# RESEARCH Appreciation Day

The Art and Science of Biomedical Research and Health

MARCH 6, 2009





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# AGENDA

7:30 - 8:00	Assemble Posters Fort Worth Community Arts Center
8:00 - 12:00	Vendor Fair Fort Worth Community Arts Center
8:00 - 9:00	Faculty/Non-Student Poster Session Fort Worth Community Arts Center
8:30 - 10:00	Poster Presentation Competition Preliminary Judging Center
10:00 - 10:30	Poster Judges Convene Judges' Headquarters
10:30 - 11:30	Poster Presentation Competition Finalist Judging Fort Worth Community Arts Center
11:30 - 12:30	Poster Judges' Final Deliberation Judges' Headquarters
11:30 - 11:45	Remove Posters
12:15 - 2:15	Lunch and Keynote Address Alcon Auditorium (CBH-220)
	<i>Welcome</i> Scott Ransom, DO, MPH, MBA President
	Overview of RAD 2009 Activities Glenn Dillon, PhD Vice President, Research
	Introduction of Keynote Speaker John C. Licciardone, DO, MS, MBA Executive Director, Osteopathic Research Center
	<i>Keynote Address</i> Josephine Briggs, MD Director, National Center for Complementary and Alternative Medicine National Institutes of Health
2:15 - 4:00	Oral Presentation Competition for GSBS
4:00 - 4:30	Oral Judges Convene Judges' Headquarters
4:30 - 5:15	Awards Ceremony (CBH-220)

# **KEYNOTE SPEAKER**

# Josephine P. Briggs, MD

Director, National Center for Complementary and Alternative Medicine (NCCAM) National Institutes of Health

On January 24, 2008, Josephine P. Briggs, M.D., was named Director of the National Center for Complementary and Alternative Medicine. An accomplished researcher and physician, Dr. Briggs brings a focus on translational research to the study of complementary and alternative medicine to help build a fuller understanding of the usefulness and safety of CAM practices.

Dr. Briggs received her A.B. cum laude in biology from Harvard-Radcliffe College and her M.D. from Harvard Medical School. She completed her residency training in internal medicine and nephrology at the Mount Sinai School of Medicine, New York, NY, where she was also chief resident in the Department of Internal Medicine and a fellow in clinical nephrology. She then held a research fellowship in physiology at Yale School of Medicine, New Haven, CT, working with Dr. Fred Wright and Dr. Gerhard Giebisch. After completing her fellowship at Yale, Dr. Briggs was a research scientist for 7 years at the Physiology Institute at the University of Munich, Munich, Germany.

In 1985, Dr. Briggs moved to the University of Michigan, Ann Arbor, MI, where she held several academic positions, including associate chair for research in the Department of Internal Medicine and professorships in the Division of Nephrology, Department of Internal Medicine and the Department of Physiology. Dr. Briggs joined the National Institutes of Health in 1997 as director of the Division of Kidney, Urologic, and Hematologic Diseases at the National Institute of Diabetes and Digestive and Kidney Diseases where she oversaw extramural research activities. While at NIDDK, she co-chaired an NIH Roadmap Committee on Translational Core Resources. In 2006, she accepted a position as senior scientific officer at the Howard Hughes Medical Institute.

Dr. Briggs' research interests include the renin-angiotensin system, diabetic nephropathy, circadian regulation of blood pressure, and the effect of antioxidants in kidney disease. She has published more than 130 research articles and has served on the editorial boards of numerous journals.

# ALCON RESEARCH, LTD. AWARDS

# THE ALCON GROUP

Alcon, the world's leading eye care company, has been dedicated to the ophthalmic industry for more than 60 years, Alcon researches, develops, manufactures and markets pharmaceuticals, surgical equipment and devices, contacts lens care solutions and other vision care products that treat diseases, disorders and other conditions of the eye.

Founded in Fort Worth, Texas in 1947, the Alcon group now employs nearly 15,000 individuals in 75 offices around the world. Total sales for 2008 were approximately \$6.3 billion, with sales activity in more than 180 markets. One of the cornerstones of Alcon's success is the company's commitment to Research and Development. Located at the company's headquarters in Fort Worth is the 700,000 square-foot William C. Conner Research Center, the largest and most sophisticated eye research center in the world. Over the next five years, Alcon plans to spend at least \$4 billion on eye related research and product development in all of its R&D centers, more than any entity outside of the National Eye Institute.

The Alcon Research, Ltd. Awards are given to the top two basic sciences student poster presentations. In addition, Alcon Research, Ltd. sponsors the Postdoctoral Fellow Poster Competition Award. All Research Appreciation Day awards are determined by a panel of judges.

# **GRADUATE STUDENT ASSOCIATION AWARDS**

The Graduate Student Association (GSA) promotes the interests and opinions of the graduate student body, sponsors projects and events beneficial to students, and acts as the voice of students on matters of policy and student welfare.

GSA has co-sponsored Research Appreciation Day since its inception.

The GSA Poster Presentation Awards are given to the top graduate student poster presentations in the basic sciences category. All Research Appreciation Day awards are determined by a panel of judges.

RAD 2009 - ABSTRACT BOOK 4

# PUBLIC HEALTH STUDENT ASSOCIATION AWARDS

The Public Health Student Association (PHSA) is a student-government organization within the School of Public Health (SPH) that provides students with a forum for promoting collegiality, engaging in service initiatives and voicing student concerns. The purpose of PHSA is to facilitate student-student and student-faculty communication and cohesiveness with respect to the students' academic, research and service experience at the school. The organization advocates on issues pertaining to curriculum revision, research opportunities, student participation, and financial needs. Ultimately, the PHSA will strive to create a strong and enduring foundation for future successors to build upon.

The objectives of the organization are: 1) provide members with resources that will enhance their educational careers; 2) foster communication among students, SPH faculty, staff, and administration; 3) promote research opportunities through collaborative public health approaches to disease prevention and health promotion; and 4) foster a prosperous graduate school experience for its members.

The Public Health Student Association sponsors Research Appreciation Day student awards for the top three oral and poster presentations as deemed by a panel of public health judges.

# SCHOOL OF HEALTH PROFESSIONS AWARDS

The School of Health Professions is committed to research excellence and will formally recognize the top two poster presentations made by its students at Research Appreciation Day. As determined by a panel of judges, this award recognizes scientific accomplishment in methods and scientific communication.

# **TEXAS COLLEGE OF OSTEOPATHIC MEDICINE AWARDS**

The Texas College of Osteopathic Medicine (TCOM) is committed to the clinical research excellence of its students and faculty. TCOM educates osteopathic physicians dedicated to careers in health care, teaching and research. By engaging in scholarly pursuits that contribute to further understanding of health and disease, the faculty and students serve the community, the state and the nation.

The Texas College of Osteopathic Medicine Poster Presentation Awards are given to the top three student/resident poster presentations as determined by a panel of judges, and a special award is given to the best poster from students enrolled in the Honors Research practicum.

# CENTER FOR COMMUNITY HEALTH COMMUNITY-BASED RESEARCH AWARDS

The Center for Community Health (CCH) is committed to partnering with the community, conducting policy-relevant health research, and enhancing the community's capacity for disease prevention. Our vision is to foster healthy, vibrant communities.

The Center for Community Health Community-Based Research Poster Awards are given to the top two student, resident, or post-doctoral poster presentations, as determined by a panel of judges representing a variety of community-based organizations.

# FOR HER AWARDS FOCUSED ON RESOURCES FOR HER HEALTH, EDUCATION AND RESEARCH

FOR HER is a collaborative health model for women of all ages and cultures that helps women understand and appreciate clinical advances and research so that they can make informed decisions about their personal health.

FOR HER is committed to fostering, facilitating and expanding collaborative basic and translational research relevant to Women's Health.

The FOR HER Poster Presentation Awards are given to the top medical student and the top resident poster presentations for a research project with findings that can be used to improve women's health across the spectrum of ages and cultures through excellence in clinical care, research or education as determined by a panel of judges.

# INSTITUTE FOR AGING AND ALZHEIMER'S DISEASE RESEARCH AWARD

The Institute for Aging and Alzheimer's Disease Research is devoted to determining the causes, diagnosis, treatment and cure for Alzheimer's disease and other neurological disease of the aged, using multidisciplinary research approaches.

The Institute for Aging and Alzheimer's Disease Research Poster Presentation Award is given to the graduate student whose research is cutting edge and addresses one of these important research issues, as determined by a panel of judges.

# NORTH TEXAS EYE RESEARCH INSTITUTE AWARD

The mission of the North Texas Eye Research Institute (NTERI) is to use interdisciplinary research to determine the causes of eye diseases and to discover new therapies. The NTERI also supports the training and education of new researchers in the visual sciences.

The UNTHSC Research Appreciation Day NTERI Poster Presentation Award is given to the deserving graduate student who has clearly demonstrated excellence in visual science research, as determined by an independent panel of judges.

# PRIMARY CARE RESEARCH INSTITUTE AWARD

The Primary Care Research Institute (PCRI) is dedicated to improving the health of Texas citizens through interdisciplinary primary care and public health service, research, and education. The PCRI provides a forum and the resources for students, residents, fellows, internal and external collaborative partners to be successful in scholarly research activities. The PCRI is proud to sponsor projects and events beneficial to primary care health issues and dissemination of research findings.

Any UNTHSC student presenting a poster in primary care or public health-related research is eligible for competition. Awardees are determined by a panel of judges.

# **TECH FORT WORTH INNOVATION AWARD**

The TECH Fort Worth Innovation Award is sponsored by TECH Fort Worth. This award is presented to the research poster which depicts the most innovative research. The award-winning poster must present cutting-edge technology which will have a high impact on both the scientific community as well as the general public.

TECH Fort Worth is a public-private partnership of the City of Fort Worth, The University of North Texas Health Science Center, and the local business community. TECH Fort Worth is a non-profit business incubator which helps entrepreneurs commercialize innovative technologies that will impact the environment, empower the community, and improve healthcare.

TECH Fort Worth manages a 20,000 sq. ft. facility that offers executive suites at the Guinn School Facility, as well as the NEW ACCELERATION LAB at UNTHSC's Center for BioHealth. On May 5<sup>th</sup>, 2009 the TECH Fort Worth IMPACT Awards will be held to recognize early stage companies that are bringing to market new technologies which will have significant impacts on our environment, our community, and our health. For more information on the TECH Fort Worth IMPACT Awards please visit <u>www.ImpactOurWorld.com</u>.

TECH Fort Worth 1120 South Freeway Fort Worth, Texas 76104 (817) 339-8968 www.techfortworth.org

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# **TRAVEL SERVICE EVERYWHERE**

Travel Service Everywhere and its affiliates are long-standing supporters of UNT Health Science Center.

Their support of RESEARCH APPRECIATION DAY 2009 includes the donation of one round-trip airline ticket for one of the first place winners of the poster competitions to travel to a national scientific meeting.

Please join us in thanking TSE and their fine team of professionals for their continued support of our activities.



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# JUDGES

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# AGING/ALZHEIMER'S DISEASE

### 100 (Poster)

First Author/Presenter: Hatoon Dablouk

Classification: GSBS Student

Hatoon Dablouk\* Daniel Tallent\*, and Hriday K. Das \* Graduate School of Biomedical Sciences Department of Pharmacology & Neuroscience

INTRAPERITONEAL INJECTION OF JNK INHIBITOR SP600125 REDUCES EXPRESSION OF PRESENILIN-1 IN MOUSE

Purpose: The purpose is to test that intraperitoneal (i.p) injection of JNK inhibitor SP600125 represses presenilin-1 (PS1) expression and gamma-secretase activity in mouse brains.

Methods: 5 months old male C57BL/6 mice (n=3) were injected i.p with DMSO (control) or with SP600125 in DMSO (23 mg/kg/day) (n=3) for 4 days. Mice were sacrificed on the 5th day and cortexes were removed to prepare protein extracts for Western blot analysis. Blood samples were also collected to prepare plasma for detection of Abeta level by Sandwich ELISA. Protein extracts (15µg) prepared from mouse cortex were fractionated by electrophoresis on 18% SDS-PAGE and analyzed by Western blotting. Control extracts (C1, C2, C3) from 3 mice and SP600125 treated extracts (S1, S2, S3) from 3 mice were subjected to Western blot analysis with anti-JNK, anti-pJNK, anti-PS1, and anti-GAPDH. Blots were developed by chemiluminescence (ECL) and protein gel bands were quantified using Labworks Image Analysis Software.

Results: PS1 produces Abeta peptide by proteolytic processing of amyloid precursor protein APP. Therefore, transcriptional regulation of PS1 controls the pathogenesis of Alzheimer's disease. Ets1/2 transcription factors activate PS1 transcription and p53 represses PS1 transcription. Previous reports showed that inhibition of basal JNK activity by JNK inhibitor SP600125 increased p53 protein level, and repressed PS1 transcription by p53-Ets1/2 interaction resulting in the reduction of PS1/gamma-secretase activity and the genesis of Abeta peptide in neuroblastoma cell lines. We now show that i.p injection of SP600125 reduced the levels of p-JNK by ~44% and PS1 by ~3 6% (S1, S2, S3) compared to DMSO treated control mice (C1, C2, C3). Total JNK levels were found to be unchanged in the brains of control and SP600125 treated mice. These results suggest that expression of p-JNK and PS1 can be inhibited in the brains of mice by i.p injection of SP600125. We could not accurately determine Abeta levels in the plasma of these mice by ELISA using mouse specific anti-Abeta. It is possible that normal APP processing in C578L/6 mice produces very low level of Abeta. Therefore, changes of Abeta levels are also undetectable in the plasma of SP600125 treated mice.

Conclusions: Data presented here suggest that i.p injection of SP600125 into TgAPPSwed/Ind mice models of AD will potentially reduce the amount of Abeta plaques, and ameliorate cognitive deficits in these mice by reducing PS1 transcription.

Sponsor: N/A

# 101 (Oral)

### First Author/Presenter: Felichia Fields

#### Classification: SPH Student

Felichia Fields, MPH1 Fernando Wilson, PhD1 Nuha Lackan, PhD1 1) Department of Health Management and Policy, School of Public Health, University of North Texas Health Science Center, 3500 Camp Bowie Boulevard, Fort Worth, TX 76107

LIKELIHOOD OF INSTITUTIONALIZATION AMONG NON-HISPANIC WHITE, AFRICAN-AMERICAN AND HISPANIC CAREGIVERS OF INDIVIDUALS WITH DEMENTIA

Purpose: To examine the likelihood of independent predictors influencing Non-Hispanic White, African American, and Hispanic caregivers of people with dementia to institutionalize.

Methods: Secondary data from the Resources for Enhancing Alzheimer s Caregiver s Health (REACH II) were examined. Likelihood to institutionalize was measured. The sample included 669 Non-Hispanic Whites, African Americans, and Hispanics. Stepwise multivariate logistic regression analyses were conducted to examine the differences in predictors of institutionalization.

**Results:** Thirty-one percent of caregivers in our sample reported being likely to institutionalize. The likelihood to institutionalize varied by race with Non-Hispanic Whites having the highest rates (38.2%) followed by African Americans (28.1%) and then Hispanics (22.6%). Stepwise multivariate analyses indicated that caregivers ages 21-55 were significantly associated with the likelihood of institutionalizing.

Conclusions: Our findings suggest that deciding to institutionalize a person with dementia is a very complex process that has racial/ethnic and income variation. Support services aimed at helping caregivers to better understand caring for a person with the dementia and the option of institutionalization to this very specific disease may be more successful if it is targeted to specific racial and ethnic groups; as well as, groups who earn less than \$50,000.

# AGING/ALZHEIMER'S DISEASE

# 102 (Poster)

#### First Author/Presenter: Felichia Fields

Classification: SPH Student

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DEPRESSIVE SYMPTOMS IN NON-HISPANIC WHITE, AFRICAN-AMERICAN AND HISPANIC CAREGIVERS OF PERSONS WITH DEMENTIA

Purpose: To examine the association between race/ethnicity and depressive symptoms in caregivers of people with dementia

Methods: Secondary data from the Resources for Enhancing Alzheimer's Caregiver Health (REACH II), a multi-site study were examined. The REACH project was designed to test promising interventions for enhancing family caregiving for persons with dementia (Wisniewski et al, 2003). Depressive symptoms were measured using the Center for Epidemiological Studies Depression Scale (CES-D). The study sample included 603 respondents and included non-Hispanic whites, African-American, and Hispanics, descriptive analyses and logistic regression analyses were conducted in order to examine the association of caregiver race and depressive symptoms.

Results: Twenty-three percent of caregivers in our sample had high depressive symptoms. Depressive symptomology varied by race/ethnicity, with Hispanics having the highest rates (28%) followed by non-Hispanic whites (24%), and African-Americans (19%). Multivariate analyses adjusting for sociodemographic characteristics, support group participation, and religious activity participation, showed that participation in a religious activity was the only significant factor across all racial/ethnic groups that decreased the likelihood of having depressive symptoms.

**Conclusions:** Our findings suggest that support services for caregivers of individuals with dementia need to be more race specifically focused. Our findings also suggest that caregivers who participate in a religious activity are less likely to report depressive symptoms, intervention programs may also need to be set up through religious outlets for non-Hispanic whites in a similar manner to those already established for African-Americans and Hispanics. Further research is needed to examine methods to influence the use of more formal support services for Hispanics and African-Americans.

Sponsor: N/A

### 103 (Poster)

First Author/Presenter: Nathalie Sumien

**Classification:** Faculty

Nathalie Sumien, Pharm & Neurosc., UNTHSC, Fort Worth, TX 76107 Uzoma Ikonne, Pharm & Neurosc., UNTHSC, Fort Worth, TX 76107 Willie Tays, Pharm & Neurosc., UNTHSC, Fort Worth, TX 76107 Michael J. Forster, Pharm & Neurosc., UNTHSC, Fort Worth, TX 76107

DOSE RESPONSE EFFECTS OF VITAMIN C AND VITAMIN E ON AGE-RELATED MOTOR DEFICITS IN C57BL/6 MICE

Purpose: These parallel studies of antioxidant dose response were designed to determine whether supplementation with increasing doses of vitamin C or vitamin E could improve motor function in aged male C57BL/6 mice.

Methods: When 20 months of age, separate groups of mice were assigned to one of the following treatment groups: vehicle (H2O or soybean oil), vitamin C (100, 200, 400, or 600 mg/kg/d ascorbate in H2O), or vitamin E (25, 50, 100, or 400 mg/kg/d a-tocopheryl acetate in soybean oil). Groups of 3-month-old mice (used as young control groups) received either the water or soybean oil vehicle. The mice were gavaged daily with their respective treatments for a period of three weeks prior to the start of behavioral testing and throughout the testing. The mice were followed for weights throughout the study and food intake was measured after 3 weeks on the treatments. Behavioral measurements encompassed motor coordination and learning (rotorod), reflexes, grip strength and balance (wire suspension and bridge tasks).

Results: Age-related deficits were evident in performance of the mice on age-sensitive tests such as bridge walking and rotorod. Performance of the mice treated with vitamin C indicated no effect of any of the doses on motor function. However, the 200 mg/kg dose seemed to have beneficial yet not significant effects on negative geotaxis and bridge walking performance. Performance of the mice treated with vitamin E indicated no significant effect of any of the doses on motor function. However, the 100 mg/kg dose had marginally deleterious effects on walking initiation (reflex) and on maximum performance on the rotorod.

**Conclusions:** Despite marginal beneficial and deleterious trends, the overall results demonstrated no significant improvement of psychomotor function in the aged mice after supplementation with vitamin C or vitamin E. These results suggest that single antioxidant supplementation, even at high concentration, does not have the capacity to improve age-related deficits in motor function in mice.

# AGING/ALZHEIMER'S DISEASE

### 104 (Oral)

First Author/Presenter: Uzoma Ikonne

Classification: GSBS Student

Uzoma Ikonne, Sujung Jun, Ladislav Dory, Michael Forster, Nathalie Sumien University of North Texas Health Science Center 3500 Camp Bowie Blvd. Fort Worth, Texas 76107

#### AN ANXIOLYTIC EFFECT IS ASSOCIATED WITH EXPRESSION OF 129 EXTRACELLULAR SUPEROXIDE DISMUTASE GENOTYPE

Purpose: Extracellular superoxide dismutase(ecSOD) is the only extracellular enzyme that provides protection against oxidative stress(superoxide) and its expression is tissue dependent.Over-expression of ecSOD has been associated with improved cognitive performance of aged mice in the radial arm maze, whereas in young mice it has been associated with deleterious effects, including impaired long-term potentiation. Previous studies have determined that expression of ecSOD is higher in plasma of 129P3 than C57BL/6 mice, strains which carry wild-type or mutant alleles for ecSOD, respectively.To determine the influence of the different alleles on brain function, congenic mice were developed carrying the wild-type(C57) or mutant(129) alleles on a C57BL/6 background.The purpose of this study was to determine the contribution of allele-dependent differential expression of ecSOD to age-related differences in psychomotor and cognitive performance.

Methods: There were four groups of congenic female C57BL/6 mice in this study 10-or17-month-old mice carrying either the 129 or wild type ecSOD gene(N=13-21).Brain function was assessed in these groups using tests of behavioral arousal,anxiety level,motor skills,and cognition.The cognitive tasks included the water maze, a measure of spatial memory, and a discriminated avoidance task. Anxiety level in the mice was measured by their avoidance of the open arms of an elevated plus maze(EPM).

Results: Age-related declines in performance were detected in most motor and cognitive tasks, independent of the ecSOD genotype. There were no allele-specific effects in the young mice; however such an effect was detected on performance in tests of behavioral arousal and anxiety in the old mice. Seventeen-month-old mice expressing the mutant(129) ecSOD spent more time in the center of an open field and in the open arms of the EPM, and their swim speed in the water maze was slower, when compared to age-matched mice carrying the wild-type(C57) allele.

Conclusions: These results suggest that the differential expression of ecSOD in C57BL/6 mice was not associated with differences in the performance of mice on the majority of the psychomotor and cognitive behavioral tasks. However, the data from the tests of behavioral arousal, the elevated plus maze, and swim speed suggest that there is an anxiolytic effect associated with the mutant(129) allele. Thus, the extracellular redox state in the brain may have a significant influence on level of anxiety.

First Author/Presenter: Alena Minton

Classification: GSBS Student

Alena Z. Minton, Myoung H. Kim, Department of Molecular Biology and Immunology, University of North Texas Health Science Center, 3500 Camp Bowie Blvd, Fort Worth, Texas 76107

NEW INSIGHTS INTO THE ROLE OF CCAAT/ENHANCER BINDING PROTEIN BETA -C IN METASTATIC GENE EXPRESSION IN PROSTATE CANCER

Purpose: C/EBPß is a transcription factor, consisting of transcription activating A and B forms (C/EBPß-AB) and transcription-inhibitory C form (C/EBPß-C). We previously reported that transcription-inhibitory C/EBPß-C was predominantly expressed in LNCaP cells which showed little or no expression of IL-6, IL-8 and anti-apoptotic gene Bfl-1 (collectively termed metastatic genes). On the other hand, transcription-activating C/EBPß-AB forms were predominant in hormone-independent prostate cancer (HI-PCa) cells which showed high levels of metastasis gene expression. IL-6 and IL-8 are known to be important in hormone-independent growth and metastasis of prostate cancer cells and Bfl-1 is an anti-apoptotic protein. All of these genes are regulated by cooperative action of C/EBPß and NF-kB. In the study, we investigate if dominant C/EBPß-C expression is inhibitory to the expression of metastatic genes in prostate cancer cells.

Methods: Reporter gene assays were used to investigate transcriptional activity of C/EBPß. Reporter gene constructs used were pGL3-Bfl-1-Luc, pGL3-IL-6-Luc and pGL3-IL-8-Luc. C/EBPß protein was depleted by siRNA-mediated silencing. C/EBPß-C was overexpressed by transient transfection of pSv5-C/EBPß-C expression vector.

Results: We determined that exogenous C/EBPB-C overexpression and siRNA-mediated C/EBPB depletion significantly reduced TNF-ainduction of BfI-1 promoter activity in DU-145 cells. Similarly, TNF-a induction of IL-6 and IL-8 promoter activity was significantly decreased C/EBPB-C overexpression or by C/EBPB depletion. The central role of C/EBPB-AB in TNF-a-induced IL-6 promoter activity was further substantiated by reporter gene assays of IL-6 promoter with mutated C/EBPB or NF-kB binding site. The reporter gene assay showed that TNF-ainduced reporter gene expression was abolished from IL-6 promoter with mutated C/EBPB binding site but showed only modest decrease from IL-6 promoter with the mutated NF-kB binding site. In addition, C/EBPB-C overexpression further decreased reporter gene, while C/EBPB-A overexpression fully restored reporter gene expression from IL-6 promoter with the mutated NF-kB binding site.

Conclusions: Taken together, these results strongly argue for the inhibitory role of C/EBPB-C in metastatic gene expression and potentially beneficial in the inhibition of metastatic growth of HI-PCa cells.

Sponsor: N/A

### 201 (Poster)

First Author/Presenter: Cherice Roth

Classification: GSBS Student

Cherice Roth - UNTHSC, Fort Worth, TX 76126 Sanjay Awasthi - UNTHSC, Fort Worth, TX 76126

### THE ROLE OF RLIP76 IN PROSTATE CANCER CHEMOTHERAPY RESISTANCE

Purpose: RLIP76 is a stress-responsive multi-specific, non-ABC transporter which represents an entirely novel link between stress-inducible Gprotein signaling, receptor tyrosine-kinase signaling, endocytosis, heat-shock and stress defense pathways, and transport mediated drugresistance. It is highly expressed in cancer cells. The purpose of this work is to analyze the role RLIP76 plays in prostate cancers.

Methods: Immunocytochemistry, western blot analysis, cell viability assays (MTT and Annexin V + PI staining), as well an murine in vivo work were all employed in this study.

