

Results: Studies have shown that poor workplace ventilation and a lack of protective clothing may increase the risk of lead exposure.

Conclusion: In conclusion, the studies demonstrated the requirement of personal protective equipment to work with lead. My recommendation is the realization of similar studies in Puerto Rico, because the information of the relation between the exposure to lead and use of personal protection equipment is very little or not available to the public. And any industry of battery recycling needs a program of occupational health, which supervises and maintains an adequate workplace for the workers.

Research supported by: UPR Industrial Hygiene Program

Abstract #: 348

Presented by: Lorraine Santiago, MS, Graduate Student

Awareness among community hospital administrators of the importance of the industrial hygiene discipline Lorraine Santiago Aguayo, USF Sunshine ERC Industrial Hygiene Program

Keywords: community hospitals, industrial hygiene, health and safety

Objective: Healthcare workers have a high risk of illness and injury with incidence rates higher than private industry (Vredenburgh, 2002).

Methods: In this study we interviewed human resources representatives working at 18 community hospitals of Puerto Rico. We asked them whether they had an industrial hygienist or an occupational health and safety department in the hospital. We also asked regarding the tasks they performed.

Results: Most hospitals had safety committees which included safety officers, nurse supervisors and other doctors taking care of health and safety, Others had a safety officer along with human resources personnel. These people reported having OSHA training to carry out health and safety tasks instead of formal university courses. Tasks such as designing ventilation systems and ergonomic adjustments are not being practiced at any of the surveyed hospitals.

Conclusion: Even though appropriate and necessary safety and health tasks are being performed at the hospitals, essential tasks are missing. Permanent industrial hygienists or a health and safety department is not needed at Puerto Rico community hospitals. Each and every hospital should be oriented on the necessity of a capable health and safety specialist to fulfill the essential missing tasks and focus on training the already working personnel to be able to carry out a complete job performance.

Presented by: April D. Schantz, Graduate Student

Antecedents to Employee Drug-alcohol-tobacco Use

<u>April D. Schantz, Armando Falcon, Julie Lanz, Archana Manapragada,</u> Florida International University Department of Psychology

Keywords: non-task organizational conflict, coping strategies, employee well-being, substance use

Objective: This paper examined the relationships between workplace conflict, coping strategies, and substance use among a diverse crowdsourcing sample of individuals employed in the United States.

Methods: Participants (N = 284) were recruited using Amazon Web Services, MTurk (2013) and represented a broad industry sample of employed individuals in the United States. Participants completed an online questionnaire containing the following measures: Michigan Organizational Assessment Questionnaire (MOAQ), Brief COPE, Non-Task Organizational (NTO) Conflict, and the Shorter PROMIS Questionnaire (SPQ).

Results: Results indicated that NTO conflict was associated with employee well-being measures of drug-alcohol-tobacco (DAT) use. Mediation analysis of coping styles on this stressor-strain relationship found avoidant coping fully mediating the stress process between NTO conflict and DAT use. NTO conflict was also associated to reduced job satisfaction and increased turnover intentions.

Conclusion: These findings concur with previous research regarding the effects of workplace conflict on employee health-related outcomes; and serve to answer recent calls to investigate the complex processes driving workplace substance use in more detail.

Abstract #: 350

Presented by: Shieloh Stephens Holland, BS, Graduate Student

Occupational Health Risks to Nontuberculous Mycobacteria

Shieloh Stephens Holland, BSN, RN, USF Sunshine ERC Occupational Health Nursing Program

Keywords: Nontuberculous Mycobateria, Atypical Mycobacteria, Occupational health

Objective: In contrast to well-developed tuberculosis programs, knowledge of nontuberculous mycobacteria (NTM) and the health hazards they pose to workers is absent in the community.

Methods: Nontuberculous Mycobacteria referred to as Atypical Mycobacteria are members of the Mycobacteria family other than M. tuberculosis and M. leprae, although symptoms from infection are similar; are not transmitted from person to person and can cause pulmonary illness, skin disease, and disseminated disease.

Results: NTM are ubiquitous in the environment found in water and soil, and are causing illness in workers at an increasing rate. Recognition of this occupational health hazard is the initial step in formulating a health and safety plan for worksites.

Conclusion: Unlike their communicable cousins M. tuberculosis and M. Leprae, NTM is not a reportable infection and can lead to serious acute and chronic conditions.

Research supported by: USF Sunshine ERC

Presented by: Zhiqing Zhou, MA, Graduate Student

Effect of Workplace Incivility on End-of-Work Negative Affect: Examining Individual and Organizational Moderators in a Daily Diary Study

Zhiqing E. Zhou, USF Sunshine ERC Occupational Health Psychology Program, <u>Yu Yan</u>, Wuhan University, <u>Xin Xuan Che</u>, University of South Florida, <u>Laurenz L. Meier</u>, University of Fribourg

Keywords: workplace incivility, negative affect, personality, stressor

Objective: This study's objective was to examine the effect of daily workplace incivility on end-of-work negative affect and explore potential individual and organizational moderators on the effect.

Methods: Data were collected from 76 full-time employees across 10 consecutive working days in China. Hierarchical linear modeling was used to examine the main effect of daily workplace incivility on end-of-work negative affect and moderating effects.

Results: Results revealed that daily workplace incivility positively predicted end-of-work negative affect while controlling before-work negative affect. Further, the relationship was stronger for people of high negative affectivity, high hostile attribution bias, external locus of control, and people experiencing less chronic workload and more chronic organizational constraints, as compared to people of low negative affectivity, low hostile attribution bias, internal locus of control, and people experiencing constraints, respectively.

Conclusion: The current study demonstrates that an individual who experiences more workplace incivility during a day's work is more likely to have stronger negative affect before leaving work on the same day. Further, this likelihood is higher for those of high negative affectivity, high hostile attribution bias and external locus of control, and those who have less workload and more organizational constraints at work. These findings suggest that workplace incivility as a daily negative event should be reduced at work by management, especially for people of certain personality traits and people working with less workload and more organizational constraints.

Research supported by: USF Sunshine ERC

Abstract #: 352

Presented by: Mohammed Al Hajji, MSPH, Occupational Safety Graduate

Workplace Injury among Waste Management Workers: Emphasis on Heat Stress Mohammed H. Al Hajji, Thomas E. Bernard, Sunshine ERC at USF, University of South Florida

Keywords: Occupational Injury, Heat Stress

Objective: Waste management includes the pick up and dumping of household garbage and trash. The employees are occupationally exposed to chemical and physical agents that might cause an injury requiring first aid to time away from work. A special consideration is the effects of heat stress on injury risk.

Methods: The injury and illness data for 6 years was examined for type of injury, severity, location (on-route or yard), and the average heat stress level. The number of labor-hours was used to calculate incident rates.

Results: Most of the injuries occurred on the routes and were dominated by musculoskeletal disorders followed by acute injuries. Most injuries were treated as first aid with less than a day of work lost. If a musculoskeletal disorder or acute injury result in more than a day away, it was more likely to be more than a week away. The rate of musculoskeletal disorders and acute injuries increased with heat stress level with a reference level at 24 °C-WBGT.

Conclusion: There was little surprise that most of the injuries were related to musculoskeletal disorders due to the manual nature of the work. The increase in musculoskeletal disorders and acute injuries due to heat stress was suspected and confirmed. The rate ratio was 1.67 just above the occupational exposure limit.

Research supported by: Kingdom of Saudi Arabia