Results: When RLIP76 antisense is given to mice in vivo prostate cancer tumor go into full remission. RLIP antisense also shows cell death in vitro.

Conclusions: RLIP76 expression seems to be vital to the ability of cancer cells to survive. Further studies include antibody deactivation of RLIP76 as well as over expression of RLIP76.

#### First Author/Presenter: Jesse Porter

#### Classification: Community Partner

KM Cardarelli, M Martin, J Porter, E Johnson, JK Vishwanatha Co-investigators: Earnestine Cole, Roy Lopez, Deborah Parish, Janet Morrison, Marva Epperson-Brown, Marcene Royster, Jesse Banda, Anna Hill, JR Newton, Pastor Preston Weaver

#### DALLAS CANCER DISPARITIES COMMUNITY RESEARCH COALITION

Purpose: The Dallas Cancer Disparities Community Research Coalition is a partnership between the South Dallas community and the Center for Community Health at the University of North Texas Health Science Center, to identify cancer disparities and jointly develop innovative communitybased interventions to reduce cancer disparities. South Dallas/Fair Park, like many inner city neighborhoods, has a population that is predominantly minority, low income and medically underserved.

Methods: To create this partnership, we adapted the five-step Community Action Model. The study was approved by the Institutional Review Board at UNT Health Science Center. In Step 1, we created and convened the Community Advisory Board (CAB), comprised of 11 individuals from the community whom we have trained to be co-investigators. The CAB completed human subject research training and reviewed existing data on cancer disparities. Next, the CAB designed and implemented 5 focus groups in order to engage the broader community to identify and prioritize cancer disparities. Each focus group was comprised of 8-12 residents from the South Dallas who were twenty-one years or older and was facilitated by a trained expert. Data collection was by audio recording and hand written notes taken by the study coordinator. Findings from the focus groups are currently being reviewed by the CAB, and an evidence-based intervention will be jointly developed by the CAB and the Center for Community Health to address the prioritized area(s). The intervention will be pilot tested in the Frazier neighborhood in South Dallas.

Results: A comprehensive evaluation of the pilot intervention will be conducted in Step 5.

Conclusions: This study demonstrates that community-based participatory research (CBPR) is a promising approach to address these important disparities, and that academicians and community members who engage in CBPR must attend to its co-learning processes in order to successfully work together.

Sponsor: National Cancer Institute

# 203 (Poster)

First Author/Presenter: Shalini Persaud

Classification: GSBS Student

S.D. Persaud, D. Pal and A. Basu. Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, TX, 76107

# DOWNREGULATION OF PKC-ETA BY DEPHOSPHORYLATION IS MEDIATED BY PROTEOSOME DEPENDENT AND INDEPENDENT PATHWAYS.

Purpose: Protein kinase C-eta, a member of the PKC family, plays an important role in cell proliferation and differentiation. Persistent activation of PKCs by tumor-promoting phorbol esters leads to their degradation or downregulation by proteasome- or calpain-mediated pathway. However, PKC-eta resists activation-induced downregulation, suggesting that PKC-eta may play a role in tumorigenesis. Targeting the downregulation of PKCs appears to prime them for activation and also decide their stability. PKCs may be autophosphorylated or transphosphorylated by other kinases, such as 3-phosphoinositide-dependent kinase 1 (PDK1). The objective of this study is to investigate how dephosphorylation of PKC-eta leads to its downregulation.

Methods: To determine if dephosphorylation of PKC-eta leads to its downregulation, we treated MCF-7 breast cancer cells with PKC inhibitors (Gö 6983 or Gö 6976) and PDK1 inhibitor Ly294002 and monitored PKC-eta expression and phosphorylation by Western blot analysis. We also examined the effect of rapamycin, an inhibitor of mammalian target of rapamycin (mTOR) which was also shown to regulate phosphorylation of PKCs and mitogen activated protein kinase (MAPK) inhibitor U0126 to check for the specificity. We next examined if inhibition of PKC-eta dephosphorylation prevents its downregulation by treating cells with pharmacological inhibitors of protein phosphatase-1 (PP1) and PP2A using calyculin A and okadaic acid or by siRNA knockdown of PH domain leucine-rich repeat protein phosphatase (PHLPP). Finally, we determined if the mechanism of PKC-eta downregulation was mediated by proteosomes or calpains by treating MCF-7 cells with calpain inhibitors (calpeptin and ALLN) or proteasome inhibitor (MG132).

Results: PKC-eta was downregulated by treatment with Gö 6983 and Ly294002 but not with rapamycin or U0126. Calyculin A, but not okadaic acid, blocked the downregulation of PKC-eta by Gö 6983 and Ly294002, suggesting that dephosphorylation of PKC-eta by PP1 induced downregulation of PKC-eta. Treatment with MG132 blocked downregulation of PKC-eta by Ly294002 but not by Gö 6983.

Conclusions: Dephosphorylation of PKC-eta induces its downregulation. In addition, dephosphorylation of PKC-eta is mediated via both proteasome-dependent and -independent pathways. (This work was supported by the grant CA1727-S1 from the NIH/NCI.)

Sponsor: This work was supported by the grant CA1727-S1 from the NIH/NCI

First Author/Presenter: Kathryn Leake

Classification: GSBS Student

Kathryn Leake, Sanjay Awasthi - UNTHSC, Fort Worth, TX 76107

#### MRP-1 DEPLETION CAUSES APOPTOSIS, KILLING MCF7/VP BREAST CANCER CELLS

Purpose: We hypothesized, Will inhibition of MRP-1 result in apoptosis? Second, Will depletion of MRP-1 simultaneously with RLIP76 result in synergistic cytotoxicity, an additive effect, or antagonism? Last, If antisense of these transporters is combined with Doxorubicin, which performs best, RLIP76 inhibition, or combined inhibition?

Methods: Following transient transfection of RLIP76 in MCF7/VP cells, expression of RLIP76 and MRP-1 cDNA in MCF7/VP cells was evaluated by RT-PCR analysis. MRP-1 antisense was designed. IC50 values of MCF7/VP cells with RLIP76, MRP-1 antisense, and RLIP76 with MRP-1 antisense together, were measured by MTT Assay. IC50 values of RLIP76 antisense versus RLIP76 plus MRP-1 antisense were both also measured in combination with Doxorubicin.

Results: We identified both transporters as expressed in the same cell line, MCF7/VP. Therefore, we inhibited MRP-1 alone and both transporters simultaneously. MTT results indicated that MRP-1 inhibition results in apoptosis of MCF7/VP cells (22%, n=5). Simultaneous inhibition of both transporters appeared synergistic at low concentrations; however, at high concentrations, there was no further additive effect. As predicted by previous studies, Doxorubicin cytotoxicity was markedly enhanced in the presence of RLIP76 antisense. No additional effect was seen by the inclusion of MRP-1 inhibition.

Conclusions: These findings indicate that MRP-1 depletion causes apoptosis, killing breast cancer cells, and that MRP-1 antisense is an antineoplastic agent by itself. Simultaneous inhibition of both transporters appears synergistic at low concentrations but does not produce synergy at higher concentrations, which may indicate a threshold effect. Finally, our findings indicate that RLIP76 may be a potential target for improving cytotoxic responses in drug resistant breast cancer cells when employed together with Doxorubicin.

Sponsor: N/A

### 205 (Poster)

#### First Author/Presenter: Angie Dao

### Classification: TCOM DO Student

Angie Dao\* and Rafael Alvarez-Gonzalez& From: \*The Texas College of Osteopathic Medicine and &The Graduate School of Biomedical Sciences, The University of North Texas Health Science Center at Fort Worth.

#### NF-KAPPA B DNA-BINDING SECIFICITY IN THE ABSENCE OR PRESENCE OF HISTONE PROTEINS

Purpose: In this research project, we aim to study if NF-kappa B-p50 regulates skin inflammatory responses by sequence specific DNA binding in the cell nucleus prior to gene expression, which may be a crucial step for the initiation phase of skin carcinogenesis at the molecular level.

Methods: We plan to use two different techniques: 1) Enzymatic labeling of the (NF-kappa B)-specific DNA binding probe. Phosphorylation of the oligodexonucleotide will be done with T4 polynucleotide kinase (PNK). For this enzyme assay, 27.0  $\mu$ l deionized water, 10  $\mu$ l oligonucleotide at 1.0  $\mu$ g/ $\mu$ l, 5  $\mu$ l 10X T4 PNK reaction buffer, 5  $\mu$ l 10 mM ATP solution, and 3 U T4 Polynucleotide Kinase, with a total reaction volume of 50  $\mu$ l, will be combined on ice. These reaction components will then typically be incubated at 37°C for 30 minutes. After 5'-end labeling, T4 PNK will be inactivated by incubating for 5 minutes at 70°C. 2) Electrophoretic Mobility Shift Assay (EMSA). We plan to use the mobility shift assay adaptation of Chang and Alvarez Gonzalez (Journal of Biological Chemistry, 2001). For the radiolabeled probe of NF-kappa B, a duplex oligodeoxynucleotide containing the consensus sequence (5 -AGTTGAGGGGACTTTCCCAGGC-3, Santa Cruz Biotechnology) will be endlabeled with gamma-[32P]-ATP (ICN) and T4 DNA polynucleotide kinase (United States Biochemical Corp. Binding will be confirmed by the autoradiographic analyses of the DNA probe with and without the histone proteins being added.

Results: The results presented on this poster were obtained from control DNA-binding experiments already done in the lab (Chang and Alvarez-Gonzalez) in the absence of histones. The experiments with the addition of precise amounts of histones are still in progress and the experiments have not been finished yet.

Conclusions: We anticipate that the addition of increasing amounts of either histone H1 or nucleosomal "core" histones will result in the competitive inhibition of the oligodeoxynucleotide-sequence specific binding of pure NF-kappa B p50.

# 206 (Oral)

#### First Author/Presenter: Shalini Persaud

Classification: GSBS Student

S.D. Persaud and A. Basu Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, TX, 76107

### DOWNREGULATION OF PKC-ETA IS MEDIATED BY PROTEOSOME DEPENDENT AND INDEPENDENT PATHWAYS

Purpose: Protein kinase C-eta (PKC-eta), a member of the PKC family, plays an important role in cell proliferation and differentiation. Persistent activation of PKCs by tumor-promoting phorbol esters leads to their degradation or downregulation by proteasome- or calpain-mediated pathway. However, PKC-eta resists activation-induced downregulation, suggesting that PKC-eta may play a role in tumorigenesis. Targeting the downregulation of PKC-eta may be an important strategy in cancer therapy. The phosphorylation status of PKCs appears to prime them for activation and also decide their stability. PKCs may be autophosphorylated or transphosphorylated by other kinases, such as 3-phosphoinositide-dependent kinase 1 (PDK1). The objective of this study is to investigate how dephosphorylation of PKC-eta leads to its downregulation.

Methods: To determine if dephosphorylation of PKC-eta leads to its downregulation, we treated MCF-7 breast cancer cells with PKC inhibitors (Gö 6983 or Gö 6976) and PDK1 inhibitor Ly294002 and monitored PKC-eta expression and phosphorylation by Western blot analysis. We also examined the effect of rapamycin, an inhibitor of mammalian target of rapamycin (mTOR) which was also shown to regulate phosphorylation of PKCs and mitogen activated protein kinase (MAPK) inhibitor U0126 to check for the specificity. We next examined if inhibition of PKC-eta dephosphorylation prevents its downregulation by treating cells with pharmacological inhibitors of protein phosphatase-1 (PP1) and PP2A using calyculin A and okadaic acid or by siRNA knockdown of PH domain leucine-rich repeat protein phosphatase (PHLPP). Finally, we determined if the mechanism of PKC-eta downregulation was mediated by proteosomes or calpains by treating MCF-7 cells with calpain inhibitors (calpeptin and ALLN) or proteasome inhibitor (MG132).

Results: PKC-eta was downregulated by treatment with Gö 6983 and Ly294002 but not with rapamycin or U0126. Calyculin A, but not okadaic acid, blocked the downregulation of PKC-eta by Gö 6983 and Ly294002, suggesting that dephosphorylation of PKC-eta by PP1 induced downregulation of PKC-eta. Treatment with MG132 blocked downregulation of PKC-eta by Ly294002 but not by Gö 6983.

**Conclusions:** Dephosphorylation of PKC-eta induces its downregulation. In addition, dephosphorylation of PKC-eta is mediated via both proteasome-dependent and -independent pathways. (This work was supported by the grant CA1727-S1 from the NIH/NCI.)

Sponsor: This work was supported by the grant CA1727-S1 from the NIH/NCI

# 207 (Poster)

### First Author/Presenter: Kristen Hahn

Classification: Staff

Kristen Hahn, MPH; Primary Care Research Institute; Fort Worth, TX 76107 Vishwam Pandya, MD, MPH; Primary Care Research Institute; Fort Worth, TX 76107 Roberto Cardarelli, DO, MPH; Primary Care Research Institute; Fort Worth, TX 76107

GEOGRAPHIC VARIATION OF MEDICAL DISCRIMINATION ON CANCER TESTING AMONG AFRICAN-AMERICANS AND WHITES

Purpose: The purpose of this study was to examine the adequacy and geographic variation of cancer testing among respondents to the 2004 Behavioral Risk Factor Surveillance System survey (BRFSS) who reported medical discrimination compared to those who did not report medical discrimination.

Methods: Data were obtained from the 2004 BRFSS Reactions to Race module administered in 7 states and the District of Columbia: South (SC, AR, and MS); Other (RI, DE, CO, WI, and DC). Among women aged 40 to 75, breast cancer testing was inadequate if a mammogram was not performed in the past 2 years. Inadequate cervical cancer testing was defined as not having a pap smear in the past 3 years and was assessed among women aged 18 to 75 with an intact uterus. Inadequate prostate cancer testing was defined as not having a PSA test in the past 12 months and was assessed among men aged 50 to 75. Inadequate colon cancer testing was defined as not having a fecal occult blood test in the past 2 years or not having a sigmoidoscopy or colonoscopy in the past 10 years and was assessed among men aged 50 to 75. Medical discrimination was evaluated with the following question: Within the past 12 months when seeking healthcare, do you feel your experiences were worse than, the same as, or better than people of other races? Respondents had experienced medical discrimination if they answered worse than other races or worse than some races, better than others. Multiple logistic regression was performed by region to assess the relationship between inadequate cancer testing and medical discrimination while accounting for complex survey weighting and sample design.

Results: With univariate analyses, the odds of inadequate cancer testing were significantly greater among respondents who had experienced medical discrimination for all regions and cancers except for prostate cancer and colon cancer in the Other region. However, when adjusted for potential confounders, none of the odds ratios remained statistically significant. Overall, the effect of perceived medical discrimination was greater in the South region versus the Other region.

Conclusions: Experiencing medical discrimination was not significantly associated with cervical, colon, breast, or prostate cancer testing in the South or the Other region after controlling for potential confounders. Additional studies examining the role of other sources of discrimination, trust in the medical system, and in other regions would be informative.

First Author/Presenter: Rebecca Johnson

Classification: GSBS Student

Rebecca Johnson Molecular Biology and Immunology Wenjun Li Neurobiology and Pharmocology Shoahua Yang M.D.PhD Neurobiology and Pharmocology

### TAMOXIFEN AS A POTENTIAL CHEMOTHERAPY FOR GLIOMA

Purpose: Gliomas are a class of tumor that develops from glial cells, which are the most common type of primary brain tumor and one of the most aggressive of all malignancies. Despite of the development of the modern diagnostic modalities, surgical and other treatment procedures, the prognosis for patients with malignant glioma has remained largely unchanged over the last two decades, with median survivals of less than a year for patient with glioblastoma, the most common and aggressive type of malignant glioma. Tamoxifen is the first selective estrogen receptor modulator (SERM) that has been successfully tested for the prevention of breast cancer in high-risk women and is currently approved for the endocrine treatment of all stages of estrogen receptor (ER)-positive breast cancer. Recently there has been increasing evidence indicates that tamoxifen may be of some benefit in treating gliomablastoma and Medullaglioma In the current study, the effect of tamoxifen in rat C6 glioma cell line were investigated.

Methods: C6 cells were seeded in 96-well plates and incubated overnight with 1- 50uM tamoxifen. Cell viability was determined using Calcein AM assay.

Results: Tamoxifen was cytotoxic to C6 glioma cells with concentrations in a dose dependent manner.

Conclusions: Though C6 glioma cells are estrogen receptor negative, tamoxifen could still decrease the cell population.

Sponsor: R01NS054687 and R01NS054651 (Shaohua Yang)

### 209 (Poster)

#### First Author/Presenter: giang zeng

N.

Classification: Postdoctoral Fellow

Q. Zeng, B. Adkins, P. Muthu Thanu, S. Sridharan, J. Borejdo and A. Basu. Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, TX, 76107

DYNAMIC SUBCELLULAR LOCALIZATION OF CASEPASE-2 IN GYNECOLOGICAL CANCER CELLS

Purpose: Caspase-2 is one of the best conserved caspases across species. It is unique among caspases in that it has features of both initiator and effecter caspases. However, basic knowledge as to the subcellular location and dynamics of caspase-2 is few. Caspase-2 is the only caspase that was found to be localized in the nucleus. Our laboratory has shown that rottlerin, an inhibitor of protein kinase C (PKC)-delta, downregulates caspase-2 via proteasome-mediated pathway independent of PKC-delta inhibition. However, inhibition of caspase-2 downregulation by proteasome inhibitor did not prevent cisplatin-induced cell death. This study is to explore if subcellular distribution of caspase-2 regulates cisplatin sensitivity in gynecological cancer cells.

Methods: In order to investigate the subcellular location and dynamics of caspase-2, we treated human cervical cancer HeLa and ovarian cancer 2008 cells with the anticancer drug cisplatin, protein kinase C-delta inhibitor rottlerin and proteasome inhibitor MG132. Subcellular distribution of caspase-2 was determined by confocal microscopy and Total Internal Reflection Fluorescence (TIRF) microscopy.

Results: Caspase-2 was present constitutively throughout the cells, including cytosol and nucleus. It translocated to plasma membrane and perinuclear region upon addition of cisplatin to HeLa and 2008 cells. Rottlerin induced downregulation of caspase-2. MG132 prevented caspase-2 downregulation but in the presence of rottlerin and MG132, caspase-2 was primarily localized in the nucleus.

Conclusions: Subcellular localization of caspase-2 is involved in apoptotic pathway in cancer cells. The intervention of these pathways may open up new potential targets for the treatment of gynecological cancer. (This work was supported by the grant CA071727 from the NIH/NCI.)

#### First Author/Presenter: Eswar Shankar

### Classification: Postdoctoral Fellow

Eswar Shankar\*, Soumya Krishnamurthy\*\* and Alakananda Basu\* University of North Texas Health Science Center, Fort Worth, TX 76107. \*Institute of Cancer Research, \*\*The Cancer Research Foundation of North Texas

### PROTEIN KINASE C-EPSILON UPREGULATES BCL-2 BY ACTIVATING CAMP-RESPONSE ELEMENT-BINDING PROTEIN

Purpose: Tumor necrosis factor-alpha(TNF-alpha) is a pro-inflammatory cytokine that regulates pleiotropic effects such as induction of apoptosis and activation of the transcription factor, nuclear factor-KappaB (NF-?B) leading to the induction of a number of anti-apoptotic proteins. Protein Kinase C-epsilon (PKCe) belongs to the novel category of PKC family and acts as an anti-apoptotic protein. PKCe has been reported to induce cell survival signals by upregulating the antiapoptotic protein, Bcl-2. Although Bcl-XL is known to be a transcriptional target of NF-?B, it is not clear as to how Bcl-2 is regulated. cAMP-response element-binding protein (CREB) has been implicated in the transcriptional regulation of Bcl-2 in B cells. CREB is reported to be activated by phosphorylation at Ser133 residue. It is not known if PKCe phosphorylates and activates CREB. Our objective was to determine if PKCe upregulates Bcl-2 via NF-?B or CREB in breast cancer cells.

Methods: Highly aggressive breast cancer MDA-MB-231 cells, which overexpress PKCe were used in the study. Western blotting was used to compare levels of various proteins. SN-50, a pharmacological inhibitor of NF-kB, was used to determine the importance of NF-kB in TNF-mediated apoptosis. Depletion of transcription factors (NF-kB subunits and CREB) and PKCe was achieved by small interference RNA (siRNA). Reverse transcriptase-polymerase chain reaction was used to measure the mRNA levels of Bcl2.

**Results:** MDA-MB-231 cells were resistant to TNF-induced apoptosis. Treatment of MDA-MB-231 cells with SN-50 resulted in TNF-induced cell death although there was no change in Bcl-2 levels. Knockdown of NF-kB subunits, p65 or p52 also did not decrease the levels of Bcl2. Knockdown of PKCe in MDA-MB-231 cells decreased. phosphorylation/activation of CREB and Bcl-2 level. Depletion of CREB in MDA-MB-231 cells decreased Bcl-2 at the protein and RNA levels.

Conclusions: These results suggest that PKCe upregulates Bcl-2 by activating CREB to attenuate breast cancer cell death. [This work was supported by the grant CA071727 from NIH/NCI (A.B.) and Predoctoral Traineeship Award BC083099 from DOD BCRP (S.K.)]

Sponsor: [This work was supported by the grant CA071727 from NIH/NCI (A.B.) and Predoctoral Traineeship Award

# 211 (Poster)

First Author/Presenter: Dilip Jain

#### Classification: GSBS Student

Dilip Jain-UNTHSC- Fort Worth, TX-76107 Wolfram Siede-UNTHSC- Fort Worth, TX-76107 Roeul Roque- University of Nevada, Las Vegas, Nevada

### POTENTIATION OF CISPLATIN THERAPY FOR OVARIAN CANCER

Purpose: We suggest that the easy-to-synthesize NSC109268 compound can be valuable as an adjuvant to Cisplatin chemotherapy. Most importantly, Cisplatin sensitivity of resistant cell lines may be greatly enhanced. The usefulness of Cisplatin may be extended to other types of cancer, where it has showed little effect previously.

Methods: Survival analysis over the wild type yeast S. Cerevisiae BY4741 and the human ovarian cancer cell lines, 2008 and 2008/C13, which are Cisplatin-sensitive and Cisplatin-resistant ovarian cancer cell lines respectively was used. Survival analysis over deletion mutants in yeast, each knocked out for a single non-essential gene of yeast, for mutants resistant or sensitive to Cisplatin/NSC109268 and the combination of Cisplatin and NSC109268 was also used. This genetic study will help identify the target of NSC109268, that causes the sensitization of cells to Cisplatin, as seen with the preliminary data procured.

Results: When Cisplatin and NSC109268 were both applied simultaneously on the ovarian cancer cell lines, 2008 and 2008/C13, and the wild type yeast BY4741, the sensitization effect of killing was found to be synergistic instead of mere additive. Since the sensitization effect of NSC109268 was not seen in the rad5 deleted background and rad10 deleted background, RAD5 and RAD10, genes that encode for proteins in the translesion replication and nucleotide excision repair pathways respectively, could be potential targets of NSC109268. These results need to be further verified by biochemical and other studies. Furthermore, the combination of NSC109268 and Cisplatin synergizes in effecting cell killing over the rad51 deletion mutant in yeast, S. Cerevisiae . Interestingly, this mutant shares characteristics of cancer cells.

Conclusions: The initial effects of NSC109268 exhibiting synergism with Cisplatin on the tumorigenic cell lines, addresses the potential of NSC109268 as a valuable adjuvant to Cisplatin, and this combination of Cisplatin and NSC109268, can result in a cost-effective way, to dramatically improve the efficacy of Cisplatin, in the treatment of ovarian cancer. Furthermore, ERCC1-negative tumours have a better Cisplatin response clinically, making RAD10, its homolog in yeast, a plausible target for NSC109268, to explain its effect of Cisplatin sensitization

# CANCER

### 212 (Poster)

First Author/Presenter: donald rozario

Classification: GSBS Student

D. Rozario and W. Siede, Graduate School of Biomedical Sciences, UNT Health Science Center, Fort Worth, Texas, 76107

### ROLE OF NOVEL PROTEIN TEL2 IN THE CELL CYCLE

Purpose: We hypothesize that Tel2 plays a vital role in the regulation of checkpoint responses by inhibiting checkpoint proteins such as Mec1 and Tel1 by interaction between superhelical folds of either protein. Furthermore such binding masks the interacting surfaces of these PIKK s. PIKK's such as ATM, ATR plays an important role in cellular responses to DNA damage while TOR is crucial to its nutritional response. Crosstalk may exist between various PIKKs and this may be mediated by Tel2. It has been shown that nutrient response versus DNA damage may be intricately linked via Tel2. Thus, a study was undertaken to find the mechanistic role of Tel2 of S. cerevisiae along with its interacting proteins.

Methods: Since Tel2 is an essential gene we used over expressed and repressed Tel2 strains. Using these strains we have tried to unmask certain Tel2 traits by carrying out survival tests under different kinds of stress. We have used random mutagenesis to build a library of mutants that will now be screened to find the important domains of Tel2 that are needed for interaction with PIKK's and possibly other functions. This would also unmask the domains of Tel2 which are required for viability which will help in determining the essential role of Tel2.

Results: Experimental results show that when Tel2 is over expressed, it prevents a filamentous phenotype under replicational stress, when the cells are grown on galactose. Further screening of strains carrying the mutant Tel2\* has shown that when treated with rapapmycin particular mutants show hypersensitivity. This is a very interesting finding and needs to confirmed by sequencing the mutant Tel2\* gene.

Conclusions: Primary studies suggest an role of Tel2 in suppressing a filamentous phenotype under specific conditions. It also is a possibility that Tel2 family of proteins link various PIKK-related cellular processes by interacting with PIKK family proteins. We do believe that Tel2 may act as an inhibitor of the TOR pathway. Tel2, thus an attractive protein, could help to shed light on the grey area linking nutritional response with DNA replication and DNA damage. This could potentially be a target for cancer therapy in the future.

Sponsor: N/A

### 213 (Poster)

First Author/Presenter: Soumya Krishnamurthy

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#### Classification: GSBS Student

Soumya Krishnamurthy+, Eswar Shankar\* and Alakananda Basu\* University of North Texas Health Science Center, Fort Worth, TX 76107 \*Institute of Cancer Research, Fort Worth, TX 76107 +The Cancer Research Foundation of North Texas, Arlington, TX 76010

### UNDERSTANDING THE REGULATION OF IKKEPSILON IN BREAST CANCER CELLS

Purpose: The novel breast cancer oncogene, the inhibitor of kappa B kinase epsilon (IKKe) was found to be overexpressed and amplified in various breast cancer cell lines and breast cancer patient samples. IKKe functions as a transforming kinase by activating nuclear factor-kappa B (NF?B). IKKe was initially discovered as a phorbol myristate acetate (PMA)-inducible kinase, although it has been observed that cytokines such as tumor necrosis factor alpha (TNFa) also induce IKKe. However, the signaling pathways leading to the activation of IKKe in breast cancer cells has not been clearly understood. Protein kinase C (PKC) is the receptor for tumor promoting phorbol esters, such as PMA. PKCe, a member of the novel category of PKC family, has been shown to function as an oncogene. Our laboratory has demonstrated that PKCe acts upstream of Akt, which is frequently deregulated in breast cancer. The objective of our study was to elucidate if PKCe could mediate the induction of IKKe.

Methods: IKKe level was compared in breast cancer cells that differ in the aggressiveness of the disease. PKCe was depleted from the metastatic breast cancer MDA-MB-231 cells, which overexpress PKCe, using small interfering RNA (siRNA). The protein levels of PKCe and IKKe were determined by Western blotting. The mRNA levels of IKKe were determined by reverse transcriptase polymerase chain reaction (RT-PCR) analysis.

Results: IKKe levels were elevated with increase in malignancy in breast cancer cell lines. Knockdown of PKCe attenuated TNFa-induced IKKe at both the protein and the mRNA levels.

Conclusions: These results demonstrate that an increase in IKKe level can contribute to the aggressiveness of breast cancer. Furthermore, PKCe regulates IKKe by acting upstream of IKKe. Thus, the oncogenic function of IKKe may be mediated via PKCe. [This work was supported by the grant CA071727 from NIH/NCI (A.B.) and Predoctoral Traineeship Award BC083099 from DOD BCRP (S.K.)]

Sponsor: Supported by the grant CA071727 from NIH/NCI (A.B.) and Predoctoral Traineeship Award (S.K.)

First Author/Presenter: Kirti Jain

Classification: GSBS Student

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### PKC-ETA SIGNALING IN BREAST CANCER

Purpose: Protein kinase C (PKC) eta is a novel PKC which is known to have oncogenic functions. Its role has been implicated in breast cancer; however the exact mechanisms are not understood. Delineating PKC-eta signaling in breast cancer necessitates the overexpression of this protein in non-malignant breast epithelial cell line e.g. MCF-10A. However usual gene delivery methods fail to overexpress a gene in MCF-10A cells. We have therefore used retroviral system to overexpress PKC-eta in these cells. Our overall aim is to dissect the molecular mechanisms responsible for oncogenic roles of PKC-eta in breast cancer.

Methods: Puromycin resistant retroviral vector, pBABE-puro, was used to clone PKC-eta. PKC-eta was PCR amplified from pcDNA3 vector. The reverse primer was designed to incorporate HinclI restriction site. The PCR products were digested using HinclI and EcoRI restriction enzymes. The digested fragments were gel purified and ligated into the pBABE-puro retroviral vector which was also digested by the same enzymes. The retroviral particle was produced by triple transfection of pBABE-puro PKC-eta, Peq Env and pEQ gag-pol into Hek 293t cells. The MCF-10A cells were infected with the retroviral particle containing pBABE-puro PKC-eta and expression was assayed using Western blotting. Puromycin was used to select PKC-eta overexpressing MCF-10A cells.

**Results:** The PKC-eta gene was successfully overexpressed in MCF-10A cells using retroviral infection. No cytotoxicity was observed in the infected cells. The PKC-eta overexpressing MCF-10A cells could be selected for stable infection using puromycin resistant gene. The level of PKC-eta in infected cells was at least 10 fold higher than the non-infected controls.

Conclusions: This work accomplished the overexpression of PKC-eta in MCF-10A cells by retroviral infection. This is the first report of overexpression of PKC-eta in non-malignant breast epithelial cells. Further characterization of this cell line would provide insight into the role of PKC-eta in breast carcinogenesis.

Sponsor: DOD-BCRP

# 215 (Poster)

First Author/Presenter: Subhamoy Dasgupta

Classification: GSBS Student

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### MEMBRANE BOUND PRENYLATED C170RF37 IS A CRITICAL REGULATOR OF CANCER CELL MIGRATION AND INVASION

**Purpose:** Our results showed that C17orf37 is predominantly a membrane bound protein. However, C17orf37 protein does not have membrane localization sequence. The purpose of this study is to understand the molecular signaling mechanism that regulates activation and translocation of C17orf37 to the cell membrane, and identify potential interactors of C17orf37 that mediate downstream signaling.

Methods: By using different prenylase enzyme inhibitors we show that C17orf37 is preferentially prenylated by geranylgerany transferase I (GGTase I) enzyme. By yeast-two hybrid, immuno precipitation and fluorescence life time imaging microscopy (FLIM) we show C17orf37 is a novel interactor of annexin A2 and this interaction is important for cancer cell migration and invasion.

Results: Overexpression of C17orf37 resulted in increased expression of MMP-9, uPA and VEGF through activation of Akt and NF-?B pathway, thus increasing migration and invasion of prostate cancer cells. Cellular localization studies using confocal and total internal reflection microscopy (TIRF) demonstrated predominant expression of C17orf37 protein in the membrane. Careful examination of C17orf37 protein sequence revealed a C-terminal prenylation motif CVIL. We hypothesized that C17orf37 acts as a membrane bound signaling molecule and facilitates migration and invasion of prostate cancer cells by NF-kB mediated downstream target genes. Using inhibitors of prenyl transferase enzymes we demonstrate that C17orf37 is preferentially geranylgeranyled by GGTase-1 enzyme and inhibition of the enzyme leads to reduced membrane localized C17orf37 protein in both breast and prostate tumor cells. By yeast two hybrid analysis we identified annexin A2 as a novel interactor of C17orf37 and by fluorescence life time imaging microscopy based FRET assay we found that these two molecules physically interact at the membrane region. Our studies show C17orf37-annexin A2 interaction is critical for tumor cell invasion and metastasis.

**Conclusions:** C17orf37 regulates the expression of proteolytic enzymes by activating NF-kB. At the membrane, C17orf37 either directly or through annexin A2 controls the Akt activity. In summary, membrane bound C17orf37 acts as a signaling molecule and regulates migration and invasion of prostate cancer cells.

Sponsor: CA109593 and MD 001633 from NIH to JKV and Predoctoral Training Award DOD-PCRP to S.D.

First Author/Presenter: Lokesh PG Dalasanur Nagaprashant Classification: GSBS Student

Lokesh P G Dalasanur Nagaprashantha (1); Sushma Yadav (1); Kevin A Schug (2); Sharad S Singhal (1); Laszlo Prokai (1); Sanjay Awasthi (1)-1-Department of Molecular biology and Immunology, The University of North Texas Health Science center, Fort worth, TX-76107 and 2-Department of Chemistry and Biochemistry, The University of Texas at Arlington, Arlington, TX-76019

# CHARACTERIZATION AND DETERMININATION OF THE ROLE OF TUMOR MARKERS MEDIATING DRUG RESISTANCE IN CANCER CELLS WITH ENHANCED EXPRESSION OF RLIP76.

Purpose: RLIP76 is a 76kDa modular membrane associated protein which is overexpressed in many types of the cancer cells and protects cells from radiation and xenobiotic toxicity. RLIP76 enhances the radiation and drug resistance of cancer cells. RLIP76 regulates the efflux of glutathione conjugates from the cells including glutathione conjugates of cancer drugs which leads to decreased therapeutic response to the conventional cancer drugs. The exposure of lung to common oncogenic insults like cigarette smoke makes it a novel model to study the role of chemical and radioactive carcinogens in transforming benign cells into cancerous cells. Studying the expression and function of molecules that mediate drug resistance in lung cancer cells with enhanced RLIP76 expression presents an aggressive and relevant tumor model which can also be tested upon to determine the therapeutic efficiency of targeting vital molecules in cancer cells.

Methods: H-358 NSCLC cells were cultured in RPMI medium with 10% fetal bovine serum. The RLIP76 antisense treated and untreated cancer cells were extracted and the left over medium was collected. The proteome of H-358 cancer cell lysate and the medium collected is currently being analyzed by Mass spectrometry. The human serum samples from cancer patients and healthy individuals will be investigated for specific secretory proteins mediating tumor aggressiveness and drug resistance following the approval and guidelines of IRB. The role of RLIP76 antisense treatment on the expression and function of markers of drug resistance will be determined by testing the expression and function of respective proteins in RLIP76 antisense treated and untreated H-358 cells.

Results: We anticipate a significant regulatory function of RLIP76 in the expression and function of vital molecules regulating the apoptosis and drug resistance in cancer cells.

Conclusions: Determining the markers of drug resistance in tumors with elevated expression of RLIP76 will yield precious therapeutic targets for formulating and developing effective therapeutic drugs for the treatment of cancer.

Sponsor: N/A

# 218 (Poster)

#### First Author/Presenter: Smrithi Rajendiran

#### Classification: GSBS Student

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### TRANSCRIPTIONAL REGULATION OF C170RF37 IN PROSTATE CANCER CELLS

Purpose: Our aim is to identify potential deregulated mechanisms for the differential expression of C17orf37. Patients suffering from prostate cancer have high levels of interleukin 4 (IL-4) and IL-13. These cytokines bind to their receptors IL-4R and IL-13R, thereby up-regulating a number of downstream genes that aid in tumor cell proliferation, invasion and migration. We hypothesize that C17orf37 is a downstream target of IL-4/IL-13 mediated signaling. In addition to this transcriptional up-regulation, in silico analysis predicts C17orf37 to be a direct target of many micro RNAs (miRNAs), a class of endogenous non-coding 22-nucleotide long RNAs, that are down-regulated in cancer.

Methods: To identify the role that IL-4 and IL-13 play, PC3 and DU145 prostate cancer cells were treated with varying concentrations of IL-4 and IL-13, either alone or in combination. Total RNA was isolated from the treated cells and quantitative real time PCR (qPCR) was performed to assess the expression of C17orf37 using GAPDH as control. Similarly, we isolated the protein and western immunoblot analysis was performed to detect the C17orf37 expression. To verify if miRNAs regulate the expression of C17orf37, we down regulated the expression of Drosha, the nuclear ribonuclease III enzyme responsible for the maturation of endogenous miRNAs. The levels of Drosha and C17orf37 were estimated by qPCR after the total RNA was isolated from the cells.

Results: Our results indicate that IL-4 and IL-13 treatment significantly increase C17orf37 mRNA expression in PC3 cells. The combinatorial treatment at 100ng/ml concentration results in a 50-fold increase of C17orf37 mRNA in comparison to untreated cells. We have also identified a set of miRNAs that may target C17orf37.

Conclusions: These preliminary studies indicate that C17orf37 expression is regulated by IL-4 and IL-13 in prostate cancer cells.

Sponsor: Supported grants from the National Institutes of Health CA109593 and MD001633 to JKV

### First Author/Presenter: Savitha Sridharan

Classification: GSBS Student

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### ROLE OF P70S6 KINASE IN APOPTOSIS AND AUTOPHAGY

Purpose: Autophagy or self-eating is a process by which a cell recycles its own components to survive under stressful or nutrient-deprived conditions. This process has been considered as a protective mechanism against cancer initiation but its role in cancer progression is ambiguous. Autophagy is inhibited under nutrient-rich conditions by the mammalian target of rapamycin (mTOR) downstream to which is the 70 kDa ribosomal S6 kinase (p70S6K). p70S6K plays important roles in protein translation, cell cycle progression and cell migration. An upregulation of p70S6K has been found in several types of cancers. Constitutively active p70S6K was associated with intrinsic resistance to cisplatin in cancer cells. Our laboratory recently showed that p70S6K is a novel substrate for caspase-3 and that its proteolytic cleavage was important for cisplatin-induced apoptosis. The purpose of this study is to investigate the role of p70S6K in apoptosis and autophagy.

Methods: To determine if prevention of caspase-3 mediated cleavage of p70S6K induces autophagy, we transfected tumor cells with an empty vector or a vector containing wild-type or mutant p70S6K in which the caspase-3 cleavage site was mutated by site-directed mutagenesis. Cells were treated with apoptotic stimuli, such as cisplatin and autophagy was monitored by the conversion of myosin-associated protein1-light chain 3B (LC3)-I to LC3-II. The levels of various proteins, including p70S6K and LC3 were determined by Western blotting.

Results: Preliminary results indicate that the prevention of p70S6K cleavage by caspase-3 in cisplatin treated cells causes an increase in LC3-II levels.

Conclusions: The induction of autophagy may be a protective mechanism and a form of resistance against chemotherapeutic agents in cancer cells.

Sponsor: N/A

# 220 (Poster)

### First Author/Presenter: Praveenkumar Shetty

Classification: Postdoctoral Fellow

Praveenkumar Shetty and Jamboor K Vishwanatha Department of Molecular Biology & Immunology, Institute for Cancer Research, University of North Texas Health Science Center at Fort Worth, TX. 76107.

### ANNEXIN A2 AS A BIOMARKER AND POTENTIAL THERAPEUTIC TARGET FOR TRIPLE NEGATIVE BREAST CANCER

Purpose: The purpose of this study is to establish Annexin A2, a known calcium-dependent phospholipid binding protein as a biomarker in TNBC and to delineate the mechanism of cancer recurrence after Herceptin therapy in breast cancer patients.

Methods: Annexin A2 and ErbB2 expression in 12 different breast cancer cell lines were analyzed by Western, qPCR and Immunohistochemistry. Dharmacon smart pool siRNA was used to knockdown Annexin A2 and HER2 in different cell lines and the expression of respective proteins and downstream signaling molecules was studied by Western analysis. AccuMax tissue micro-array was used to study the expression of these proteins in different breast cancer cases.

Results: : In this study, we show that Annexin A2 is over expressed in different TNBC cell lines, where there is a basal or very low level of HER2 expression or vice-versa. Here we demonstrate for the first time that blocking HER2 expression in SK-BR-3 cells, lead to increased levels of Annexin A2. In addition, we found that inhibition of both Annexin A2 and HER2 in cells over expressing HER2 blocked all the downstream signaling mechanism that helps in cancer cell growth. Conversly, in TNBC cell lines that lack HER2 expression, we could successfully block the metastatic function of cancer cells (AKT downstream signaling) by down regulating only Annexin A2. Although the Annexin A2 is not a secretory protein, we noticed that large amounts of Annexin A2 is secreted from these cancer cells. This unique property could help us in developing tools using Annexin A2 as a marker to identify TNBC cases.

**Conclusions:** This current observation addresses the concern about the low response of TNBC to Herceptin therapy in treatment of basal carcinoma and the recurrence of cancer after HER2 blocking. This particular study, HER2/Annexin A2 cross talk opens up a new horizon in this area and we are in the process of establishing Annexin A2 involved therapeutic intervention of TNBC.

Sponsor: P20MD001633 from the National Center On Minority Health And Health Disparities (JKV).

#### First Author/Presenter: Linda Mooberry

Classification: GSBS Student

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### TARGETED NANOPARTICLES FOR ANTICANCER DRUG DELIVERY

Purpose: The purpose of these studies was to determine if anticancer drugs, encapsulated into reconstituted high density lipoprotein (rHDL) are taken up through an HDL receptor-mediated mechanism.

Methods: [3-H]-paclitaxel or [3-H]-cholesteryl ester was used to form rHDL particles and incubated with parental and SR-BI (HDL receptor) transfected IdI A7 cells. The uptake of the drug was measured in the radiolabeled cell lysate. Double-labeled particles were prepared using 14C-paclitaxel and [I-125]-labeled Apo A-1. The double-labeled rHDL/Ptx preparations were incubated with prostate cancer cells (PC-3), to determine the extent of the drug uptake via a selective uptake mechanism. In addition, uptake was also determined in the presence of a 10-fold excess of Apo A-1, discoidal Apo A-1/Phosphatidyl choline and native HDL derived from plasma.

Results: When cholesteryl ester and paclitaxel uptake from rHDL was measured in SR-BI transfected cells, the uptake was 3-fold compared to parental control cells. When paclitaxel uptake was measured in PC-3 prostate cancer cells, 82% of the paclitaxel was delivered selectively compared to 18% by internalization. When the uptake was measured in the presence of a 10-fold excess of HDL derived from plasma, the paclitaxel uptake was decreased to 30% of control.

Conclusions: Uptake in the IdI A7 cell line was dependent on SR-BI expression. Prostate cancer cells take up paclitaxel from rHDL/Ptx in a mechanism similar to that of the HDL receptor, which can be blocked by native plasma HDL. Anticancer drugs, such as paclitaxel show potential for specific receptor targeting to cancer cells.

Sponsor: N/A

### 222 (Poster)

First Author/Presenter: Adrienne Badeaux

Classification: GSBS Student

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#### THE MEMBRANE ANDROGEN RECEPTOR AS A THERAPEUTIC TARGET FOR BRAIN CANCER

Purpose: To determine if activation of the mAR, using a pharmacological tool, increases the amount of cell death induced by TMZ.

Methods: Cell culture: Two cell lines have been chosen for our experiments. They are the A172 cells (a model of GBM) and the C6 cells (a model of glioma, consisting of astrocytes and oligodendrocytes). A172 cells and C6 cellswill be grown and maintained in DMEM media (ATCC) with 10% FBS; 24hrs prior to experiments media will be changed to DMEM media with 10% charcoal stripped FBS. Assessment of cell viability: Caspase 3/7 assay. The Apo-One Homogenous Caspase-3/7 assay will be used according to the manufacturer s specification (Promega). In essence, cells will be plated in 96 well plates at 30,000 cells/well the day prior to the experiment. Cells will then be treated for 6hrs with the proper compounds after which 100µl of the Apo-One Caspase-3/7 reagent will be added to each well. The plate will then be put on a plate shaker for 30 minutes and incubated at room temperature for 1- 2hrs. Following the incubation the active caspase 3/7 levels will be determined by measuring fluorescence at the 485 nm excitation and 530 nm emission wavelengths in a plate reader. Statistical Analysis Caspase 3/7 level fluorescence values will be obtained and averaged from triplicate samples to produce a single n. The experiment will then be replicated to give a sample size of 3. The data will then be analyzed using an ANOVA followed by post hoc analysis to determine differences between groups.

Results: To date, the experiments conducted have been to validate the experimental models. To this end we show data that confirms the ability of TMZ to induce cell death, in a concentration and time-dependent manner, in both experimental models.

Conclusions: The data support the use of these cell lines in testing our hypothesis that activation of the mAR will promote the cell death elicited by TMZ. Specifically, we expect the concentration response curve for TMZ-induced cell death to be shifted to the left, indicating an enhanced sensitivity to the chemotherapeutic. Funding support: The National Institution of Aging (AG022550, AG023330, AG027956), and The Alzheimer s Association (IIRG) awarded to MS, and a grant from the Center for Disease Control (MiHERO).

#### First Author/Presenter: Cody Scott Cruz

#### Classification: SPH Student

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# FACTORS ASSOCIATED WITH ADHERENCE TO FOLLOW-UP PROGRAMS IN CHILDHOOD CANCER SURVIVORS AT UT MD ANDERSON CANCER CENTER

Purpose: Today in children and adolescents with cancer, approximately 80% will survive 5 or more years and essentially be cured of the disease. (NCI-SEER 2005) There are very serious and high morbidity- and mortality-related chronic health problems that occur in latent form (7-24yrs after treatment). (Wallace et al, 2004) Latent late effects include, the association of chemotherapy and radiation therapy with the development of Cardiovascular disease, and the development of secondary malignant neoplasms as a result of radiation therapy. A substantial barrier to late effects clinics has become the attrition of childhood cancer survivors to a regimented follow-up program. This pilot study investigates the association of a number of variables that may be identified as factors to non-adherence of follow-up at UT MD Anderson Cancer Center-Children s Cancer Hospital.

Methods: A retrospective cohort study was selected and patients at UT MD Anderson, diagnosed with childhood cancer between 1996-2000, were identified (Cohort=600). Medical records were reviewed and the demographic, clinical and socio-economic data were collected on all childhood cancer survivors. These variables were collected as of Nov. 2008 and were used in the comparison. From the original cohort only those who were alive and successfully off cancer treatment were used in analysis (n=444). Some variables of interest used as comparison to test include ethnicity, disease diagnosis, and health insurance status.

Results: Within the cohort of the original 600 patients identified, 156 patients were not eligible to be analyzed (134 (22.33%) were deceased, and 22 (3.67%) were still on treatment/relapsed). Analysis found that childhood cancer survivors who contained health insurance were 2.21 times as likely (95% CI,1.71-2.85) to adhere to a follow-up regimen as those cancer patients who did not. Adherence was not shown to be associated with ethnicity(95% CI,.88-1.07).

**Conclusions:** The availability of health insurance is shown to be significant in childhood cancer survivors coming to follow-up after cancer treatment. Follow-up care for the surveillance of late effects of cancer treatment is important to catch the development of the associated chronic diseases in their earliest stages. Possible bias could surface as a result of the inability to find certain demographic information on childhood cancer survivors due to this info not being available in the patient s medical records.

Sponsor: N/A

# 224 (Poster)

First Author/Presenter: Archana Archana

Classification: GSBS Student

Archana, Yadav S, Singhal S, Awasthi Sanjay

ROLE OF SINGLE NUCEOTIDE POLYMORPHISM ACROSS RLIP76 GENE IN DRUG RESISTANCE

Purpose: The purpose of this study is to identify Single Nucleotide Polymorphism across RLIP76 gene associated with drug resistance.

Methods: There are three nonsynonymous SNPs already known in RLIP76.We constructed the mutants of RLIP76 (Lys [K] 149 ? Glu [E] 149 and Arg [R] 208 ?Gln [Q] 208) by incorporating the known SNPs. Purified proteins (wild type as well as mutant RIP76) from transformed E. coli were reconstituted into artificial liposomes and their transport properties for doxorubicin and DNP-SG was measured.

Results: Mutant Lys [K] 149 ? Glu [E] 149 shows 30% less activity than the wild type RLIP76 for both doxorubicin and DNP-SG while there is no significant change in the activity of mutant, Arg [R] 208 ?Gln [Q] 208.

Conclusions: Single nucleotide polymorphism in RIP76 affects its transportation activity and may be associated with drug resistance.
## 300 (Poster)

## First Author/Presenter: Nicole Beltran

Classification: Staff

Anna Espinoza, MD\*; Nicole Beltran, BA\*; Lorna Brooks\*; Roberto Cardarelli, DO, MPH\*; Kimberly Fulda, DrPH\*; Joan Carroll, PhD~;\*Primary Care Research Institute; \*Department of Family Medicine; ~Department of Integrative Physiology University of North Texas Health Science Center, Fort Worth, TX 76107

THE ASSOCIATION OF BINGE DRINKING AND CORONARY ARTERY CALCIFICATION BY RACE/ETHNICITY-THE NORTH TEXAS HEALTHY HEART STUDY

Purpose: The purpose of this analysis is to assess the association of binge drinking and coronary artery calcification (CAC) by race/ethnicity.

Methods: Participants were recruited from the North Texas Primary Care Practice-Based Research Network (NorTex), from April 2006 to May 2008, for the North Texas Healthy Heart (NTHH) Study. NTHH is a cross-sectional study involving non-Hispanic whites, non-Hispanic African Americans, and Hispanics. Participants were screened for eligibility: 45 years and above and no prior or current history of heart disease. Participants had a one-hour face-to-face interview. Body measurements, lab analyses, and multi-slice computed tomography of the heart and abdomen were taken. Race/Ethnicity and binge drinking were self-reported. Binge drinking was ascertained from the question, How often do you have four or more drinks on one occasion? Responses were dichotomized to No or Any. Multiple logistic regression was performed for each race/ethnicity, odds ratios (OR), and 95% confidence intervals (CI) are presented. CAC was categorized as 0 or > 0. Regression analyses controlled for known risk factors for CAC: age, gender, education, smoking, BMI, hypertension, diabetes, hyperlipidemia, and family history.

Results: Of the 571 participants, 146 (26%) were White, 205 (36%) were African American, and 210 (37%) were Hispanic. 350 (62%) were female, 164 (30%) responded Yes to binge drinking, and 186 (37%) had a CAC > 0. After controlling for known risk factors the association between binge drinking with CAC was not statistically significant [OR=0.99; 95% CI (0.58, 1.67)] with all race/ethnicities combined and individually; Whites, [OR=2.17; 95% CI(0.84, 5.60)] Hispanics, [OR=0.81; 95% CI(0.31, 2.16)] and African Americans [OR=0.37; 95% CI(0.14, 1.02)].

Conclusions: The association between binge drinking and CAC was not statistically significant among all racial/ethnic groups. However, among African Americans, the association between CAC and binge drinking approached significance in a protective manner with those who binge drink being 63% less likely to have a CAC greater than 0. This association should be further explored with a larger sample size.

Sponsor: National Center of Minority Health and Health Disparities

## 302 (Poster)

### First Author/Presenter: Eric Johnson

### Classification: TCOM DO Student

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# DOES INTERMITTENT HYPOXIC CONDITIONING CONFER PROTECTION AGAINST ISCHEMIA-REPERFUSION INJURY IN SWINE MYOCARDIUM?

Purpose: Intermittent hypoxic conditioning (IHC) produces potent protection against myocardial ischemia-reperfusion injury in dogs and rats1. This investigation sought to determine the effect of IHC in a large species with a coronary microcirculation more similar to humans.

Methods: Eight Yorkshire pigs of either sex were studied, four of which underwent IHC. For twenty consecutive days, pigs undergoing IHC were placed in a normobaric chamber in which the fraction of inspired oxygen was decreased to 9.5-10% by introduction of N2. This conditioning progressively increased from 5 min to 10 min during 5 to 8 daily cycles of hypoxia with intervening 4 min periods of normoxia for a total of 20 sessions. The pigs showed no discomfort during IHC. In an acute experiment one day following IHC completion, the left anterior descending coronary artery (LAD) was occluded for 60 min and then reperfused for 3 hr. Hemodynamic variables and lead II ECG were monitored throughout the experiment; arrhythmias were assessed by applying a standard scoring system. After reperfusion, the LAD was reoccluded, and dye was infused into the remainder of the coronary circulation to demarcate the area at risk of infarction (AAR) due to LAD ligation. The AAR was then stained with 2,3,5-triphenyl tetrazolium chloride to identify infarcted myocardium.

Results: While too few animals completed the protocol to generate statistically significant data, trends have begun to emerge. All control pigs (n=4) had ventricular tachycardia (VT) and/or ventricular fibrillation (VF); two of these animals could not be defibrillated. Only two pigs in the IHC group suffered VT or VF. Arrhythmia score for control pigs was 4.5±0.5 (SE) versus 2.7±0.8 for IHC pigs (p=0.13). Infarct size (IS) as a function of the AAR (IS/AAR) tended to be less in pigs that had undergone IHC (n=3) compared to control pigs (n=2). IS/AAR for control pigs was 57.3±7.3% compared to 29.3±15.5% for IHC pigs (p=0.27). As expected, mean arterial pressure (MAP) dropped significantly after LAD occlusion in both groups. MAP in control pigs decreased 21.7±4.1 mmHg compared to 18.7±3.4 mmHg in IHC pigs (p=0.59). However, during reperfusion, MAP of control pigs increased 0.9 ± 0.4 mmHg, whereas MAP of IHC pigs fell by 4.2±1.8 mmHg (p=0.12).

Conclusions: These preliminary data suggest that IHC protects swine from life threatening cardiac arrhythmias and infarction during ischemiareperfusion. This intriguing possibility merits further research.

## 303 (Poster)

First Author/Presenter: Dinesh Jasti

Classification: GSBS Student

Dinesh Jasti, Jasenka Zubcevic and Jeffrey T. Potts, Dept. of Integrative Physiology, University of North Texas Health Science Center, Fortworth, TX - 76107.

ROLE OF GLIAL CELL METABOLISM IN NUCLEUS TRACTUS SOLITARII (NTS) IN REGULATION OF ARTERIAL BAROREFLEX FUNCTION IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR)

Purpose: Nucleus Tractus Solitarii (NTS) is a major integrative centre for cardiorespiratory homeostatic reflex pathways. Immunohistochemical staining for the glial cell marker, glial fibrillary acidic protein (GFAP), demonstrated that glial cells were strongly activated in the NTS of the spontaneously hypertensive rat (SHR) compared to its normotensive control, the Wistar-Kyoto (WKY) rat. Since glial cells are a major source of angiotensin II (Ang II) synthesis by the brain, we are currently testing the novel hypothesis that glial cells modulate arterial baroreceptor signaling in the NTS via ANG II-dependent mechanisms.

Methods: In our preliminary experiments we blocked the glial cell metabolism acutely by microinjection of fluorocitrate (FC, 40ng in 50nl) into the NTS 24 to 48 hrs prior to characterizing arterial baroreflex control of heart rate (HR) in juvenile WKY and SHR using the in situ, arterially-perfused preparation.

Results: We found that pretreatment with FC significantly improved arterial baroreflex function in the SHR (HR barogain: -1.29 vs. -2.82 bpm/mmHg, control vs. FC-treated). In contrast, FC had little effect on arterial baroreflex function in WKY (HR barogain: -3.74 vs. -3.61 bpm/mmHg, control vs. FC-treated).

Conclusions: This data supports our hypothesis that activated glial cells in the NTS contribute to baroreceptor reflex gain dampening in the SHR. This may be by increased synthesis and release of angiotensinogen, an Ang II precursor, from the activated glial cells. We are currently investigating the contribution of glial cells to the overall Ang II level using ELISA for angiotensinogen following FC pretreatment in the NTS of SHR and WKY.

Sponsor: N/A

## 304 (Poster)

## First Author/Presenter: Eugenia Manukhina

### **Classification:** Faculty

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### METABOLIC SYNDROME IMPAIRS NITRIC OXIDE STORAGE IN CORONARY VESSELS

Purpose: Nitric oxide (NO) in vivo forms complexes (NO stores) for transport and intracellular storage of NO. A key function of NO stores is defense against NO toxicity during NO overproduction. Metabolic syndrome (MS) is associated with NO overproduction, which is detrimental for endothelium function.

Methods: NO storage was evaluated in coronary vessels of 4 dogs with MS induced by a high fat diet and in coronary vessels of 4 control dogs. NO stores were indexed by relaxation of isolated left circumflex artery (LCA) rings, precontracted with a thromboxane A2 mimetic, U46619 (625 nmol/L), to N-acetylcysteine (NAC, 10-3 M). To estimate capacity of NO stores, LCA was incubated with a NO donor, dinitrosyl iron complex (10-5 M) for 20 min. After washout, LCA was precontracted with U46619, and NAC was added to release NO from the accumulated NO stores.

**Results:** NAC-induced relaxation of LCA from dogs with MS was larger than in control ( $11.1\pm1.6$  vs  $3.1\pm1.4$ %, respectively, P<0.01). This is consistent with NO overproduction in MS. After NO loading, relaxation of LCA from control dogs was significantly greater than that of LCA from dogs with MS ( $62.4\pm7.3$  vs.  $33.9\pm5.9$ %, respectively, P<0.03). This is consistent with reduced NO storage in MS vessels.

Conclusions: In conclusion, these findings are consistent with NO overproduction in MS, and with depressed ability of MS coronary vessels to bind excessive NO into NO stores. Thus, an intrinsic defense of coronary vessels against NO toxicity is impaired in MS.

Sponsor: Cardiovascular Research Institute

## CARDIOVASCULAR

## 305 (Poster)

#### First Author/Presenter: Ana Wilson

### Classification: Dual Degree Student: DO/PhD

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EFFECTS OF TESTOSTERONE ON OBESITY-RELATED CARDIAC HYPERTROPHY AND FIBROSIS

Purpose: Both testosterone and obesity are known to increase renin-angiotensin system activity, leading to cardiovascular dysfunction. This study determined whether testosterone potentiated the effects of obesity on renin-angiotensin system activity to worsen left ventricular hypertrophy and cardiac fibrosis.

Methods: Male New Zealand White rabbits were fed either a maintenance diet or 10% added fat diet; diet groups were further divided into control, castrated and losartan-treated groups. Multiple linear regression was used to determine independent or interactive effects of obesity, testosterone, and renin-angiotensin system on indices of cardiac hypertrophy and fibrosis.

Results: After 12 weeks, there was not an interaction between obesity and testosterone to potentiate plasma renin activity or aldosterone. Further, analyses revealed that obesity, testosterone, and renin-angiotensin system were all independently associated with increased ventricular weights and myocyte cross sectional area. Unexpectedly, neither obesity nor testosterone was associated with increased interstitial or perivascular cardiac collagen, while losartan treatment tended to independently increase interstitial collagen. However, obesity independently increased left ventricular matrix metalloproteinase-2 activity, while testosterone tended to decrease matrix metalloproteinase-2 activity. Tissue inhibitors of matrix metalloproteinases were not altered by obesity, testosterone, or renin-angiotensin system activity.

Conclusions: These data suggest that testosterone contributes to obesity-related left ventricular hypertrophy and tends to decrease degradation of collagen independent of the renin-angiotensin system.

Sponsor: American Heart Association

## 307 (Poster)

### First Author/Presenter: Christina Pacchia

Classification: GSBS Student

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## EFFECT OF VAGAL ACTIVATION ON VENTRICULAR RHYTHM IN ATRIAL FIBRILLATION

Purpose: The purpose of this study was to determine if sinusoidal fluctuations in vagal activity on the ventricular result in an entrainment of the ventricular rhythm in humans and a porcine model of atrial fibrillation.

Methods: : Forced vagal oscillations at two different frequencies were produced by employing deep breathing (0.125 Hz) and neck suction (0.25 Hz) in humans and pigs with AF. In the pig model, glycopyrrolate was administered to block peripheral muscarinic receptors, thus inhibiting vagal transmission to the heart. Vagal activity was evaluated using power spectral analysis of heart rate variability in order to determine the contribution of the vagus to ventricular irregularity in AF.

Results: In 2 of our human subjects, power spectral analysis showed no significant difference between oscillations in heart rhythm during neck suction (0.25Hz) and deep breathing (0.1 Hz) compared to baseline. In addition, the standard deviation of RR intervals was not significantly different with or without neck suction. In one subject, however, there was a significant increase in power during both neck suction and deep breathing increased power at 0.25 and 0.125 Hz respectively and vagal blockade abolished power in both frequencies.

Conclusions: In humans, neck suction (vagal activation via baroreflex) did not have a clear effect on RR interval in AF. We are unable to draw a definitive conclusion based on the data in humans because of the small number of subjects. However, data from the pig experiments suggest the vagus does, in part, mediate ventricular irregularity. The difference between the human and porcine models may be attributed to the fact that the humans had chronic AF whereas the pigs had acute AF. Chronic AF may produce changes in baroreflex function, i.e. no change in vagal tone with neck suction. In addition, there may be some level of parasympathetic neuropathy which makes the heart unresponsive to the vagus.

## 308 (Poster)

### First Author/Presenter: Gayathri Shankar

### Classification: SPH Student

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CHARACTERISTICS OF AGGRESSION AS PREDICTORS OF INFLAMMATION: THE NORTH TEXAS HEALTHY HEART STUDY

Purpose: The purpose of this study is to assess the contribution of each of the antagonistic attributes - physical aggression, verbal aggression, anger aggression, hostility aggression, and total aggression scores along with other psychosocial factors in elevating inflammatory biomarker levels: C-reactive protein (CRP) and Interleukin - 6 (IL 6).

Methods: Data for this study were obtained from The North Texas Healthy Heart Study (NTHHS). The participants for the NTHHS included 571 Caucasians, African Americans and Hispanics recruited from participating sites of the North Texas Primary Care Practice-Based Research Network (NorTex) and within Tarrant County. For this study, we excluded individuals with active infection, CRP levels greater than 10 mg/l and BMI greater than 60, cancer, diabetes and auto-immune problems. Our analyses included 260 subjects on whom CRP was measured and 243 subjects on whom IL-6 was measured. We ran 10 Multiple Regression models 5 for CRP and 5 for IL-6 - with demographic factors (age, gender, race, education, family history of CHD), lifestyle factors (smoking, drinking, regular exercise, BMI, TC:HDLc), and psychosocial factors (social support, perceived discrimination, depression, sense of control) with each of physical, verbal, anger, hostility and total aggression scores. Log transformed CRP and IL-6 were used for all the analyses. Analyses were performed using SPSS.

**Results:** A moderate association was observed between hostility aggression (p=0.073) and CRP. When an interaction term between hostility and depression was added into the hostility aggression model, a strong association was found both in hostility (p=0.011) and the interaction term (p=0.049), and a weak association in depression (p=0.096). Association between anger aggression and IL-6 (p=0.025) was significant and total aggression and IL-6 (p=0.055) trended towards significance. When the interaction term between anger aggression and sense of control was introduced into the anger aggression model, anger aggression (p=0.030) continued to be significant, as was the interaction term (p=0.049).

Conclusions: Increased CRP levels were associated with hostility aggression in combination with depression, whereas moderate CRP levels were associated with only hostility. Increased IL-6 levels were associated with anger aggression - alone and in combination with sense of control. Increased IL-6 levels were also associated with total aggression score.

Sponsor: The project was supported by the National Center on Minority Health and Health Disparities

## 309 (Poster)

First Author/Presenter: Vanessa Pickard

Classification: School of Health Professions MPAS Student

Vanessa Pickard, PA-S Kerbi Elsenbroek, PA-S Michael Clark, PhD, PA-C Olive Chen, PhD

### COMPARING CLASSES OF DRUGS USED TO TREAT STAGE I HYPERTENSION IN WOMEN OF DIFFERENT ETHNICITIES

Purpose: This systematic chart review was designed to compare the use of anti-hypertensive medications for treatment of Stage I hypertension in Caucasian, African American, and Hispanic women in an outpatient setting.

Methods: After gaining IRB approval, this study identified 504 outpatient charts from a multi-provider family practice site that were eligible for inclusion: female, ages 18-60, diagnosed with stage I hypertension according to JNC VII guidelines, and ethnicity. After using a random sampling method to identify 200 charts, 48 charts were unable to be located, possibly due to being in use at the time or misfiled. Of the remaining 152 charts, another 48 did not contain adequate information. Therefore, 104 charts were used for data analysis. Information was gathered on patient age, ethnicity, blood pressure at start of treatment, blood pressure approximately one year later, drug classes prescribed for the treatment of hypertension and co-morbidities from the charts. This data was analyzed using chi-squared tests and logistic regression.

**Results:** Among 104 reviewed charts 56% were Caucasian, 36% African American and 12% Hispanic. Overall, 64.4% of patients studied were treated to target blood pressure. Five medications were studied: beta blockers, diuretics, calcium channel blockers (CCB), angiotensin converting enzyme inhibitors, and angiotensin II receptor blockers (ARB). Results demonstrated that there was no significant relationship between ethnicity and total number of medication classes (x24=5.074, P=.280), as well as no significant relationship between ethnicity and class of medication (x210=8.318, P=.598).

Conclusions: The results reveal that the relationship between classes or quantities of medications used to treat women of different ethnicities was not significant. However, there were general trends observed from the data. For example, Hispanic women on 3 medications were treated to goal more often than those on 1 or 2 medications, while African American and Caucasian women were treated to goal most often if using 1 medication class. Caucasian women had better results if they were on a beta blocker. African American women were treated to goal most often on a beta blocker, a diuretic or a CCB. Hispanic women were best treated on a diuretic or an ARB. A prescriber can use this information when initializing a treatment plan for a female patient newly diagnosed with hypertension. Future studies should include a larger sample size with diverse clinic sites.

## CARDIOVASCULAR

## 310 (Poster)

### First Author/Presenter: Hunaid Gurji

Classification: Dual Degree Student: DO/PhD

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### PRYUVATE-FORTIFIED FLUID RESUSCITATION DURING HEMORRHAGIC SHOCK AND HINDLIMB ISCHEMIA

Purpose: Typical fluid resuscitation for hemorrhagic shock can elicit an intense inflammatory response and metabolic stress. Pyruvate, a natural metabolite, possesses anti-inflammatory and anti-oxidant properties. We are testing whether pyruvate-enhanced fluid resuscitation can mitigate systemic inflammation and its sequelae.

Methods: Anesthetized goats (20-30kg) were assigned to 3 groups. Shams (n=2) were surgically prepared, but were not hemorrhaged nor subjected to hindlimb ischemia-reperfusion. The other 2 groups underwent hemorrhage to reduce mean arterial pressure (MAP) to 50mmHg while a tourniquet and vasoclamp were applied to impose ischemia in the right hind limb. The control group (n=4) received lactate-enriched Ringer s solution iv, beginning 30 min after hemorrhage and ending 30 min after hindlimb reperfusion. The pyruvate group (n=4) received Ringer s fortified with pyruvate instead of lactate. Hemodynamics and ECG were monitored, and plasma pyruvate and lactate were measured by spectrophotometry. At 4 h hindlimb reperfusion, left ventricular (LV) myocardium and ischemic gastrocnemius (IG) were biopsied for measurements of lactate dehydrogenase (LDH) and glucose-6-phosphate dehydrogenase (G6PDH) activities.

Results: Pyruvate infusion achieved peak pyruvate concentrations of 3.03±0.83 mM, vs. 0.46±0.15 mM in controls (p<0.05) and 0.15±0.002 mM shams. During infusion, peak lactate was 5.4±1.4 mM in the pyruvate group vs. 10.4±1.6 mM in controls and 0.60±0.10 mM in shams. During infusion, systemic redox state (lactate/pyruvate ratio) was higher in the control group (30.32±4.47) vs. pyruvate (1.92±0.27; p<0.001) and sham (3.71±0.11; p<0.01). At 4 h reperfusion, systemic redox state remained high in controls (10.04±3.66) vs. pyruvate (3.04±0.76) and sham (3.94±0.60) groups. MAP decreased throughout the protocol in all groups, while pulse pressure - an indirect measure of vascular resistance - was steady in the pyruvate group (6.5% increase), but increased in controls and shams (84% and 76% respectively) during reperfusion. LDH and G6PDH activities in LV and IG were similar among the groups, as were ECG P wave dispersion and QTc duration.

Conclusions: We have developed a hemorrhagic shock model in the goat to test pyruvate-fortified resuscitative solution. Pyruvate-infusion minimized systemic vasoconstriction while normalizing the redox state. The latter effect could decrease availability of NADH to NAD(P)H oxidase, a major source of pro-inflammatory reactive oxygen species.

Sponsor: Department of Defense

## 311 (Poster)

First Author/Presenter: Sam Selby

Classification: TCOM DO Student

William Betz OMSII; Matthew Garcia OMSII; Sam Selby OMSI; UNTHSC-TCOM Fort Worth, TX 76107

## SUBCLAVIAN STEAL SYNDROME IN A 52 YEAR OLD MAN

Purpose: A 52-year-old male was evaluated at a primary care clinic regarding a 9-10 month history of numbness in his right shoulder and arm. He also reported having occasional leg pain when walking. Upon examination no palpable pulse in the patient s feet was discovered. Patient did have good capillary refill in both feet.

Methods: Blood pressure measurement revealed 185/96 in the right arm and 117/84 in the left arm. Vascular imaging revealed significant peripheral vascular disease and monophasic waveforms in the left subclavian artery with retrograde flow noted in the left vertebral artery. There was a 50 mm blood pressure difference noted in both arms, left side being lower. All of these findings are consistent with left subclavian steal syndrome.

Results: This man was evaluated for peripheral vascular disease upon diagnosis and referred to a cardiovascular surgeon for further evaluation for his symptomatic subclavian steal and his lower extremity claudication.

Conclusions: Peripheral vascular disease should be suspected and evaluated upon diagnosis of Subclavian Steal syndrome.

## 312 (Poster)

#### First Author/Presenter: Ashton Tassin

## Classification: SPH Student

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RACIAL/ETHNIC DIFFERENCES IN THE RELATIONSHIP BETWEEN CHRONIC DISEASE AND CARDIOVASCULAR INFLAMMATORY MARKERS: THE NORTH TEXAS HEALTHY HEART STUDY

Purpose: African-Americans and Hispanics suffer from a disproportionate amount of cardiovascular mortality despite the former having lower cholesterol than Caucasians. Major risk factors for cardiovascular disease include hypertension (HTN), diabetes milletus (DM), and hypercholesterolemia. The purpose of this study was to assess whether there are racial/ethnic disparities in the association between having one or more of these conditions and inflammatory processes associated with plaque instability. This study examined racial/ethnic distributions in the relationship between HTN, hypercholesterolemia, DM and inflammatory markers interleukin-6 (IL-6), fibrinogen, and cardiac sensitive C-reactive protein (hsCRP).

Methods: A total of 571 participants were recruited from NorTex member clinics from April 2006 to June 2008. Participants underwent body measurements and lab analyses. Race/ethnicity was self-reported. Serum levels of IL-6, hsCRP, and fibrinogen were measured. Participants with hsCRP levels greater than 10 or reporting active infection were excluded, resulting in a final sample of 429. The independent variable grouped by ethnicity was chronic disease state which consisted of a composite score, summing diagnoses of HTN, high cholesterol, and DM. Variables of interest include IL-6, CRP, and fibrinogen.

**Results:** Of the 429 participants, 112 were white (25.7%), 155 were African American (35.6%), and 162 were Hispanic (37.2%). Of these, 111 had none of the three chronic diseases (25.5%), 156 had one of the three (35.9%), and 166 had 2-3 diseases (38.2%). African-Americans showed the most pronounced trend in mean CRP levels with increasing number of diseases, while Caucasian and Hispanic mean levels declined slightly. With mean IL-6 levels, Caucasians showed an increasing trend with disease while the other groups did not. Fibrinogen activity showed a slight increasing trend with disease for African-Americans and Caucasians, but not for Hispanics (See Table 2).

**Conclusions:** This is the first study to examine the number of chronic diseases and inflammatory markers. Our results revealed some ethnic differences in cardiovascular markers with an increasing number of chronic diseases. This warrants further investigation. Future studies will need to examine to what extent these differences contribute to cardiovascular mortality so appropriate treatments and their intensification can be developed. (Grant Number P20MD001633 from the National Center on Minority Health Disparities)

Sponsor: National Center on Minority Health and Health Disparities

## 313 (Oral)

First Author/Presenter: Devin Flaherty

#### Classification: Dual Degree Student: DO/PhD

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# PYRUVATE-ENRICHED RINGER'S RESUSCITATION BOLSTERS CYTOPROTECTIVE DEFENSES IN REPERFUSED HINDLIMB IN THE SETTING OF HEMORRHAGIC SHOCK

Purpose: The purpose of this study is to test the hypothesis that resuscitation with Ringer s solution containing pyruvate, an antioxidant and antiinflammatory metabolite, may mitigate hindlimb ischemia-reperfusion injury in the setting of hemorrhagic shock.

Methods: Isoflurane-anesthetized male goats were hemorrhaged to lower mean arterial pressure (MAP) to c. 50 mmHg, then the right femoral artery and vein were occluded for 90 min. Lactate- (LR) or pyruvate-fortified Ringer s solution (PR) was infused iv (10 ml/min) from 30 min occlusion until 30 min after release of occlusion. At 4 h post-occlusion, gastrocnemius was biopsied for analyses of antioxidative enzymes (spectrophotometry) and pro- and anti-apoptotic proteins (actin-normalized immunoblot).

**Results:** [\*P < 0.05 vs. sham; P < 0.05 vs. LR]: At 4 h post-occlusion, MAP (mm Hg) was better maintained following PR (64 ± 6 ) than LR (44 ± 4). PR increased activities (mU/g) of antioxidant enzymes glutathione reductase (Sham 4.1 ± 0.2, LR 6.9 ± 0.7\*, PR 9.8 ± 1.0\* ) and glutathione peroxidase (Sham 11.3 ± 2.7, LR 14.0 ± 0.9, PR 17.4 ± 1.2\* ). PR also stabilized muscle contents of the antiapoptotic protein Bcl-XL (Sham 1.95 ± 0.02, LR 1.25 ± 0.12\*, PR 1.77 ± 0.15 ) and the ratio of uncleaved (i.e., inactive)/cleaved (i.e., pro-apoptotic) poly-ADP ribose polymerase (PARP) (Sham 3.53 ± 0.57, LR 2.27 ± 0.23\*, PR 3.90 ± 0.44 ).

**Conclusions:** Relative to conventional LR, resuscitation with PR more effectively stabilized MAP, and bolstered the post-ischemic hindlimb's antioxidant and anti-apoptotic phenotype. Resuscitation with pyruvate-enriched fluids may provide protection superior to conventional resuscitative solutions in the setting of hemorrhagic shock and hindlimb ischemia-reperfusion.

Sponsor: US Dept. of Defense

## 314 (Poster)

### First Author/Presenter: Kelly Sprawls

### Classification: Dual Degree Student: DO/MS

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### CHRONIC DISEASE STATUS, SLEEP QUALITY, AND TNF-ALPHA - UNDERSTANDING PATHOPHYSIOLOGIC PROCESSES

Purpose: As the prevalence of cardiovascular co-morbidities continues to rise within the United States, the quality of sleep continues to deteriorate. Recent evidence suggests inflammatory mediators, such as tumor necrosis factor-alpha (TNF-alpha), play a role in mediating this process. The goal of this study is to examine the association between: sleep quality and TNF-alpha; chronic disease and sleep quality; and whether chronic diseases modify the association between sleep quality and TNF-alpha.

Methods: This pilot study uses a cross-sectional design nested within a larger cohort study, The North Texas Healthy Heart (NTHH) Study. Sixty participants have been administered the Sleep Quality Questionnaire and undergone body measurements, lab analyses, and a multi-slice computed tomography of the heart. Simple linear regression analyses will be performed to evaluate the association between sleep quality and TNF-alpha, chronic disease status and sleep quality, and the number of chronic diseases and sleep quality. Multiple linear regression analyses (hypertension, dyslipidemia, coronary calcium score, diabetes mellitus, and metabolic syndrome) and sleep quality. Multiple linear regression analyses will also be used to explore whether chronic disease status, type and number modify the association between sleep quality and TNF-alpha.

Results: There are currently 60 participants; however an additional 20 are scheduled for February. To date, we have received TNF-alpha serum levels for 18 participants. The statistical analyses are pending until all the data are collected in February.

Conclusions: We expect our results to reveal an association between sleep quality and TNF-alpha. In addition, we anticipate our results will suggest that chronic diseases and sleep quality act synergistically to alter the serum level of the inflammatory mediator, TNF-alpha.

Sponsor: N/A

## 315 (Poster)

#### First Author/Presenter: Robert Mallet

#### Classification: Faculty

Robert T Mallet, Myoung-Gwi Ryou, Devin C Flaherty, Besim Hoxha, Jie Sun, Monica Bellard, Lisa M Hodge, Albert H Olivencia-Yurvati

### ANTI-INFLAMMATORY EFFECTS OF PYRUVATE-ENRICHED CARDIOPLEGIA IN PIGS UNDERGOING CARDIOPULMONARY BYPASS

Purpose: Reactive oxygen species produced during cardiopulmonary bypass (CPB) can elicit inflammation. Cardioplegia enriched with the intermediary metabolite pyruvate exerts antioxidant protection in myocardium of pigs subjected to CPB. The purpose of this study is to test the hypothesis that pyruvate-fortified cardioplegia mitigates myocardial inflammation by increasing anti-inflammatory cytokines, enhancing myocardial antioxidant defenses, and suppressing matrix metalloproteinase activity and neutrophil infiltration.

Methods: In situ swine hearts were arrested for 1 h with 4:1 blood:crystalloid cardioplegia, where the crystalloid component contained 188 mM glucose ± 24 mM pyruvate, then the hearts were reperfused and the pigs weaned from CPB. At 4 h post-CPB, left ventricular myocardium was sampled for immunoblot analyses of the acute inflammation marker C-reactive peptide (CRP), matrix metalloproteinase-3 (MMP3) and tissue inhibitor of metalloproteinase-2 (TIMP2), and to assess neutrophil infiltration by histology and myeloperoxidase activity.

Results: Myocardial CRP content increased over fivefold following CPB with control cardioplegia, but pyruvate cardioplegia prevented this increase. Circulating IL-10 temporarily increased during and immediately after CPB; pyruvate cardioplegia provoked more sustained and robust enhancement of this anti-inflammatory cytokine. CPB increased myocardial neutrophil infiltration and myeloperoxidase activity, but pyruvate-fortified cardioplegia prevented these effects.

Conclusions: Pyruvate-enriched cardioplegia suppresses CPB-induced inflammation, an effect potentially mediated by anti-inflammatory cytokines and TIMP-2. Thus, pyruvate-fortified cardioplegia provides anti-inflammatory protection superior to that afforded by conventional cardioplegia solutions.

Sponsor: Osteopathic Heritage Foundation

## **CELLULAR & MOLECULAR SCIENCE**

### 400 (Poster)

First Author/Presenter: Sarabeth Graham

Classification: GSBS Student

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REGULATION OF TRPC6 CHANNEL ACTIVITY BY HYDROGEN PEROXIDE

Purpose: Our hypothesis is that canonical transient receptor potential 6(TRPC6) is a redox-sensitive channel and therefore, a target for reactive oxygen species (ROS) in the regulation of cellular events

Methods: Human embryonic kidney (HEK) cells were cultured using standard tissue culture techniques. Conventional cell-attached and insideout excised patch clamp approaches were used to measure single-channel cationic currents. Cytosolic Ca2+ transients were examined using membrane-permeable fura-2 fluorescent ratiometry.

Results: We found that in TRPC6-overexpressed HEK293 cells, application of 100 uM 1-oleoyl-2-acetyl-sn-glycerol (OAG), a membrane permeable analogue of diacylglycerol and a known TRPC6 channel activator, significantly stimulated Ca2+ entry measured by fura-2 fluorescence. This response was not observed in untransfected or mock-transfected cells and was nearly abolished by 20 uM La3+, a TRPC channel blocker, suggesting a contribution of TRPC6 to the Ca2+ influx. In this heterologous TRPC6 expression system, we found that H2O2 stimulated Ca2+ entry in a dose-dependent manner and a 10 uM concentration of hydrogen peroxide (H2O2) induced nearly the maximal response. Importantly, H2O2 (10 uM) significantly enhanced the OAG-induced response, suggesting that ROS function not only as an activator, but also as a regulator that may sensitize the TRPC6 channel to physiological stimuli. In agreement with the Ca2+ imaging data, electrophysiological studies showed that H2O2 (10 uM) significantly increased channel open probability (NPO) and enhanced OAG-induced channel activation in TRPC6-overexpressed HEK293 cells.

Conclusions: TRPC6 is a redox-sensitive channel and H2O2 can regulate intracellular Ca2+ signaling by regulating TRPC6 channel activity.

Sponsor: American Diabetes Association

## 401 (Poster)

### First Author/Presenter: Marcus Hadley

Classification: GSBS Student

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## MECHANISMS OF UV-INDUCED DAMAGE IN RETINAL PIGMENTED EPITHELIAL (RPE) CELLS

Purpose: Studies in our laboratory as well as by others have shown that LPO products generated during oxidative stress can induce apoptosis in various cell types both via death receptor Fas- mediated as well as p53-mediated apoptotic signaling. However, the role of these signaling pathways in the mechanisms of UV-induced apoptosis in RPE cells is not clear. Present studies were designed to investigate the effect of UV radiation on the cultured RPE cells with respect to the cellular redox conditions, expression and functions of tumor suppressor protein p53

Methods: Chemicals: All chemicals unless otherwise mentioned were obtained from Sigma Aldrich Chemical Company Antibodies: ß-actin, Bax, p21, p53 antibodies were obtained from Santa Cruz Biotechnology Cell Culture: RPE (SV-40) cells were grown DMEM low glucose medium supplemented with 10% fetal bovine serum (FBS), 2 mM L-glutamine and 1% penicillin and streptomycin and maintained in a humidified incubator at 37°C with 95% air and 5% CO2. Irradiation: Irradiation of RPE cells was performed with energy 1J/cm2 (wavelength 254nm) control and for times including 2, 5, 10 and 20 minutes with and without antioxidant

Results: UV-C exposure at 1J/cm2 for 2-20min induces cell death in RPE cells. Exposure of RPE cell to UV exposure causes increase in lipid peroxidation. Pre-treatment of cells with 100µM hydralazine attenuates LPO. Exposure of RPE cells with UV-C radiation causes up-regulation of p53 and pro-apoptotic Bax proteins. Pre-treatment of RPE cells with 100µM hydralazine hydrochloride makes these cells resistant to UV induced cell death Pre-treatment of hydralazine to RPE cells alters the redox conditions in cells by changing GSH/GSSG ratios.

Conclusions: UV radiation resulted in the activation of p53 and its phosphorylation. Up-regulation and phosphorylation of p53 were found to be accompanied with the activation of pro-apoptotic protein Bax. Pretreatment of these cells with anti-oxidant chemical hydralazine caused attenuation of LPO levels with concomitant increase GSH/GSSG ratios resulting in resistance of these cells to UV-induced cell death. As it was observed, our studies also exhibited a decrease in intracellular peroxides and an increase in total GSH concentrations suggesting changes in cellular redox status upon treatment with antioxidant.

## **CELLULAR & MOLECULAR SCIENCE**

## 402 (Poster)

### First Author/Presenter: Priya Muthu

Classification: GSBS Student

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### STUDY OF CROSS BRIDGE KINETICS IN HYPERTROPHIC VENTRICULAR MUSCLE

Purpose: FHC is known to have an estimated prevalence of about 1 in 500. It is a heart disease characterized by ventricular hypertrophy and sudden cardiac death. In this study, we aim towards unraveling the molecular mechanism behind this disease. We look at one particular mutation, Asp166Val in regulatory light chain of myosin in the left ventricular heart muscle. We hypothesize that FHC might in part be caused by an inefficient utilization of ATP by cardiac muscle due to mutation-mediated alterations of the kinetics of myosin cross-bridges.

Methods: We examined whether the environment of an active cross-bridge in cardiac myofibrils from transgenic (Tg) mice is altered by the Asp166Val mutation in RLC. The cross-bridge environment was monitored by tracking the fluorescence lifetime (t) of Alexa 488-phalloidin labeled actin. In addition, using a sensitive EM CCD, we measured the fluorescence of actin protomer labeled with rhodamine phalloidin during isometric contraction.

Results: We observed that the lifetime was high when cross-bridges were bound to actin and low when they were dissociated from it. The duty ratio expressed as a fraction of time that cross-bridges spend attached to the thin filaments during isometric contraction was similar in Tg-WT and Tg- Asp166Val muscle. Since independent measurements showed a large decrease in the cross-bridge turnover rate in Tg-D166V muscle compared to Tg-WT, the fact that the duty cycle remains constant suggests that the Asp166Val mutation of RLC causes a decrease in the rate of cross-bridge attachment to actin. Also, it was seen that the rate of dissociation of force generating myosin cross-bridges (g) was significantly lower compared to Tg-WT and NTg control fibers.

Conclusions: Our data indicate that the Asp166Val mutation may exert its action through changes in the kinetics of myosin cross-bridges leading to an inefficient utilization of ATP by the mutated myocardium. The failure of the myocardium to maintain the energy levels necessary for contraction may ultimately lead to cardiac dysfunction and sudden cardiac death as observed in individuals carrying the Asp166Val mutation. This study will enable us to gain an insight into the disease pathology which could well result in improved risk assessment and ultimately to development of specific treatments. The results of our studies may, in the future, contribute to the development of targeted cellular therapeutic approaches to limit FHC related cardiac dysfunction.

Sponsor: N/A

## 403 (Poster)

First Author/Presenter: Shahzeb Niazi

Classification: TCOM DO Student

### Shahzeb Niazi Texas College of Osteopathic Medicine Fort Worth, TX, 76107

### PILOCARPINE INDUCED ACTIVATION OF MITOGEN-ACTIVATED PROTEIN KINASE IN SALIVARY CELLS

Purpose: Muscarinic receptors mediate parasympathetic nerve induced salivary gland fluid secretion. These receptors are G protein-coupled receptors (GPCR) and thought to mediate their responses by activating an intracellular calcium cascade. However, recent studies have indicted that GPCR may activate mitogen-activated protein kinase (MAPK) pathway, a cascade traditionally linked to the epidermal growth factor receptors (EGFR). Activation of EGFR may cause cell proliferation and differentiation. In this study, we studied the effect of muscarinic agonist on the MAPK pathway in a human salivary gland cell (HSY).

Methods: HSY cell line was cultured and treated with a muscarinic agonist (pilocarpine) for various times. The cells were then lysed and the proteins were separated using gel electrophoresis and transferred to a membrane, followed by Western blot analysis using antibodies against phosphorylated Extracellular Signal-Regulated Kinases 1/2(ERK1/2) that is an activated form of ERK1/2 (MAPKs). Western blot using antibody against total ERK1/2 was used for monitoring protein loading in each lane.

**Results:** Pilocarpine induced a time-dependent increase in ERK phosphorylation that peaked after ten minutes and gradually sustained at a lower level up to sixty minutes. The normalization of phosphorylated ERK1/2 by ERK1/2 in each lane showed that pilocarpine induced a  $10.5 \pm 2.2$  fold (n=6) increase in ERK1/2 activation at 10 minutes. When HSY cells were treated with an EGFR inhibitor, AG1478 (5x10-6M), for 30 min prior to addition of pilocarpine (10-4M) for 10 minutes, ERK1/2 were not activated (phosphorylated).

Conclusions: Our results indicated that pilocarpine induces activation of ERK1/2 in a time dependent manner, which may mediate through transactivation of the EGFR.

## **CELLULAR & MOLECULAR SCIENCE**

## 404 (Poster)

First Author/Presenter: Sujung Jun

Classification: GSBS Student

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### ALLELE-SPECIFIC EFFECTS ON EXTRACELLULAR SUPEROXIDE DISMUTASE SYNTHESIS AND SECRETION

Purpose: Extracellular superoxide dismutase (ecSOD) protects the extracellular space from oxidative stress. We previously reported a new allele for ecSOD, expressed in 129P3/J mice (sod3\*129), which differs from the wild-type (sod3\*WT), expressed in C57BL/6J and other strains. It is associated with increased level of enzyme in several tissues, and also with different localization in heparin accessible area in the tissues. However, the congenic mice expressing the sod3\*129 allele express only a fraction of the corresponding mRNA levels, when compared to mice with the sod3\*WT allele. These results suggest significant allele-specific differences in the regulation of ecSOD synthesis, intracellular processing and secretion, independent of the genomic context. Thus, we hypothesize that the primary structure of the ecSOD transcript has an effect on the rates of enzyme synthesis and/or secretion.

Methods: Stably transfected CHO cells (WT or 129 allele of ecSOD) were pulsed for 1 hour with met- and cys-free medium, supplemented with [35S]-met and -cys (5Q.Ci/ml) and chased with regular medium for up to 6 hours. In long-term labeling experiments cells were exposed to radiolabeled amino acids for up to 8 hours and cellular and medium ecSOD were immunoprecipitated in 30 min -1 hour intervals, and incorporation into cellular and medium ecSOD was determined. To be able to distinguish the relative translational efficiency of the transcripts of the two ecSOD alleles, we also employed the in vitro translation system using rabbit reticulocyte lysate and in vitro generated ecSOD mRNA of both alleles.

**Results:** Both synthetic as well as secretory rates of the products of the two distinct alleles are significantly different. The processing of ecSOD\*129 was appears to be faster than that of the wild-type enzyme.

Conclusions: The altered ecSOD sequence in sod3\*129 may be responsible for increased rate of processing and secretion of ecSOD\*129. This may most likely be the result of an amino acid substitution [N(-4)D] in the signal peptide sequence of the 129 allele. This observation may also be responsible for the higher steady-state levels of plasma ecSOD in the 129 strain or the congenic mice expressing this allele and their apparently increased resistance to select diseases.

Sponsor: RO1-HL70599

## 405 (Oral)

First Author/Presenter: Jerel Fields

### Classification: GSBS Student

Jerel A. Fields, Kathleen Borgmann, Anuja Ghorpade. University of North Texas Health Science Center Fort Worth, TX 76107

## MOLECULAR REGULATION OF ASTROCYTE-TIMP-1 EXPRESSION IN NEUROINFLAMMATION

Purpose: Many neurodegenerative disorders, including HIV associated dementia (HAD), are exacerbated by an imbalance between matrix metalloproteinases and their inhibitors, tissue inhibitors of metalloproteinases (TIMPs). Primary human astrocyte-TIMP-1 expression was initially increased in response to the inflammatory cytokine interleukin (IL)-1\$ but was down regulated during chronic stimulation. Regulation of the TIMP-1 promoter contributed to a decrease in astrocyte-TIMP-1 expression, and deletion of a CCAAT box in the TIMP-1 promoter restored expression levels during chronic activation. The purpose of this project is to test the hypothesis that astrocyte-TIMP-1 expression is regulated via a CCAAT element at -310 in the TIMP-1 promoter during neuroinflammation.

Methods: We investigated the role of CCAAT enhancer binding protein & (CEBPß) and CCAAT displacement protein (CDP) in astrocyte-TIMP-1 expression during chronic neuroinflammation. Primary human astrocytes were treated with II-13, for varying periods, to simulate neuroinflammation. siRNA was used to transiently knockdown suspected transcription factors, CCAAT displacement protein (CDP) and CCAAT enhancer binding protein (CEBPß). Quantitative real time polymerase chain reaction, western blot and TIMP-1 ELISA were used to measure gene expression levels.

Results: Treatment with IL-13 resulted in robust increases in CEBPß mRNA and to a lesser extent, increases in CDP mRNA levels. Transient knockdown of CDP, by siRNA, increased TIMP-1 mRNA levels at 72 and 168 hour time points and increased the level of TIMP-1 in supernatants of chronically activated astrocytes. Western blot analysis of nuclear extracts of IL-13 treated astrocytes revealed increases in CEBPß and CDP protein levels. Furthermore, the ratio of transcriptional silencer to activator isoforms of CEBPß increased in response to IL-13 treatment.

Conclusions: This work shows CDP and CEBPß may contribute to the intracellular signaling cascade leading to decreased astrocyte-TIMP-1 expression during chronic neuroinflammation.

Sponsor: Neurobiology of Aging Training Grant

First Author/Presenter: Liem Nguyen

Classification: McNair/SMART Participant

Liem Nguyen, Arti Sharma and James L. Caffrey Department of integrative physiology at University of North Texas Health Science Center

### NON-INVASIVE METHODS TO EVALUATE EARLY INDICATORS FOR DIABETES

Purpose: We hypothesize that changes in autonomic reflexes as measured by Valsalva sensitivity will be predictive indicators of metabolic syndrome and diabetes and will serve as early indicators of these conditions in those at higher risk within ethnic minority populations.

Methods: Total of 85 subjects from three different ethnic groups (Caucasian, Hispanic and African Americans). Each group was categorized into three sub-groups: control, diabetes, and metabolic syndrome (NCEP criteria). Each subject performed three Valsalva maneuvers. In the Valsalva maneuver subjects forcefully exhale from the diaphragm into a mouthpiece connected to a pressure transducer and maintain a constant pressure of 30mmHg for 10 seconds. Heart rate and blood pressure are recorded during Valsalva maneuver by a finger plethysmography (Finapress). Valsalva delay, ratio, and sensitivity measurements are analyzed by using computer software Windag.

Results: Valsalva sensitivity is depressed in MS and DM, and there was not a significant difference between MS and DM. Insulin sensitivity and Valsalva sensitivity are both greater in control than in MS and DM. This relationship appears to persist within the ethnic groups studied though additional subjects will be needed to verify that observation statistically. There also appears to be a positive correlation between the insulin sensitivity and Valsalva sensitivity.

Conclusions: Valsalva sensitivity may have potential value as an early indicator of changing autonomic reflexes and may help able to identify those at higher risk of diabetes including ethnic minorities.

Sponsor: N/A

## 501 (Poster)

### First Author/Presenter: Joan Carroll

### Classification: Faculty

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#### VISCERAL ADIPOSE TISSUE AND INSULIN RESISTANCE AFTER LAPAROSCOPY ADJUSTABLE BANDING SURGERY

**Purpose:** Visceral adipose tissue (VAT) is implicated as contributing to metabolic syndrome-related pathologies such as insulin resistance. Laparoscopic adjustable banding surgery (LGBS) is increasing recognized as reducing insulin resistance in obese patients. The purpose of this study was to examine the relationships between changes in insulin resistance and VAT after LGBS.

Methods: Patients (n=19) were tested prior to LGBS (T1), and 6 (T2) and 12 months (T3) after LGBS. Body weight and body mass index (BMI) were measured. Insulin resistance was estimated using the HOMA index and VAT was measured at the L4L5 spinal level using computed tomography. Data from the three testing periods were compared using repeated measures ANOVA. Patients were also compared to a normal weight control group (n=10) using t-tests. Data are presented as mean±SD.

Results: At T1, BMI values for patients and controls were  $41.8\pm4.8$  and  $22.2\pm1.8$  kg/m2 respectively (p=0.05). BMI was still significantly higher in patients at T3 ( $33.7\pm4.8$  vs  $23.1\pm21.8$  kg/m2, p=0.05). T1 HOMA values were  $3.67\pm2.80$  and  $0.78\pm0.39$ , respectively (p=0.05). HOMA values for patients at T2 and T3 were  $1.90\pm1.62$  and  $1.82\pm1.10$ , respectively. While HOMA values were significantly reduced at T2 and T3 compared with T1, HOMA values did not change significantly from T2 to T3. T3 HOMA values did not differ significantly between patients and controls ( $1.32\pm0.75$ ). As expected, L4L5 VAT at T1 was significantly higher in patients compared with controls ( $245\pm76$  and  $82\pm35$  cm2, respectively, p=0.05). L4L5 VAT in patients was reduced at T2 and T3 ( $177\pm58$  and  $151\pm52$  cm2, respectively, p=0.05) compared with T1. Although VAT at T3 was somewhat lower than at T2, the change was not significant. Combining data from all three time points, patients values of HOMA were more strongly related to L4L5 VAT (r=0.79, p=0.0001) than to body weight (r=0.37, p=0.004) or BMI (r=0.36p=0.006).

Conclusions: These data suggest that the most striking changes in body composition and insulin sensitivity occur within the first 6 months after LGBS. The data further suggest that improvements in insulin sensitivity are more strongly related to changes in VAT than to changes in other anthropometric measures.

### Sponsor: NIH H75/CCH224064

### First Author/Presenter: Eva Evans

#### Classification: SPH Student

Eva L. Evans, Rohit P. Ojha, Lori A. Fischbach, Department of Epidemiology, University of North Texas Health Science Center

NON-INVASIVE DIAGNOSTIC MODELS TO IDENTIFY UNDIAGNOSED DIABETICS AND FACTORS DIVERGENT FROM DIAGNOSED DIABETICS

Purpose: The substantial proportion of undiagnosed diabetics in the United States warrants the development of an effective non-invasive method for identifying such individuals. Therefore, we evaluated putative factors to develop diagnostic models that may identify undiagnosed diabetics and factors divergent from diagnosed diabetics.

Methods: We utilized self-reported data for adults age =20 years (n = 8,881) in the United States from combined (1999-2004) National Health and Nutrition Examination Surveys (NHANES). Undiagnosed diabetics were participants who reported that they had never been diagnosed with non-gestational diabetes by a healthcare professional, but had a fasting blood glucose (FBG) >126mg/dL upon laboratory examination. Diagnosed diabetics were participants who reported that they had been diagnosed with non-gestational diabetes by a healthcare professional. Factors associated with undiagnosed and diagnosed diabetics were identified using best subset selection in weighted logistic regression models. Discriminatory accuracy was assessed using the concordance (c) statistic for each model.

**Results:** Male gender, family history of diabetes, hypertension, BMI>25, ever smoker, age>40, single, and sedentary lifestyle were factors associated with undiagnosed diabetics. White race, male gender, family history of diabetes, hypertension, age>40, sedentary lifestyle, and physician examination within 1 year of the interview were factors associated with diagnosed diabetics. The discriminatory accuracies for the models were relatively comparable (Undiagnosed: c=0.78; Diagnosed: c=0.81).

**Conclusions:** Our model for undiagnosed diabetics has respectable discriminatory accuracy in our study population and may be a useful noninvasive screening tool in a variety of settings for simple and rapid identification of individuals who would benefit from confirmatory testing. Factors that distinguish undiagnosed and diagnosed diabetics may indicate strengths and weaknesses of the current diabetes detection paradigm.

Sponsor: N/A

### 503 (Poster)

First Author/Presenter: Susan Franks

#### Classification: Faculty

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EATING BEHAVIOR PATTERNS AND WEIGHT LOSS ONE YEAR AFTER LAPAROSCOPIC BANDING SURGERY

Purpose: Successful weight loss with laparoscopic banding surgery (LBS) depends largely on life-long behavioral changes. The possible reemergence of habitual eating patterns creates a risk for behavioral non-compliance. We previously reported differences in eating patterns between normal weight (NW) and LBS subjects (LB) prior to LBS (T1), and their normalization 6 months post-LBS. The purpose of this study was to examine the stability of these effects on eating behavior and weight loss one-year post-LBS (T2).

Methods: Subjects included 29 LB and 30 NW. All subjects completed the Eating Inventory to assess Cognitive Restraint (CR), Disinhibition (DI) and Hunger (HN) at T1. LB were retested at T2, and compared using repeated measures ANOVA. Percent excess weight loss (EWL) was calculated for LB based on pounds to achieve a BMI of 25.0. LB was split high (73.38±4.62%) and low (25.57±13.51%) EWL at T2. Point-biserial correlations were used to determine the relationships between EWL, EI scores at T1 and T2, and change in EI scores (T2-T1).

**Results:** Results indicated significant improvement in eating behaviors from T1 to T2 for CR ( $6.7\pm3.8$  vs.  $14.0\pm4.1$ , p=0.000), DI ( $10.7\pm3.6$  vs.  $6.2\pm2.8$ , p=0.000), and HN ( $8.2\pm3.7$  vs.  $3.3\pm1.8$ , p=0.000). T2 values for CR and DI were higher than NW ( $11.1\pm5.0$ , p=0.017 and  $4.0\pm3.0$ , p=0.005), but not for HN. EWL group membership was significantly correlated with T1 HN (r=.45, p=.03) and T2-T1 DI (r=-.45, p=.03).

Conclusions: Improved eating behavior patterns after LBS appear to be maintained at one year. LBS was most effective for LB with higher presurgical hunger and with greatest improvement over periodic loss of control of eating. LB who are at-risk for poor weight loss may gain greater benefit from post-surgical behavioral interventions. The mechanisms underlying greater post-surgical outcomes should be further investigated. (Funding from H75/CCH224064, CDC, Division of Diabetes Translation, UNTHSC DREAMS project)

Sponsor: Funding from H75/CCH224064, CDC, Division of Diabetes Translation, UNTHSC DREAMS project

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# DOES PERCEIVED STRESS AND COPING MODERATE CENTRAL ADIPOSITY AND INSULIN RESISTANCE IN MORBIDLY OBESE SUBJECTS?

Purpose: Maladaptive coping with stress has been implicated as contributing to metabolic syndrome through its effect on key physiological pathways that predominately influence central adiposity (CA) and insulin resistance (IR). Thus, the purpose of this study was to investigate the effect of coping style and psychological stress these two essential components of the metabolic syndrome in morbidly obese subjects. It was hypothesized that coping style and perceived stress would interact to increase central adiposity and insulin resistance.

Methods: Subjects included 70 morbidly obese men and women who were evaluated prior to undergoing laparoscopic banding surgery (X BMI=43.2 kg/m2 +.07). Perceived Stress (PS) and Coping (COP) were assessed using the Multidimensional Health Profile Psychosocial. Visceral adipose tissue was measured at the L4L5 spinal level using computed tomography. Insulin resistance was estimated using the HOMA index. Subjects were divided into high and low COP and PST conditions based on a median split. VAT and HOMA were analyzed separately in 2 x 2 ANOVAs. Gender was entered as a covariate due to significant differences in both VAT and HOMA.

Results: The interaction of PST and COP was non-significant for VAT. It approached significance for HOMA (F=3.60, p=.06) but was opposite the hypothesized direction so that poor coping/high stress had the lowest HOMA score. There was a significant difference in VAT for high and low COP (F=6.688, p=.01) but also opposite the hypothesized direction, with poor coping having the lowest VAT. All other results were non-significant.

Conclusions: Results did not support previous work showing a strong linear relationship between maladaptive coping with stress to indicators of metabolic syndrome such as central adiposity and insulin resistance. However, several features of the study design may have affected the findings including subject and test characteristics. Future studies should include subjects from mild to morbidly obese, restrict the focus to high chronic stress conditions and examine a broader range of coping. (H75/CCH224064, CDC, Div of Diabetes Translation, UNTHSC DREAMS Project)

Sponsor: H75/CCH224064, CDC, Div of Diabetes Translation, UNTHSC DREAMS Project

## 505 (Oral)

### First Author/Presenter: Anna Shurtleff

### Classification: SPH Student

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### MOW DIABETIC CLIENTS NEEDS IDENTFICATION AND MANAGEMENT PROGRAM: MEALS ON WHEELS, INC. OF TARRANT COUNTY

Purpose: "Evaluate potential correlation between high depression levels and uncontrolled diabetes. "Establish medical and social needs which may be attributing to high levels of depression. "Develop prospective policy initiatives for assisting this population.

Methods: Participants in the 2008 program were required to be active recipients of Meals on Wheels services and diagnosed diabetics. In the Fall of 2007 surveys were mailed to each of the potential participants based partially on their participation in the project the previous year and identification of unmet needs by caseworkers. The project was conducted from February 2008 until August 2008. The University of North Texas Health Science Center assigned a geriatric medical social worker to conduct testing and assist with referrals in the program. Also the university provided a student from the public health program and medical school to collect clinical data during the home visits.

Results: "110 identified diabetes were evaluated for depression through home assessments. 26 clients self reported depression and an additional 10 clients were identified for high depression scoring during the evaluation. "33.3% of participants were found to have positive depression scores. This is above the 13% expected depression for community dwelling older adults. These results are between older acute care patients (24%) and nursing home dwelling older adults (43%) (7). "110 Client were provided with potential social and health services options via mail and followed up a few months later through home visit on results. "Mini Mental State Examination (MMSE) results show 20.7% (23 out of 110participants) exhibit mild to severe impairments "95% of clients are content with their living conditions.

Conclusions: This project demonstrated the positive correlation between high depression needs and high A1C level in the community based elderly population. Through this project Meals on Wheels of Tarrant County has begun to evaluate expanding their services to include Geriatric Health Care Management. Currently Tarrant County MOW assigns a caseworker to each of their clients; these services may need to be expanded to include more extensive health and social programs. As a result of this study, starting in 2010 first year TCOM student will be paired with elderly individuals for healthcare home management.

First Author/Presenter: Kathryn Dolan

Classification: Faculty

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### MEDICAL EDUCATION AND COMMUNITY HEALTH RESOURCES

Purpose: Evidence suggests that healthcare workers feel ill-prepared when caring for vulnerable patients, such as those who are chronically ill, victims of violence, the elderly, and people with disabilities, addictions and mental illness. The purpose of this study is to evaluate the Community Resources course for pre-doctoral TCOM students as a tool for familiarizing these students with the intersections between the health care system and community based health and human services in urban and rural settings.

Methods: TCOM faculty have developed an innovative pre-doctoral curriculum, Community Resources, designed to provide educational experiences that: 1. Develop recognition of the social, economic, cultural and psychological factors that affect health and access to care. 2. Develop insight into the complementary roles and skills of medical, allied health, mental health and social service professionals as members of the health care team. 3. Increase knowledge of community health, mental health and social service resource referral options for a comprehensive care and support system. The educational methods during this two-year period include panel presentations on 16 specific topics, observation site visits at community based organizations and student small group presentations. Professionals and experts from the community present information on each topic, including groups most affected, barriers in accessing health care and supportive services available through community based organizations.

Results: The information presented in Community Resources contributes to medical students appreciation of the challenges vulnerable patients face and the community supports available to reduce health disparate outcomes. Topics are re-arranged to improve correlation with a systembased curriculum. Observation site visits allow student physicians to directly observe the diverse health and human service settings in the community, and develop an understanding of the roles and skills of allied health and social service professionals as members of the health care team. Adding content on signs and symptoms for each topic as well as textbook readings will enhance learning.

Conclusions: Community Resources is an effective way to increase medical students knowledge of community health, mental health, social service resources and referral options. Continued reassessment of curriculum content by course directors however, is critical to successful implementation.

Sponsor: N/A

## 601 (Poster)

### First Author/Presenter: Sha Maresh

### Classification: SPH Student

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## COMPASSION FATIGUE AND ITS EFFECT ON THE REGISTERED NURSE AND THEIR FAMILY MEMBERS

Purpose: The purpose of this study is to determine the level of compassion satisfaction, burnout, and compassion fatigue for registered nurses at HMFW; determine if there is a correlation of these concepts with a selected family member; design and implement interventions to assist employees improve family interactions.

Methods: The study is quasi-experimental and a pilot study and only survey registered nurses in order to provide a homogeneous sample for study. Anyone under 18 years old excluded from eligibility for this study. The Caregiver's Family QOL Scale is a new survey, developed by the PI, which is designed to elicit the family member's response to the caregiver's level of compassion satisfaction, burnout, and compassion fatigue. Demographic data will be obtained; however, reporting will only occur in the aggregate. Participants instructed to obtain a complete packet that contains: Cover letter with instructions for RN and family member, Demographic sheet with code number, ProQOL-CSF-R-IV with corresponding code number, and Self-addressed, stamped envelope with HMFW return-address (to maintain anonymity for respondent) for family member to return survey to study team.

Results: Validity and reliability test will be performed, plus further analysis possible, it s all depended on how the data processing. Possible subscales are Perception of family member of nurse s satisfaction, Perception of family member of nurse s fatigue, Family member s satisfaction with interactions with RN, Family member s fatigue/burnout with interactions with RN and the validity and reliability of this instrument will be tested in this pilot study.

Conclusions: Compassion fatigue (CF) is a secondary traumatic stress reaction (STSR) resulting from helping, or desiring to help, a person suffering from traumatic events. It has been well documented that nurses can and do suffer from compassion. Figley (2002) also found that some clinicians in healthcare do not practice a high level of self care, so knowing that they are suffering from CF does not always lead them to seek help to relieve this condition. Sherman, Zanotti, and Jones (2005) summarized studies that reflect on the importance of family members being involved in the treatment of post traumatic stress disorder (PTSD). There is a gap in the literature related to knowledge about nurses participation in interventions to relieve CF when they learn how their CF impacts family members.

## EDUCATION

## 602 (Poster)

First Author/Presenter: Laura Solano

Classification: School of Health Professions MPAS Student

Laura Solano, PA-S, Daniella Ramirez, PA-S, Olive Chen, PhD, Ruthie Kested, MS, PA-C

INCREASING WOMEN S AWARENESS OF PREMENSTRUAL DYSPHORIC DISORDER

Purpose: The purposes of this project were to: 1) develop a brochure that would increase awareness of Premenstrual Dysphoric Disorder (PMDD) in women of reproductive age, 2) investigate the brochure s effectiveness, 3) investigate differences in previous knowledge about PMDD prior to an educational activity and 4) investigate if the brochure influenced participant s willingness to seek medical care for PMDD.

Methods: The researchers developed a brochure about PMDD. The brochure included information about PMDD s risk factors, differences between PMS and PMDD, diagnostic criteria, symptoms, treatment options, how to get non-pharmacological relief, and where to seek medical treatment. A survey was developed to measure the brochure efficacy in increasing women s knowledge about PMDD. The survey contained a total of 14 questions about PMDD and demographic characteristics. After receiving IRB approval, the researchers recruited participants from waiting areas in two clinics. There were 44 participants but only 40 participants completed the activity. Participants were between the ages of 18 and 40, had the ability to speak, read, and write English, and were (to their knowledge) not pregnant. The survey was administered twice, one before the educational activity and one afterwards. One-way ANOVA s and a paired T- test were used to analyze the results.

**Results:** This study showed that the brochure presented in this study increased the participants knowledge about PMDD (t39=8.98; p<.001). Further, no significant differences were found in PMDD knowledge between different educational levels (F3,36=1.29; p=.295) or between different ethnicities (F2,34=0.762; p=0.475). Finally, the brochure did not change the participants' willingness to seek medical care.

Conclusions: The data supported that the brochure presented in this educational activity effectively improves awareness of PMDD. The brochure is a useful educational tool to increase awareness of PMDD in women. Therefore, this brochure can be widely distributed to women in clinics, health fairs, and women s affiliations for the purpose of increasing awareness of PMDD. A possible limitation of this study is the location from which participants were recruited from. Since participants were already in a medical waiting area, they may have been more likely to seek medical care for PMDD or any health related illness.

Sponsor: N/A

## 603 (Poster)

First Author/Presenter: Heather Schulze

Classification: School of Health Professions MPAS Student

Tate Rubley, PA-S; Heather Schulze, RD, PA-S; Patti Pagels, MPAS, PA-C; Sarah Brown, MPH; Olive Chen, Ph.D. University of North Texas Health Science Center, Fort Worth, Tx 76108

WILL AN INTERACTIVE EDUCATIONAL SEMINAR IMPROVE LEVEL OF CONFIDENCE AND KNOWLEDGE IN PHYSICIAN ASSISTANT STUDENTS REGARDING HOSPICE AND PALLIATIVE MEDICINE?

Purpose: The purpose of this study was to assess if an interactive educational seminar would increase awareness and positively affect attitudes of PA students towards hospice and palliative medicine.

Methods: This study was a prospective single group educational design. The researchers developed and implemented an educational seminar designed to enhance end of life (EOL) care competencies, addressing 5 domains of hospice. The program contained a 40-minute lecture and a case-based role play followed by a panel discussion. The outcomes measured before and after the seminar, included: (1) confidence and knowledge regarding the principles of hospice and palliative medicine; and (2) attitudes concerning the patient when relating to pain management, emotional support, addressing the patient s family, the need for open communication, and addressing spirituality. The project was approved by IRB and the data was analyzed using Wilcoxen test and linear regression analysis.

**Results:** A total of 30 PA students participated in the seminar. The majority of participants were female (77%) with mean age of 29.8 yrs. The majority of participants had no prior hospice experience (67%) and a mean prior healthcare experience of 41.6 mos. After completion of the seminar, participants overall attitude and knowledge increased in 9 of the 10 areas evaluated (p<.01), the exception being the participant's level of comfort when addressing the emotional needs of a patient. The data also showed that past healthcare experience is a positive predictor on the knowledge of hospice and palliative medicine (P=.011). Healthcare and prior hospice experience are positive predictors on the level of confidence when describing hospice (P=.028, P=.045, respectively). Age is also a positive predictor on level of understanding regarding effects of spirituality on the patient at EOL (P=.021) and on level of comfort when addressing the subject of spirituality (P=.024).

**Conclusions:** The results demonstrate that the interactive educational seminar increased PA students self-reported awareness and knowledge of hospice and palliative medicine. This rise in awareness, accompanied by the increase in self-reported confidence when treating a patient at EOL, illustrates the benefit of this seminar for future PAs. By increasing awareness and improving the skills of the PA students, the patients they will treat will be given better care, and ultimately a better quality of life.

## First Author/Presenter: Anirudh Sethi

### Classification: GSBS Student

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TRANSFORMING GROWTH FACTOR BETA INDUCES EXTRACELLULAR MATRIX CROSSLINKING ENZYME LYSYL OXIDASE AND OTHER LOX FAMILY PROTEINS

Purpose: Glaucoma is a leading cause of irreversible blindness in the world and is associated with elevated intraocular pressure due to increased aqueous outflow resistance in the trabecular meshwork (TM). Increased deposition of extracellular matrix (ECM) material in the TM appears to be responsible for this glaucomatous IOP elevation. Lysyl oxidase (LOX) is a collagen and elastin polymer crosslinking enzyme, and recent genome wide association studies showed that SNPs in LOXL1, a LOX family member, significantly increased the risk of developing exfoliation glaucoma. Aqueous humor levels of transforming growth factor beta (TGF-b) are elevated in glaucoma patients, and TGF-b itself can cause increased ECM deposition in the TM and elevated IOP. Our lab has recently showed that TGF-b2 induced tissue transglutaminase (TGM2), another family of cross linking enzymes, in humanTM cells. The objective of the current study is to evaluate the effects of exogenous TGF-b (1, 2 and 3) treatment on LOX and LOXL1-4 mRNA and protein expression in cultured human TM cells.

Methods: Primary glaucomatous and normal TM cells were grown in DMEM containing 10% FBS until 80% confluent and transferred to serum free medium for 24hrs prior to TGF-b treatment. Both cell associated and secreted LOX protein levels were analyzed using western immunoblotting. mRNA levels were determined by RT-PCR.

Results: After 48hrs, protein levels of both LOX and LOXL2 were induced by all three isoforms of TGF-b (5ng/ml). TGF-b2 caused elevated LOX and LOXL2 levels in the conditioned medium. TGF-b2 also causes a dose dependent increase in both secreted and cell associated LOX and LOXL2 proteins. We are examining the expression of other members of the LOX family (LOXL1, LOXL3, LOXL4) using RT-PCR.

Conclusions: Our studies indicate that there is an increased induction of LOX and LOXL2 proteins in TM cells treated with TGF-b and that TGF-b2 can cause secretion of these proteins in a dose dependent fashion.

Sponsor: NEI grant, EY017374

## 701 (Poster)

First Author/Presenter: Weiming Mao

#### Classification: Postdoctoral Fellow

Weiming Mao, Robert J. Wordinger, Abbot F. Clark Department of Cell Biology & Genetics and the North Texas Eye Research Institute U. North Texas Health Science Center, Ft. Worth, TX

### THE EXISTENCE OF A CANONICAL WNT SIGNALING PATHWAY IN GTM-3 CELLS

Purpose: Increased intraocular pressure (IOP) is the primary risk factor of glaucoma, and we have previously shown that the canonical Wnt signaling pathway plays a role in regulating IOP. In order to better understand Wnt signaling in the trabecular meshwork (TM), we investigated whether a similar canonical Wnt signaling pathway exists in GTM-3 cells, a transformed glaucomatous TM cell line widely used in glaucoma research.

Methods: The Wnt signaling pathway in GTM-3 cells was examined using a TCF dual-luciferase reporter gene assay, and we determined the effects of Wnt signaling on the endogenous ß-catenin levels with Western immunoblots. For the dual luciferase assay, reporter vectors containing TCF cis-elements were transfected into GTM-3 cells, which were then treated with recombinant Wnt3a, Wnt5a with or without SFRP-1 at different concentrations. For Western blots, nuclear and cytoplasmic proteins were extracted from GTM-3 cells treated with or without Wnt3a and/or SFRP-1 for 4 hours. ß-catenin, Lamin A/C and GAPDH (nuclear and cytoplasmic protein loading controls, respectively) were probed with corresponding antibodies.

Results: The dual-luciferase assay showed that Wnt3a dose-dependently induced luciferase expression in GTM-3 cells. The normalized relative luminescence unit (RLU) in GTM-3 cells increased 10 fold with 100ng/ml Wnt3a and 40 fold with 500ng/ml Wnt3a (both p<0.01). In contrast, Wnt5a only regulated luciferase expression with low efficacy. Treating GTM-3 cells with SFRP-1, an inhibitor of Wnt pathway, dose-dependently blocked the effect of Wnt3a with complete inhibition at 10ug/ml (p<0.01). Wnt3a caused the accumulation of endogenous ß-catenin in the nucleus and cytoplasm in GTM-3 cells, and this accumulation was also inhibited by SFRP-1.

Conclusions: GTM-3 cells have a canonical Wnt signaling pathway. These cells will be useful in further examining Wnt/?-catenin signaling and identifying Wnt regulated genes in the TM.

### First Author/Presenter: Ankur Jain

### Classification: GSBS Student

Ankur Jain(1); John A. Fuller(1, 2); Robert J. Wordinger(1, 3); and Abbot F. Clark(1, 3) 1-Department of Cell Biology and Genetics, UNT Health Science Center, Fort Worth, TX 2-Ophthalmology and Neuroscience, Johns Hopkins University, Baltimore, MD 3-North Texas Eye Research Institute, UNT Health Science Center, Fort Worth, TX

### CHARACTERIZATION OF CULTURED PRIMARY BOVINE TRABECULAR MESHWORK CELLS

Purpose: Glaucoma is a leading cause of visual impairment and blindness in the world. Elevated intraocular pressure (IOP) is a major causative risk factor for the development and progression of glaucoma. This IOP elevation is caused by glaucomatous damage to the trabecular meshwork (TM), a reticulated tissue found at the junction of the cornea and iris. Although human TM cells have been cultured and characterized to study glaucoma pathogenesis, there is limited access to human donor eyes and only relatively small numbers of human TM cells can be grown. The purpose of the present study is to grown TM cells from more readily available bovine eyes and to determine whether these bovine TM cells have similar responses to the glucocorticoid dexamethasone (DEX).

Methods: TM tissues were carefully dissected from bovine eyes and cultured as explants. Primary bovine TM cells grown in DMEM containing 10% FBS with or without 100nM (DEX) for various time periods were subjected to biochemical and molecular manipulations. The cells were examined for DEX effects on the actin cytoskeleton using Phalloidin-Alexa staining and Epifluorescence microscopy. The effects of DEX treatment on fibronectin and myocilin expression were analyzed using Western immunoblots and RT-PCR.

Results: 14 days treatment with DEX resulted in increased protein expression of fibronectin. Three or more days of DEX treatment caused a reorganization of microfilaments to form cross-linked actin networks (CLANs). We currently are examining the expression of myocilin mRNA in DEX treated cells.

Conclusions: Our studies indicate that cultured bovine TM cells share some classic characteristic features with cultured human TM cells like DEX-induced CLANs formation and increased fibronectin expression.

Sponsor: N/A

## 703 (Poster)

### First Author/Presenter: Ashley Fitzgerald

Classification: GSBS Student

Ashley Fitzgerald1, Anirudh Sethi1, Abbot Clark1,2, Robert Wordinger1,2 Department of Cell Biology and Genetics1 and North Texas Eye Research Institute2, University of North Texas Health Science Center at Fort Worth, TX., 76107

### GENE EXPRESSION OF TGF-BETA/SMAD SIGNALING PROTEINS IN HUMAN TRABECULAR MESHWORK CELLS

Purpose: Glaucoma is a leading cause of blindness affecting over 70 million people worldwide. Important risk factors for glaucoma include age, race, and elevated intraocular pressure (IOP). Elevated IOP results from increased resistance of aqueous humor (AH) outflow through the trabecular meshwork (TM). Resistance to AH outflow in the TM has been attributed to increased deposition of extracellular matrix proteins (ECM). Glaucoma patients have elevated levels of transforming growth factor-beta2 (TGF-ß2) in the AH, consequently this growth factor is known to increase the deposition of ECM proteins. Our lab has previously reported that exogenous TGF-ß2 causes an upregulation of secreted and cross-linked ECM proteins in cultured human TM cells. However, TGF-ß2 can utilize several different signaling pathways. The purpose of this study was to compare and contrast the gene expression of several TGF-ß2 (a) canonical signaling pathway proteins and (b) anchoring/accessory proteins in normal and glaucomatous TM cells.

Methods: Primary normal (NTM) and glaucomatous (GTM) TM cells were cultured and treated with TGF-ß2 (5ng/ul) for 48hrs. Following treatment, RNA was extracted from the cells, and RNA was synthesized to cDNA. Changes in gene expression of betaglycan, endoglin, Smad2, Smad3 and thrombospondin were analyzed by reverse transcriptase polymerase chain reaction (RT- PCR).

**Results:** Gene expression results indicate that betaglycan was only expressed by GTM cells, but not NTM cells. Endoglin was expressed by both GTM cells and NTM cells. Smad2 gene expression was high in GTM cells and NTM cells following TGF-ß2 treatment. Interestingly, Smad3 was expressed only in GTM cells. Thrombospondin was highly expressed in GTM cells with and without TGFb2 treatment and in NTM treated cells.

Conclusions: TGF-ß2 treatment of NTM and GTM cells resulted in differences in gene expression of TGF-ß2-Smad signaling and anchoring/accessory proteins. The anchoring protein betaglycan, and signaling protein Smad2 were elevated in the NTM cells following TGF-ß2 treatment. These data indicate that exogenous TGF-ß2 can upregulate proteins related to TGF-ß2 signaling and may lead to up-regulation of both secreted and cross-linked ECM proteins in the TM.

Sponsor: NIH

## **EYE/VISION**

### 704 (Poster)

First Author/Presenter: Jacquelyn Garcia

Classification: TCOM DO Student

Jacquelyn Garcia, Weiming Mao, Robert J. Wordinger, Abbot F. Clark from The Texas College of Osteopathic Medicine and The Graduate School of Biomedical Sciences

## TGF-B2 INDUCED REORGANIZATION OF THE HUMAN TRABECULAR MESHWORK ACTIN CYTOSKELETON

Purpose: Glaucoma is one of the leading causes of worldwide blindness. TGF-?2 is elevated in the aqueous humor in glaucoma, and it increases aqueous humor outflow resistance leading to elevated intraocular pressure. The purpose of this study is to determine whether treatment with TGF-b2 alters the trabecular meshwork (TM) actin cytoskeleton to form CLANs (cross-linked actin networks) in cultured human TM cells.

Methods: Human trabecular meshwork cells cultured in Dulbecco s Modified Eagle s Medium (DMEM) were treated with TGF-B2. Previous studies have shown that the glucocorticoid dexamethasone (Dex) reorganizes the actin filament bundles to form geodesic dome-like structures of CLANs. Therefore, Dex-treated cells were used as a positive control to visualize CLANs within the TM cells. The cells were treated under two conditions with their respective controls. The TM cells were exposed to dexamethasone (0.1 uM) and its control, and TGF-B2 (5 ng/ml) and its control for three, seven, and ten days. The cells were then formalin fixed, extracted with Triton X-100 and stained with Alexa 594-phalloidin. The cells were visualized by epifluorescence, microscopy and analyzed for the amount of CLAN formation.

Results: As expected, Dex treated cells (positive control) had CLANs. The TM cells treated with TGF-B2 (for three, seven, and ten day treatments) also had increased CLAN formation compared to control cells.

Conclusions: There was an increase in CLAN formation in the cells treated with TGF-B2 compared to the control, so TGF-B2 may have a direct role in altering the trabecular meshwork cytoskeleton leading to the formation of these CLANs. CLAN formation may play a role in the TGF-B2 induced aqueous outflow resistance and elevated intraocular pressure in glaucoma patients.

Sponsor: N/A

## 705 (Poster)

### First Author/Presenter: Amber Ondricek

### Classification: GSBS Student

Amber Ondricek, Department of Cell Biology and Genetics, UNT Health Science Center, Fort Worth, TX, 76107 Anindita Mukerjee, Department of Molecular Biology and Immunology,UNT Health Science Center, Fort Worth, TX, 76107 Jamboor Vishwanatha,Department of Molecular Biology and Immunology,UNT Health Science Center, Fort Worth, TX, 76107

# FORMULATION AND CHARACTERIZATION OF N-ACETYL CYSTEINE LOADED PLGA NANOPARTICLES FOR NEUROPROTECTION TO RETINAL GANGLION CELLS IN AN IN VITRO MODEL OF GLAUCOMATOUS CELL DEATH

Purpose: The eye is a preferential environment to study sustained delivery methods due to its isolation from peripheral circulation via the blood retina barrier. Likewise, poly-L-lactic-co glycolic acid (PLGA) is a preferential polymer to encapsulate drugs for sustained delivery because it is biodegradable, biocompatible and FDA approved. The purpose of this study is to formulate and characterize N-acetyl cysteine (NAC) loaded PLGA nanoparticles and study the effect of them delivering neuroprotective antioxidants to retinal ganglion cells. We hypothesize that NAC loaded PLGA nanoparticles (NAC-PLGA nps) will afford sustained neuroprotection to retinal ganglion cells (RGCs) via activation of cell survival pathways when compared to NAC alone.

Methods: PLGA nanoparticles were synthesized utilizing double emulsion solvent evaporation technique. Nanoparticles were then characterized for size using a particle size analyzer, Nanotrac. Intracellular localization in RGC-5 and to the RGC cell layer in pig eyes was determined using Nile Red. Encapsulation efficiency was determined by direct method utilizing the thiol-reactive probe, Ellman s Reagent. Cell survival assay was carried out using Calcien AM assay. Western blotting analysis was used for determination of cell signaling events.

Results: NAC-PLGA nps were optimized based on preferred size (100-250 nm) and encapsulation efficiency. It was found that NAC-PLGA nps localize intracellularly in vitro in RGC-5s and ex vivo to RGCs in pig eyes. NAC-PLGA nps affords neuroprotection to RGC-5s against lodoacetic Acid induced cytotoxicity. NAC-PLGA nps induce sustained phosphorylation of ERK1 and 2, and S6 over 24 hours compared with control.

Conclusions: NAC-PLGA nanoparticles have potential to become an effective treatment, in vitro, against the generation of oxidative stress and cytotoxicity. They are a plausible for application in glaucoma because of the ability to localize intracellularly in RGCs. The application of such a sustained delivery method could improve patient outcomes and compliance when combined with IOP-lowering treatments or in normal tension glaucomas alone.

Sponsor: Neurobiology of Aging

## **EYE/VISION**

## 706 (Poster)

First Author/Presenter: Jwalitha Shankardas

Classification: Postdoctoral Fellow

Jwalitha Shankardas, Integrative Physiology, Fort Worth, TX 76107 Dan.S.Dimitrijevich, Integrative Physiology, Fort Worth, TX 76107

INTRACELLULAR DISTRIBUTION OF P63 DURING PROLIFERATION AND DIFFERENTIATION OF THE CORNEAL EPITHELIUM

Purpose: To study the role of DNp63 in proliferation and differentiation of human corneal epithelial cells Need to put in why p63.

Methods: Indirect immunofluorescence was used to determine the localization of TAp63 and DNp63 in the central and limbal epithelial cells of the corneal epithelium. Primary human corneal epithelial cells from the central cornea (hCEC) and hCEC ectopically expressing hTERT were cultured under proliferation and differentiation conditions. Localization of DNp63 was determined by indirect IF and compared with that in proliferating controls. The quantitated expression levels of DNp63 were derived from western blot analysis.

**Results:** TAp63 expression was observed in the superficial layers of the central cornea and was absent in the limbus. DNp63 localization is nuclear in the basal cells of the corneal epithelium and cytosolic in the superficial / differentiated cell layers of the central cornea and the limbus. Western blot analysis of lysates from cultured primary cells showed that DNp63 expression decreases under differentiation conditions. Indirect immunofluorescence of cells cultured under differentiation conditions showed translocation of DNp63 from the nucleus to the cytoplasm.

Conclusions: Primary cultures of hCEC contain a heterogeneous population of proliferating and cells at different stages of differentiation. The presence of differentiated cells may be characterized by the cytosolic localization of DNp63. The translocation of DNp63 is more prominent in the hTERT CEC cells in which DNp63 in completely nuclear, but after 2-weeks under differentiation conditions; small populations of cells begin to show cytosolic localization of DNp63. Since there is no known cytosolic function for DNp63, its translocation to the cytosol could be an indication of targeted degradation.

Sponsor: N/A

## 707 (Poster)

### First Author/Presenter: Grant Herndon

Classification: TCOM DO Student

Grant Herndon 1, Weiming Mao 2, Abbot F. Clark 2, Robert J. Wordinger 2 1 TCOM 2 Dept. Cell Biology & Genetics and the North Texas Eye Research Institute

### DO LAMINA CRIBROSA CELLS DIFFERENTIATE INTO OPTIC NERVE HEAD ASTROCYTES?

Purpose: Primary open angle glaucoma (POAG), the most common form of glaucoma, leads to progressive, irreversible loss of retinal ganglion cell (RGC) axons at the level of the optic nerve head (ONH). This is usually in response to abnormally elevated intraocular pressure (IOP). One of the features of the glaucomatous ONH is remodeling of the extracellular matrix at the lamina cribrosa layer which is partly orchestrated by activated ONH astrocytes. Activated ONH astrocytes are known to have increased expression of glial fibrillary acidic protein (GFAP) and neural cell adhesion molecule (NCAM). Because astrocyte activation can take place in the absence of astrocyte mitotic proliferation, we hypothesize that LC glial cells are immature, quiescent glial cells capable of undergoing differentiation to GFAP-positive, NCAM-positive ONH astrocytes when subjected to glaucomatous conditions, thus contributing to the increase in expression of GFAP and NCAM observed at the glaucomatous optic nerve head.

Methods: Human LC cells were cultured on coverslips in Dulbecco s Modified Eagle s Medium (DMEM) + 10% fetal bovine serum (FBS) until confluent, followed by incubation in DMEM + 0.5% FBS with factors known to be present in glaucomatous optic neuropathy, specifically TGF-ß2 (5 ng/mL), endothelin-1 (100 nM), or glutamate (100  $\mu$ M), or DMEM + 0.5% FBS alone as controls. Cells were treated for 10, 7, and 3 days. The LC cells were then incubated with fluorescent antibodies specific for GFAP and NCAM. Fluorescent microscopy was used to visualize staining for GFAP and NCAM in the LC cells compared with human brain astrocytes acting as positive controls.

Results: Treated LC cells were negative for GFAP and NCAM as were the untreated control LC cells. Posititve control brain astrocytes stained for GFAP and NCAM. There was no discernable production of GFAP or NCAM by LC cells treated with TGF-ß2, endothelin-1 or glutamate.

Conclusions: LC cells do not have the ability to differentiate into ONH astrocytes following exogenous treatment with TGF-ß2, endothelin-1 or glutamate.

## **EYE/VISION**

## 708 (Poster)

First Author/Presenter: Donald Daudt III

Classification: GSBS Student

D.R. Daudt, III, R. Krishnamoorthy, T. Yorio. Pharmacology & Neuroscience, UNT Health Science Center, Fort Worth, TX 76107.

FK506 BINDING PROTEIN 51 (FKBP51) MEDIATED NEUROPROTECTION AGAINST GLUTAMATE EXCITOTOXICITY IN RGC-5 CELLS

Purpose: Glaucoma is a progressive optic neuropathy characterized by loss of retinal ganglion cells (RGC) and optic nerve degradation. Existing treatments focus on lowering intraocular pressure (IOP); however, vision loss may still progress. Neuroprotectant drugs are useful as an adjunct approach in preventing further loss of RGCs; though, candidate genes are lacking. FK506, a widely used immunosuppressant drug, has profound neuroprotective and neuroregenerative properties throughout the central nervous system, including the eye. FK506 achieves these properties through interaction with FK506 Binding Proteins (FKBP). In this study, we investigate FKBP51s neuroprotective properties.

Methods: Retinal ganglion cells (RGC-5s) were stably transfected with FKBP51 overexpression vector. Cells were subjected to excitatory glutamate toxicity. Cell death was measured through calcein-AM/propidium iodide cell-survival assay. Western blot analysis was used to determined cytochrome c release from the mitochondria during apoptosis.

Results: In RGC-5 cell cultures, stably transfected cells overexpressing FKBP51 showed increased cell viability during calcein-AM/propidium iodide cell-survival assay compare to negative control. Furthermore, RGC-5 cells overexpressing FKBP51 had a decrease in cytochrome c release into the cytosol and an increase of cytochrome c in the mitochondria.

Conclusions: These data provide strong evidence that FKBP51 promotes anti-apoptotic action in retinal ganglion cells during excitatory glutamate toxicity. Further investigation is needed to determine which pathways FKBP51 activates to achieve these neuroprotective action.

Sponsor: NIH Grant T32 AG020494

## 710 (Poster)

### First Author/Presenter: Jwalitha Shankardas

Classification: Postdoctoral Fellow

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### EFFECT OF DOWN-REGULATION OF AQUAPORINS IN THE HUMAN CORNEA.

Purpose: The purpose of this study is to determine the effects of down-regulation of Aquaporin 1(AQP-1) and Aquaporin 5(AQP-5) in human corneal endothelial cells (HCEC) and human corneal epithelial cells respectively.

Methods: AQP-1 and AQP-5 were down-regulated using siRNA following lipofectamine mediated transfection in corneal endothelial and epithelial cells respectively. Down-regulation was confirmed using RT-PCR, Indirect Immunofluorescence and western blot analysis. Cell proliferation was determined by SRB assay. Cell migration was determined by scratch wound healing assay and also using the boyden assay.

Results: AQP-1 down-regulation results in decrease in HCEC cell proliferation and a corresponding decrease in pERK. In addition AQP-1 downregulation causes a decrease in cell migration. AQP-5 protein expression is membrane associated and cytosolic in corneal epithelial cells (Primary and SV-40 transformed corneal epithelial cell line). AQP-5 down-regulation results in an increase in proliferation while there is no significant difference in pERK. There is an increase in cell migration following AQP-5 down-regulation.

Conclusions: AQP-1 is involved in HCEC proliferation and migration and therefore may have significant implications in corneal endothelial dysfunction. AQP-5 may play an indirect role in human corneal epithelial cell proliferation and migration. There is however no significant difference in the MAPK kinase signaling cascade suggesting the involvement of an alternate pathway.

Sponsor: This research was partially supported by a grant from the Alcon Research Ltd. to JKV

### First Author/Presenter: Tasneem Putliwala

Classification: GSBS Student

Tasneem Putliwala1, J. Shankardas2, R. Arafeh1; S. D. Dimitrijevich2. 1. Graduate School of Biomedical Sciences, UNTHSC, Fort Worth, TX, 76107. 2. Integrative Physiology, UNTHSC, Fort Worth, TX, 76107.

## ASSEMBLY OF A THREE DIMENSIONAL LAMELLAR MODEL OF THE CORNEA

Purpose: We hypothesize that optical transparency of the cornea may be recapitulated in vitro by lamellar organization of thin transparent films into laminated stacks. Assembly of the stacks will also depend on alignment of collagen fibrils and cells on the collagen films which will be demonstrated using Cy-5 labeled collagen in combination with fluorescently labeled cells. By incorporating PMMA membranes into separate stacks, we will determine the feasibility of assembling a biocompatible corneal prosthesis with appropriate optical and physical properties.

Methods: Thin films of neutralized collagen type I solution, PMMA coated glass coverslips producing thin films and commercially available collagen films were utilized. Each film was seeded with normal human keratocytes (1x105 cell/film) which had been labeled with Cell Tracker Green® (CTG) and Cell Tracker Orange® (CTO) for 24 hours. PMMA films were then peeled off the coverslips and assembled as alternating CTG and CTO layers lamellar stacks to mimic the stroma s structure. Scanning laser confocal microscopy was used to demonstrate this. The tricompartment Cy5 labelled collagen model, populated with CTG labeled keratocytes, corneal epithelial cells and corneal endothelial cells was also assembled.

Results: Stacks of collagen films were assembled using the above protocol. Scanning laser confocal microscopy showed the series of lamellae populated with alternating layers of green and red fluorescently labeled cells cells. The keratocytes plated on in-house generated collagen films were aligned and when assembled into a stack. Commercially available collagen type I, and PMMA films, did not have aligned cells but could still be assembled into stacks. Alignment of collagen fibrils and cells was visualized using Cy-5 labeled collagen (conjugated) and CTG labeled keratocytes. The three different compartments were examined using confocal microscopy following Z-sectioning.

Conclusions: It is possible to efficiently and reproducibly assemble lamellar stroma model composed of layers of collagen (~ 150 µm thick) and commercially available collagen films populated by keratocytes. The cells cultured on the collagen films were shown to adopt a parallel unidirectional alignment in accordance with the proposed alignment of collagen fibrils which was visualized using Cy5 dye. The stratified corneal epithelial layer and the basal endothelial layer can also be successfully incorporated to complete the corneal construct.

Sponsor: N/A

## 712 (Poster)

### First Author/Presenter: Mallika Valapala

### Classification: GSBS Student

Mallika Valapala1, Julian Borejdo2, Tchedre KT3 and Jamboor K Vishwanatha1,2 1Department of Biomedical Sciences and 2Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, Texas, 3Schepens Eye Research Institute, Harvard Medical School, Boston

### GLUTAMATE INDUCES CELL SURFACE TRANSLOCATION OF ANNEXIN A2 IN RETINAL GANGLION CELLS

Purpose: The role of annexin A2 in the retina is not known, this study provides certain molecular insights into its function as an active plasmin generating extracellular receptor.

**Methods:** Glutamate-induced intracellular Ca2+ dynamics was studied by ratiometric Ca2+ imaging and confocal microscopy. Cell surface biotinylation and versene elution were used to recover cell surface annexin A2. Time-lapse confocal microscopy were used to show the cell surface translocation of annexin A2. Site directed mutagenesis was used to study the involvement of key residues in the translocation process. Immunoprecipitation was used to detect the phosphorylation status of cell surface annexin A2. A fluorogenic in vitro plasmin generation assay was used to study annexin A2-mediated plasmin generation.

Results: Glutamate treatment resulted in the mobilization of intracellular Ca2+ in RGC-5 cells. Both endogenous and GFP fused annexin A2 translocated to the cell surface on glutamate treatment in a process dependent on the activity of the NMDA receptor and independent of de novo protein synthesis. Among the two phosphorylation sites in the N-terminus of annexin A2, Y23 and S25, we observed that Y23 is crucial for the translocation process. Mutation of Y23 to a non-phosphomimetic Y23F inhibited the translocation process whereas mutation of S25 to S25A did not have any effect. Double mutants at Y23 and S25 showed similar effects as single mutants. N-terminal deletion mutants have indicated that N-terminus by itself can translocate to the cell surface but it cannot be mobilized in response to changes in intracellular Ca2+. The C-terminal deletion mutant does not translocate to the cell surface suggesting that the C-terminus of annexin A2 imparts the Ca2+-dependent cell surface binding ability. Immunoprecipitation studies indicated that cell surface annexin A2 is tyrosine-phosphorylated and serine-phosphorylated annexin A2 was not detected. Translocation of annexin A2 was inhibited by genistein, augmented by sodium orthovandate and not influenced by okadaic acid. Annexin A2 forms an active plasmin generating complex and this activity is inhibited by an antibody or a peptide directed against the N-terminus of annexin A2.

Conclusions: These results suggest that annexin A2 potentiates excitotoxic loss of RGC-5 cells and modulating its activity can confer neuroprotection.

Sponsor: P20MD001633 from the National Center On Minority Health And Health Disparities (JKV) and Alcon Res.

First Author/Presenter: Pankaj Chaudhary

Classification: Postdoctoral Fellow

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### 4-HYDROXYNONENAL INDUCES P53-MEDIATED APOPTOSIS IN RETINAL PIGMENT EPITHELIAL CELLS

Purpose: Since generation of 4-hydroxynonenal (4-HNE) after lipid peroxidation has been shown to induce apoptosis in various cell types through multiple apoptotic pathways, the present studies were designed to investigate the mechanism of 4-HNE induced apoptosis in RPE cells and its regulation by glutathione S-transferase (GST) A4-4.

Methods: RPE and ARPE-19 cells were grown in DMEM medium containing 10% fetal bovine serum and antibiotics in a humidified incubator at 37oC in 5% CO2 atmosphere. RPE cells were transfected with either empty pTarget-T vector (VT) or the pTarget vector with the hGSTA4 sequence (hGSTA4-Tr), using Lipofectamine PLUS reagents (Invitrogen, Carlsbad, CA) as per the manufacturer s instructions. RPE and ARPE-19 cells were exposed to various concentrations of 4-HNE and the cytotoxic effects were measured by MTT assay. The effect of 4-HNE (20µM) on the p53 and other components of apoptotic pathway was compared in control and GSTA4-transfected cells.

Results: The results of present studies indicate that 4-HNE is toxic to RPE and ARPE-19 cells. The IC50 values for 4-HNE for the RPE and ARPE-19 cells were found to be  $52 \pm 1.4$ , and  $46 \pm 3.2 \mu$ M, respectively. Upon 4-HNE treatment, a dose and time dependent increase in the intracellular levels of p53 and phospho p53 were observed in RPE/ARPE-19 cells. A dose-dependent up-regulation of Bax, p21, JNK and caspase-3 were also observed in 4-HNE treated RPE/ARPE-19 cells. The silencing of p53 expression in RPE cells attenuated 4-HNE-induced cell death. Over-expression of either human GSTA4-4 in RPE or mGsta4-4 in ARPE19 cells acquired significant resistance to apoptosis as judged by the lack of caspase-3 activation in 4-HNE treated GSTA4-transfected cells. GSTA4-4 over-expression also attenuated the expression of p53, phospho-p53 and Bax in 4-HNE treated cells. In vivo studies also indicated that p53 expression was significantly up-regulated in the tissues of mGsta4 null mice having 2-3 fold higher 4-HNE levels in their tissues as compared to the wild type mice.

Conclusions: These studies suggest that 4-HNE is involved in p53-mediated apoptotic signaling in-vitro cell cultures as well as in-vivo that can be regulated by GSTs.

Sponsor: N/A

First Author Presenter: Furth Pickedon

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Like Smith, MLS UNTHISC, For Westh, TX, 2010/10/ke Claim, PhG UNTHISC, Fort Westh, TX, 26102

Purpose. This study designed a two part intelst therapy controllary involving classroom wolkars and a practical application with parasits of phototric politicity and ovaluated its effectiveness. The goal was to platernize base the controllars effected physician excitated (PA) students of the controllars effective context (PA) students and the controllars effective context (PA) students and the context of th

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## **GENERAL MEDICINE**

## 800 (Poster)

## First Author/Presenter: Michael Dunn

### Classification: Dual Degree Student: DO/MS

Principle Investigator: Roberto Cardarelli, D.O., M.P.H UNT Health Science Center, Department of Family Medicine Acting Chair/Family Medicine, Associate Professor/Family Medicine, Director/Division of Research (DOR), Director/Center for Evidence-Based Medicine, Executive Director and Founder/Primary Care Research Institute/NorTex Address:855 Montgomery Street, Fort Worth, TX 76107 Student Investigator: Michael A. Dunn, D.O./M.S. Candidate, 2009 UNT Health Science Center: TCOM, GSBS

# UNDERSTANDING THE PSYCHOSOCIAL FACTORS OF COMMUNICATION THAT UNDERLIE COLORECTAL CANCER SCREENING ADHERENCE

Purpose: To investigate physician-patient interpersonal factors of communication and the extent to which they impact a patient s adherence to the recommendation for a colorectal cancer screening test by their physician through use of a validated instrument: The Interpersonal Processes of Care (IPC) Survey.

Methods: Potential participants were recruited from billing records of the Texas College of Osteopathic Medicine, Department of Family Medicine with a minimum goal of recruiting 50 participants. Eligibility was assessed prior to recruitment according to age (50 years and over) and previous preventive visit with their primary care physician (having been seen by their primary care physician during the 2007 calendar year for a preventive visit/ well-woman/well-man visit, or yearly physical). Eligible participants were then identified through the billing department of Family Medicine and mailing labels developed accordingly. The study included two procedures: 1) a self-administered survey and 2) a medical chart review. The 70-question survey contained validated scales related to demographics, health history, interpersonal processes of care, barriers and facilitators to cancer screening, recent (if any) colorectal cancer screening tests, and other health related measures. The survey was mailed to eligible participants and included with it was a packet explaining the study and that by completing the survey the eligible participant was providing consent to use their responses for research purposes and to have their medical chart reviewed for colorectal cancer screening tests had their medical chart reviewed by mail, participants who reported receiving any of the approved colorectal cancer screening tests had their medical chart reviewed by the Student Researcher (SR) to corroborate such reports. Testing results, consult letters, and clinic note documentation were used to corroborate participants reports of receiving tests.

Results: Data collection in progress.

Conclusions: To be determined.

Sponsor: N/A

## 801 (Poster)

### First Author/Presenter: Ruth Pinkerton

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## LEARNING THROUGH OUTREACH: THE EFFECT OF A HEALTH LITERACY CURRICULUM ON PHYSICIAN ASSISTANT STUDENTS

Purpose: This study designed a two part health literacy curriculum involving classroom lectures and a practical application with parents of pediatric patients and evaluated its effectiveness. The goal was to determine how the curriculum affected physician assistant (PA) students knowledge, attitudes, and confidence related to health literacy and how the educational program was received by PA students.

Methods: The classroom curriculum was a 4 hour presentation using a PowerPoint from the American Medical Association. It contained four sections: overview of health literacy, creating a shame-free environment, enhancing patient interaction and communication, and cultural competence and the use of an interpreter. The second component was an outreach activity in which students gave presentations on using the website Medline Plus for health questions to parents of pediatric patients. The curriculum took place with first year physician assistant students in North Texas after receiving IRB approval. The curriculum was evaluated using tests before and after the curriculum, a survey of students opinions following the curriculum, and worksheets students filled out after their outreach activity. Analysis was conducted using a paired t-test to measure change in student knowledge and Wilcoxon tests to measure change in student confidence, as well as descriptive statistics.

Results: Thirty three students completed the curriculum and evaluation. There were no significant changes in participants knowledge, attitudes, or confidence from pretest to posttest. There was, however, a significant increase in participants self-reported knowledge of health literacy from a median of 6 to 8 (p<0.001). Participants approved of the curriculum; 82.4% found both components of the curriculum beneficial to their future as PA's. In their responses to qualitative questions, participants noted that the curriculum improved their awareness of health literacy issues, gave them skills for addressing health literacy problems, and provided a practical experience teaching patients.

Conclusions: The participants expressed satisfaction with both components of the curriculum and stated that the curriculum was beneficial to their future clinical practice. This curriculum should be employed by other health professional programs or schools interested in increasing their students competency in health literacy issues and skills. Some modifications should be made to make the curriculum fit the circumstances of individual programs.

Sponsor: National Institutes of Health Department of Health Services

## IMMUNOLOGY

## 900 (Poster)

## First Author/Presenter: Kim Aldy

Classification: GSBS Student

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### IDENTIFYING HIV EPITOPES THAT CAUSE AN EFFECTIVE CD8+ T CELL RESPONSE FOR USE IN AN HIV VACCINE

Purpose: Acquired immune deficiency syndrome (AIDS), caused by Human Immunodeficiency virus (HIV) is the most devastating global health problem. Although it is one of the most studied diseases in the world there are still few preventative treatments available. Many groups of individuals have different outcomes in HIV infection and AIDS progression. One of these groups contains seropositive individuals, Long Term Non Progressors (LTNP), that have delayed progression to AIDS. It has been shown that a potent anti-HIV CD8+ T cell response is associated with this group; therefore, an effective cytotoxic T cell (CTL) response is vital for the immune system to control HIV. Human leukocyte antigen (HLA) B14 and HLA B27 types are present in LTNP. We propose that by taking advantage of this population s ability to combat the virus we can expand our treatment methods. We have identified the 2B4 (CD244) receptor expressed on NK cells and some populations of CD8+ T cells. Although the function of 2B4 in T cells and its role in HIV remains unexplored, the expression of 2B4+CD8+ T cells has been shown to increase during HIV disease progression. This study is the first to establish an in vitro model comparing this receptor s role in T cell cytotoxicity towards HIV infection.

Methods: To study the ability of conserved HIV peptides to bind HLA B14 and B27 BLCLs (B Lymphoblastoid cell lines) we used an in vitro model where we removed the self peptides from their MHC class I using a mild citric acid treatment and exogenously added synthetic HIV peptides. Once the binding affinities of these epitopes to the BLCLs were established, we cultured the peptides with dendritic cells to create antigen presenting cells (APC). These APC s were used to prime two populations of CD8+ T cells, 2B4- and 2B4+ CD8+ T cells after which we measured IFN-gamma production and cytotoxicity of the activated CD8+ T cells.

Results: Eleven HIV peptides were screened for their binding affinity to HLA B14 and B27 BLCLs and only peptides IK-9 and IY-11 showed binding. Preliminary data using non HLA-B14 and B27 donors showed 2B4+CD8+ T cells secrete higher levels of IFN-gamma as compared to 2B4-CD8+ T cell populations in response to APC priming.

Conclusions: These results suggest that 2B4+CD8+T cells play a role in immune regulation by secreting IFN-gamma upon recognizing HIV peptides presented by APC. Further immunogenicity studies to stimulate an effective CTL response can eventually help in the development of an effective HIV vaccine.

Sponsor: Supported by Grant# P20MD001633 from the National Center for Minority Health and Health Disparities

## 901 (Oral)

#### First Author/Presenter: Karen Meeks

#### Classification: GSBS Student

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### IL-23 AND THE IL-17 RECEPTOR ARE REQUIRED FOR PROTECTION AGAINST LISTERIA MONOCYTOGENES

Purpose: Listeria monocytogenes (LM) is a gram-positive, intracellular bacterium that can induce spontaneous abortion, septicemia, and meningitis. Recently, it has been demonstrated that interleukin (IL)-17A is necessary for an optimal immune response against LM in the liver. As IL-23-dependent cytokines, IL-17A and IL-17F induce the mobilization of neutrophils to sites of infection. We hypothesize that IL-23 has a critical role during LM infection.

Methods: We utilized mice deficient in either IL-23 (IL-23p19 KO) or the IL-17 receptor A (IL-17RA KO)in order to investigate the role of these cytokines during infection with LM. Mice were infected for 1, 3, 5 or 7 days with ~10,000 LM. In addition to splenic and hepatic bacterial burden, neutrophil numbers were assayed in the spleen, liver, and peripheral blood via flow cytometry. IL-17A and IL-17F ELISAs were performed on LM-infected spleen and liver culture supernatants.

Results: During infection with LM, IL-23p19 KO and IL-17RA KO mice have increased susceptibility to infection and increased bacterial burden in the spleen and liver. We demonstrate here that IL-23 and the IL-17RA, which mediates both IL-17A and IL-17F signaling, are necessary for resistance against LM infection. IL-17A and IL-17F are decreased in spleen and liver culture supernatant from LM infected IL-23p19 KO mice. Furthermore, neutrophil numbers are reduced in IL-23p19 KO and IL-17RA KO mice at early time points. When IL-23p19 KO mice are rescued with the administration of exogenous IL-17A, spleen and liver LM burdens are reduced to levels equivalent to wild-type B6 mice.

Conclusions: Therefore, it is likely that IL-23 regulates the optimal production of IL-17A/F during LM infection which results in early neutrophil recruitment and bacterial clearance.

Sponsor: NIH AI064592

First Author/Presenter: Amy Graham

Classification: GSBS Student

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INTERLEUKIN-23 IS IMPORTANT FOR THE MUCOSAL IMMUNE RESPONSE AGAINST LISTERIA MONOCYTOGENES INFECTION

Purpose: Listeria monocytogenes (LM) is a gram-positive bacterium commonly found in soil and water. This intracellular pathogen is a common contaminant in processed meats and dairy products. In humans, ingestion of LM results in infection in the spleen and liver, which can ultimately lead to septicemia, meningitis, and spontaneous abortion. Interleukin (IL)-23 is a cytokine that regulates immune responses by inducing the production of IL-17A, IL-17F, and IL-22, and is important for clearance of bacteria at mucosal surfaces, including the intestine. IL-17A and IL-17F have been shown to recruit neutrophils to sites of infection, while IL-22 can induce the secretion of anti-microbial peptides. However, the role of IL-23 during an intra-gastric (i.g.) LM infection is unknown. We hypothesize that intestinal IL-23 induces the production of IL-17A/F and/or IL-22, which is able to influence neutrophil recruitment and/or anti-microbial peptide production during LM infection.

Methods: At days one and three post i.g. inoculation with LM, bacterial burdens in the spleen and liver were quantified in C57BI/6 and IL-23 deficient mice. The percentages of neutrophils in the blood and spleen were measured using flow cytometry.

Results: We have found that mice lacking IL-23 have higher bacterial burdens in the spleen and liver compared to wild type C57BI/6 mice one day after i.g. infection, suggesting that IL-23 is necessary for resistance to LM. Interestingly, neutrophil percentages do not differ in IL-23 deficient versus wild type C57BI/6 mice in the blood or spleen at one day post infection.

Conclusions: These findings suggest that mice lacking IL-23 are not able to clear LM as efficiently as wild type mice at early time-points following i.g. infection. Since neutrophil numbers were similar in both strains of mice, IL-17A/F production may not be the mechanism by which IL-23 confers resistance in an oral model of LM infection. Another cytokine downstream of IL-23, IL-22, is known to induce the production of antimicrobial peptides during mucosal infections. IL-23 induced IL-22 production may play a major role in LM clearance from the mucosal surfaces. Future studies will include comparing wild type to IL-23 deficient mice using the oral LM infection model to determine the rate of dissemination to the spleen and liver from the mucosal intestinal surface, anti-microbial peptide production, and cytokine production. In addition, IL-22 deficient mice will be studied using this oral LM model.

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## 903 (Oral)

First Author/Presenter: Adam Odeh

### Classification: GSBS Student

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# REGULATORY T CELLS DAMPEN MYCOPLASMA RESPIRATORY DISEASE SEVERITY WITHOUT IMPACTING CLEARANCE OF INFECTION

Purpose: By dampening the immune response, Tregs may have a negative effect, contributing to persistence of infection in some cases. However, depletion of Tregs in some models has resulted in damaging immunopathology, autoimmunity, and graft rejection. Our lab proposed to study the role of Tregs in the context of chronic mycoplasma infection in a mouse model. We hypothesized that depletion of Tregs would cause more severe disease, but would also result in increased clearance of the mycoplasma.

Methods: Balb/c mice were administered an anti-CD25 antibody to deplete Tregs (defined as CD4+CD25+FoxP3+) or PBS control. Mice were then infected intranasally with Mycoplasma pulmonis or broth control. Mice were weighed every other day, and then sacrificed at 14 days post-infection. Lungs were harvested, visually scored for the presence of lesions, and processed for flow cytometry staining or for counts of colony forming units (CFU). In addition, serum was collected and ELISA s run for immunoglobulin levels.

Results: Mice that were Treg-depleted and infected lost significantly more weight compared to mice that were only infected, only Treg depleted, or neither (negative control). Lungs of Treg-depleted mice showed significantly more lesions compared to mice that were infected only. Serum levels of IgG, IgM, and IgA were all significantly higher in Treg-depleted and infected mice compared to mice that were infected only. Despite drastic differences in disease severity, no difference in lung CFU counts was observed at any time point.

Conclusions: In keeping with our hypothesis, depletion of Tregs resulted in increased severity of disease in infected mice, demonstrating that Tregs are important in suppressing damaging inflammatory responses during mycoplasma respiratory disease. However, in contrast to our hypothesis, Tregs played no role in persistence of infection.

## IMMUNOLOGY

## 904 (Poster)

First Author/Presenter: Nathan Horton

Classification: GSBS Student

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CLONING OF THE LIGAND FOR NATURAL CYTOTOXICITY RECEPTOR, NKP44

Purpose: Natural killer (NK) cells represent a specialized lymphoid population of the innate immune response against tumor or virally infected cells. NK cell cytotoxicity is closely regulated by numerous inhibitory and activating receptors. Major Histocompatibility Complex (MHC) I acts as an inhibitory receptor by presenting normal self antigen on nucleated cells, thus sparing the healthy cell from NK cell mediated lysis. On cells lacking MHC I other activating receptors, such as 2B4, NKG2D, and a group termed the Natural Cytotoxicity Receptors (NCRs), induce cytotoxicity and subsequent target cell death. The NCRs play a key role in recognition and killing of MHC I deficient cells and include the receptors NKp30, NKp46, and NKp44. Binding of one or more of these receptors to specific, pathologically induced ligands induces strong NK mediated cytotoxicity, and involved in HIV infection. Ligands for NKp44 have been reported but not yet characterized. Previous work in our lab utilizing a NKp44-IgG fusion protein and FACS analysis has shown that a B cell lymphoma cell line (DB) expresses a ligand for NKp44. The purpose of this study is to clone and characterize this ligand to further understand the interactions between NKp44 and target cells.

Methods: Messenger RNA was isolated from DB cells and constructed into a directional complimentary DNA (cDNA) library for transformation into ultra competent E. coli bacteria. The cDNA library was amplified and then transiently transfected into Cos cells.

Results: The cDNA encoding the NKp44 ligand was isolated utilizing mammalian expression cloning and sequenced.

Conclusions: Characterization of this ligand and further understand of ligand/receptor interactions of NKp44 will help to develop future strategies in NK cell modulation in immunotherapy.

Sponsor: N/A

## 905 (Poster)

### First Author/Presenter: Timothy Break

Classification: GSBS Student

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# THE EXPRESSION OF EXTRACELLULAR SUPEROXIDE DISMUTASE DETERMINES THE SUSCEPTIBILITY OF MICE TO LISTERIA MONOCYTOGENES INFECTION

Purpose: Listeria monocytogenes (LM) is a gram positive bacterium used to study immune responses against intracellular bacterial infections. Neutrophils are the front-line defense of the immune system and are essential for clearance of LM by generating reactive oxygen and/or nitrogen species (ROS and RNS). These ROS and RNS contribute to inflammation, along with pro-inflammatory cytokines like interferon-gamma (IFN-g), and are neutralized by the enzyme superoxide dismutase (SOD). Previously, it was shown that extracellular SOD (ecSOD) also affects the recruitment and survival of neutrophils. The immune response to LM in the absence or overexpression of ecSOD serves as a novel approach to determine how an extracellular enzyme can affect an intracellular pathogen. In these studies, we utilize congenic mice that have varying levels of ecSOD and determine how this affects their ability to respond to infection with LM.

Methods: Mice expressing high levels of ecSOD (ecSOD high), low levels of ecSOD (ecSOD low), or lacking ecSOD (ecSOD KO), all on the C57 background, were infected with LM for 1 or 3 days and blood, spleen, and livers harvested. Spleen and liver colony forming units (CFUs) were counted to determine bacterial load. Blood and spleen neutrophil percentages were determined by flow cytometry. IFN-g concentrations were measured by ELISA in serum and cultured splenocyte supernatant.

Results: In this study, both the spleen and liver had higher bacterial burdens in the ecSOD high mice as compared to the ecSOD KO mice 3 days pi, with ecSOD low mice showing intermediate burdens. At days 1 and 3 pi, ecSOD high mice have a higher percentage of neutrophils in the blood compared to ecSOD low and ecSOD KO mice. In the spleen, higher total numbers of neutrophils were evident in the ecSOD KO mice compared to ecSOD high mice. IFN-g levels were found to be greatest from cultured splenocytes isolated from ecSOD KO mice at day 3 pi, while ecSOD high mice had very low concentrations of IFN-g.

Conclusions: The fact that ecSOD high mice are more susceptible than those lacking ecSOD, infers that ecSOD is detrimental during the early response to LM infection. Trafficking or survival of immune cells may be impaired by high levels of ecSOD, which would account for high levels of neutrophils in the blood, but reduced numbers in the spleen when compared to mice lacking ecSOD. The amount of IFN-g in the spleens 3 days pi could be indicative of the ability of mice lacking ecSOD to mount a better immune response to LM.

## IMMUNOLOGY

## 906 (Poster)

First Author/Presenter: Mukesh Sahu

Classification: GSBS Student

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ROLE OF RLIP76 IN ANTIGEN ENDOCYTOSIS AND ITS PRESENTATION

Purpose: The purpose of this study is to understand the role of RLIP76 in receptor mediated antigen endocytosis and presentation on the cell surface needed for immune response.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from human blood using Ficol-Paque Plus gradient. Adherent peripheral blood mononuclear cells (PBMCs) were cultured in medium containing GM-CSF and IL-4 for 2 to 7 days. Dendritic cell phenotype was checked for the presence of characteristic markers by flow cytometery. The effect of RLIP76 inhibition on dendritic cell maturation was checked using anti-RLIP antibody in the presence of lipopolysaccharide (LPS).

Results: The presence of RLIP76 on the plasma membrane was higher in immature dendritic cells compared to mature dendritic cells. In the presence of RLIP76 antibody, there is reduced expression of maturation markers such as: CD83, CD80, CD38, CD209, CD11c.

Conclusions: Absence of maturation markers in the presence of anti-RLIP antibody, shows that inhibited RLIP76 activity disrupts dendritic cells maturation.

Sponsor: N/A

## 907 (Poster)

### First Author/Presenter: Mayela Pedrueza

### Classification: GSBS Student

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### CHARACTERIZATION OF ANTI-MADB106 TUMOR IMMUNE RESPONSES IN VITRO

Purpose: The significance of the lymphatic system in maintaining health has been extensively recognized by the osteopathic medical profession. One method of manipulation utilized by osteopathic physicians to treat edema and infectious disease is the lymphatic pump technique (LPT). Our long-range goal is to test the efficiency of LPT at increasing anti-tumor immune responses and providing protection against tumor metastasis and development. The purpose of this study was to characterize anti-MADB106 tumor response in Fisher 344 rats. MADB106 is a chemically induced adenocarcinoma originally isolated from the lung of a Fisher 344 rat. It is commonly used to study the effects of tumor metastasis in rats.

Methods: MADB106 mammary adenocarcinoma cells were injected either intravenously or subcutaneously at concentrations ranging from 2.5-10x10<sup>6</sup> cells/ml. Fourteen days post-injection, spleens were removed and stimulated with either LPS or MADB106. Spleens from naive rats were included as controls. Enzyme linked immunosorbent assays (ELISAs) and flow cytometry were used to analyze IFN-gamma production and lymphocyte proliferation from in vitro stimulated splenocytes. Specifically, leukocyte proliferation was measured using CFSE proliferation assay.

Results: MADB106 injected animals did not develop significant indicators of cachexia such as weight loss, pain, or distress. Splenocytes from naive or MADB106 injected rats did not proliferate and did not produce IFN-gamma when cultured with media alone. However, when co-cultured with MADB106, splenocytes from MADB106 injected rats proliferated and produced similar concentrations of IFN-gamma as naive splenocytes.

Conclusions: This finding suggests that MADB106 mammary adenocarcinoma induces proliferation and IFN-gamma production by splenocytes in vitro; however, this tumor response is not mediated by antigen specific memory cells, but most likely by natural killer cells.

Sponsor: AOA 08-11-573

First Author/Presenter: Byung-Jin Kim

Classification: GSBS Student

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ADMINISTRATION OF NEUROENDOCRINE RECEPTOR ANTAGONIST AMELIORATES PULMONARY STREPTOCOCCUS PNEUMONIAE INFECTION CAUSED BY RESTRAINT STRESS IN MICE

Purpose: Stress is believed to be a link between psychosocial input and a number of factors that influence health outcomes. We previously demonstrated stress-induced modulation of pulmonary innate immune system against Streptococcus pneumoniae (S. pneumo.) infection using restraint stress (RS) mice model. We also have demonstrated that epinephrine and corticotrophin releasing hormone (CRH) can directly modulate cytokine production through receptor binding on antigen presenting cells (APC) in vitro. Furthermore, we have shown that different Th priming of CD4+ T cell was generated by epinephrine and CRH-primed bone marrow derived-dendritic cells. However, further investigations are still required to identify mechanisms of stress-related neuroendocrine factors that influence all aspects of the immune defense system. Therefore, we hypothesize that blockade of neuroendocrine factors using receptor antagonists may ameliorate the alteration of immune responses imposed by RS against S, pneumo, infection in mice.

Methods: Beta 2 adrenergic receptor antagonist, butoxamine (2 mg/kg) and CRH receptor 1/2 antagonist, astressin2B (100 ug/kg) were administered by intraperitoneal injection to 6<sup>-8</sup> week old female CD-1 mice prior to RS paradigm (each 3 hr stress for 4 days), and then S.pneumo. were inoculated intranasally (2 x 10<sup>-5</sup> CFU/ mouse).

Results: Lung CFUs in RS group was significantly higher than non-stressed (NRS) mice after 18 hr of infection; however, butoxamine and astressin2B administered mice showed significantly lower CFUs compared with RS. A similar result of CFUs was shown in spleen. In blood, astressin2B administered-mice showed significantly higher CFUs compared with NRS, RS and butoxamine administered-mice.

Conclusions: Our findings suggest that catecholaminergic neurotransmitters (CLNT) and CRH would directly and compartmentally influence generation of immune responses related with bacterial clearance or dissemination against S.pneumo. infection through receptor mediatedmechanism on immune cells or indirect mechanisms with other pathways. As a future study, we will test the direct effect of neuroendocrine factors on immune cells using adoptive transfer system of CLNT and CRH primed APC or lymphocytes to naïve animal before S.pneumo. infection. These results will provide understandings for possible mechanisms how stress can affect immune responses and, consequently, modulation of overall pathologic controls.

Sponsor: NCMHD P20MD001633

## 909 (Poster)

### First Author/Presenter: Prachi Dongre

1 in

### Classification: GSBS Student

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### MOLECULAR CLONING AND CHARACTERIZATION OF THE PROMOTER REGION OF NATURAL KILLER CELL RECEPTOR CS1

Purpose: CS1 (CRACC or CD319) is a unique member of the SLAM (Signaling Lymphocyte Activation Molecule) family. Unlike other SLAM members CS1 shows SAP (SLAM Associated Molecule) independent but EAT-2 (Ewings Sarcoma Associated Transcript) dependent signaling in human and murine NK cells. SAP is mutated in X- linked Lymphoproliferative Disease (XLPD). The SAP independent signaling property of CS1 could be harnessed to device immunotherapy for XLP. Recently multiple myeloma (MM) cells were demonstrated to over-express CS1. Humanized monoclonal antibody against CS1 is generated. It is known to induce NK mediated MM cell lysis by ADCC (Antibody Dependent Cellular Cytotoxicity). Understanding transcriptional regulation of CS1 will help identify the specific transcription factors that control CS1 expression in normal and MM cells. This information may be useful in devising immune based therapy for MM.

Methods: Transcriptional studies began with isolation of B6 mouse genomic DNA. The mouse CS1 promoter region was identified by aligning Gen Bank Accession numbers NT\_039185 and NC\_000067 using BLASTtn search program. The region upstream of the cDNA start site was identified. The putative promoter region was amplified using the Step down protocol of Polymerase Chain Reaction using sequence specific primers. The amplified fragment was gel purified and cloned into TA vector pCR2.1 from Invitrogen. Promoter deletion mutants were generated to identify the exact location of the promoter region. The promoter fragments were sub-cloned into pGL2 Basic reporter vector. Murine cell lines were screened using RT-PCR to identify cells expressing murine CS1. pGL-2- promoter constructs will be transfected into SP2/O cells. Region bearing promoter activity will be identified by luciferase assay. Gel Shift Assays will be performed to identify major transcription factors that regulate gene expression.

Results: The 5 flanking region of the murine CS1 gene was isolated by PCR. The identity of the fragment was confirmed by DNA sequencing. The isolated fragment is cloned into pCR2.1 vector. Promoter deletion mutants were generated and sub-cloned into pGL2 basic reporter vector. SP2/O cells were found to express CS1.

Conclusions: Transcriptional regulation studies will prove beneficial towards understanding the functional relevance of CS1 in the immune system and to understand its significance in XLP patients.

## IMMUNOLOGY

## 910 (Poster)

#### First Author/Presenter: Kay Kayembe

Classification: GSBS Student

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BASIC FUNCTION OF BONE MARROW DENDRITIC CELLS UNDER NEUROENDOCRINE CONTROL BRIDGES THE GAP BETWEEN STRESS AND DISEASE PATHOGENESIS DURING STREPTOCOCCUS PNEUMONIA INFECTION

Purpose: In the presence of stress, the central nervous system can communicate with the immune system to coordinate selective cellular responses. Our previous studies demonstrated contrasting immune responses during primary and secondary pneumococcal infection. Whereas stressed mice infected for the first time showed localized bacterial growth within the lung resulting in delayed sepsis, a re-infection of the stressed survivors resulted in diminished protective immunity leading to increase lethality and chronic pulmonary disease. We hypothesize that the different types of neuroendocrine factors have regulatory effects on antigen presenting cell s (APC) function during stress. The purpose of our study is to begin to define the mechanism by which neuroendocrine factors modulate dendritic cell (DC) maturation and function.

Methods: "Bone marrow-derived dendritic cells (BMDCs) were generated from bone marrow precursor cells using ecSOD congenic and knockout mice, which have C57/BL6 background. "BMDCs were cultured in the presence of epinephrine, CRH (corticotrophin releasing hormone), LPS (lipopolysacharide), and heat-killed Streptococcus pneumoniae at various concentrations and time points. "Cytokine activity by BMDCs was determined by ELISA and quantitative RT-PCR. "EcSOD expression was determined using western blotting. "MHC II and co-stimulatory surface molecule expression by BMDCs was determined by flow cytometry techniques in evaluating phenotype and maturation status.

Results: Our previous results demonstrate that exposure to CRH impacts inflammatory cytokine activity by BMDC and their ability to mediate CD4 T-cell effectors function.

Conclusions: In conclusion, we anticipate that defining the maturation and phenotype of DC in the presence of CRH will reveal hidden mechanisms through which stress can modulate protective and sensory responses associated with s. pneumonia.

Sponsor: NCMHD P20MD001633

## 911 (Poster)

### First Author/Presenter: Jong-Rok Kim

Classification: GSBS Student

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ANALYSIS OF SLAM FAMILY RECEPTORS 2B4, CS1 AND NTB-A IN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Purpose: Systemic lupus erythematosus (SLE) is a female-prone, chronic autoimmune inflammatory disease, characterized by improper regulation of B cells that leads to the production of auto-antibodies. Defective clearance of apoptotic cells by phagocytes is important contributor to the development of SLE. Linkage analyses of human chromosome and genomic characterization of murine SLE susceptible genes have suggested strong association of SLE with SLAM family receptors, such as NTB-A, 2B4 and CS-1. We hypothesize that the alterations in expression of 2B4, CS1, and/or NTB-A may mediate the immune dysregulation observed in patients with SLE. The purpose of this study is to compare surface expression of 2B4, CS1 and NTB-A on T, B, NK (natural killer) cells, and monocytes in SLE subjects versus those of healthy controls and to analyze the differential expression of splice variants of 2B4 and CS1 at molecular level.

Methods: Blood samples were obtained from 45 patients diagnosed in SLE and 31 healthy volunteers. Peripheral blood mononuclear cells were stained with fluorochrome-labeled antibodies for CD3, CD19, CD14, CD56, 2B4, CS1 and NTB-A, and analyzed by flow cytometry. Total RNA was isolated from PBMC and RT-PCR was performed for 2B4, CS1 and NTB-A. Single-stranded conformational polymorphism (SSCP)-heteroduplex mobility shift assay (HMA) was conducted for analysis of 2B4 and CS1 polymorphism.

Results: 2B4 and NTB-A expression was upregulated on T cells in patients with SLE compared to healthy controls. However, 2B4 expression was downregulated on NK cells from patients with SLE. Interestingly, SLE B cells expressed high level of CS1 and low level of NTB-A compared to healthy controls. Moreover, decreased expression of 2B4 and increased expression of NTB-A was observed on SLE monocytes compared to monocytes from healthy controls. In addition, we found different expression ratios of 2B4-A and 2B4-B as well as CS1-L and CS1-S isoforms in total PBMC in patients with SLE compared to healthy controls. SSCP-HMA analysis suggests that some SLE subjects have polymorphism in 2B4 and CS1 genes.

Conclusions: 2B4 expression was upregulated on SLE T cells but downregulated on SLE NK cells. CS1 and NTB-A was counter-regulated in SLE B cells, while 2B4 and NTB-A was counter-regulated in SLE monocytes. Differential expression of 2B4 and CS1 splice variants was also observed in SLE subjects. Therefore, SLAM family receptor 2B4, CS1, and NTB-A may play critical role in the pathogenesis of SLE.

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CHEMOKINE NEUTRALIZATION MODULATES RECRUITMENT OF INFLAMMATORY CELLS IN MYCOPLASMA PULMONIS RESPIRATORY DISEASE

Purpose: Mycoplasma pneumoniae is responsible for up to 30% of cases of pneumonia in the US each year. The murine model of M. pulmonis respiratory infection is used in our lab due to the similarities in disease pathogenesis shared with the human mycoplasma infection. Previous studies have shown the importance of inflammatory cells, notably T cells, in development of the lesions seen in this chronic respiratory disease. The goal of these experiments is to better characterize the role of chemokines in recruiting the immune cells responsible for immunopathology. This could lead to therapies that efficiently modify the immune response to diminish immunopathology and increase bacterial clearance.

Methods: Balb/c mice were infected intranasaly with 2\*10^5 CFU M. pulmonis. On days 0, 3, 6, 9, and 12 mice were given i.p. injections of antichemokine antibodies diluted in rabbit serum in order to neutralize the effects of a given chemokine or rabbit serum alone as a control. On day 14 post-infection lung tissue sections were taken and H&E stained. A previously established protocol of lung lesion scoring was used to assess immunopathology. In subsequent studies lung cells were isolated on day 14 and stained for flow cytometry with fluorochrome bound antibodies specific for CD3, CD4, CD8, B220, F4/80, CD11b, and Gr-1.

Results: Based on the lung lesion scores of the initial eleven chemokines studied, four were chosen for further investigation by flow cytometry. CCL3 and CXCL2 neutralization led to increased and decreased epithelial hyperplasia, respectively. Loss of CXCL11 resulted in a decrease in lymphoid infiltration and, unexpectedly, an increase in alveolar lesions. Neutralization of XCL1 caused marked decreases in lymphoid infiltration as well as alveolar lesions. Preliminary flow cytometry studies have not shown any statistically significant changes in cell populations and require further attention.

Conclusions: Chemokines are responsible for the recruitment of inflammatory cells to the lungs during M. pulmonis respiratory infection. Further investigation is required in order to elucidate the mechanism involved and to identify the chemokines that play the largest role in immunopathology.

Sponsor: N/A

## 913 (Poster)

### First Author/Presenter: Nicole Dobbs

124

### Classification: GSBS Student

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# MYCOPLASMA SPECIFIC LYMPHOCYTES FROM INTERFERON-GAMMA KNOCKOUT MICE DO NOT CONVEY INCREASED PROTECTION OR PATHOLOGY DURING MYCOPLASMA PULMONIS INFECTION

Purpose: Chronic mycoplasma respiratory disease has an immune response that is both protective and damaging. T cell depletion studies have demonstrated that CD8+ T cells dampen the immune response, while CD4+ T cells increase pathology and clinical disease. CD4+ T helper (Th) cells can be divided into two subclasses. Th1 cells are identified by the secretion cytokines such as interferon gamma (IFN-g), whereas Th2 cells are identified by the secretion type 2 cytokines such as interleukin 4 (IL-4). Th2 cells have been implicated in the exacerbation of airway hypersensitivity reactions in such conditions as asthma and allergies. We hypothesize that similar these diseases, Th2 cells lacking the capability to make IFN-g and forcing a Th2 phenotype, will exacerbate pathology and clinical disease when adoptively transferred into wild-type mice infected with M. pulmonis.

Methods: Wild-type (WT) Balb/cJ mice from Jackson Labs and IFN-? knockout (KO) mice (strain C.129S7(B6)-Ifngtm1Ts/J) were immunized intranasally with 5  $\mu$ g/20 $\mu$ l of mycoplasma membrane protein twice in two weeks. Lymphocytes were harvested from the lungs and LRNs and adoptively transferred into WT Balb/cJ mice via tail vein injection at 10^6 lymphocytes per mouse. Half of the recipient mice were infected with M. pulmonis and the infection was monitored for 14 days. Mice were harvest 14 days post-infection and gross lesions and colony forming units obtained.

Results: Infected mice that received KO lymphocytes demonstrated a slight increase in weight loss compared to those infected mice that received lymphocytes from WT mice. However, this difference is not statistically significant. Infiltrating lymphocyte numbers, gross lesion scores and CFUs demonstrate little to no difference between mice receiving mycoplasma specific WT lymphocytes versus KO lymphocytes, which demonstrate a Th2 phenotype.

Conclusions: In contrast to our initial hypothesis, these Th2-type mycoplasma specific lymphocytes did not have and increased pathology or clinical illness on the host during a mycoplasma respiratory infection. However, this difference may be due to the fact that the recipient mice s immune response is capable of making the critical cytokine IFN-g and thus may over compensate for the lack of IFN-g production from adoptively transferred lymphocytes. Understanding the pathologic components of the immune response to mycoplasma respiratory infections can lead us to create a vaccine that will provide protection against this communal respiratory pathogen.

Sponsor: NIH

## **MICROBIOLOGY/INFECTIOUS DISEASE**

## 1000 (Poster)

### First Author/Presenter: Sally Hoger

#### Classification: SPH Student

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### ANTIMICROBIAL PROFILING OF UNIQUE NATURAL PRODUCT AND SYNTHETIC COMPOUNDS INDICATES ACTIVITY AGAINST CLINICALLY SIGNIFICANT GRAM-POSITIVE BACTERIA

Purpose: Methicillin-resistant Staphylococcus aureus (MRSA) infections of soft tissues account for most hospital-acquired, nursing homeacquired and community-acquired infections and are a leading cause of mortality due to infection. Also other gram-positive cocci such as coagulase-negative staphylococci and streptococci have acquired significant resistance to many antimicrobial agents. Fears of further resistance of these bacteria to antibiotics have fueled efforts by us and others to discover new antimicrobial pharmacophores, because a limited number of antibiotic pharmacophores have been introduced into the clinic over the last 30 years.

Methods: Using standardized bacterial strains, growth and biofilm formation was tested by broth macrodilution assay. Briefly, tubes containing 2 mL of tryptic soy broth media were seeded with bacteria, in the presence or absence of test compound (30 μM) or antibiotic or vehicle controls, and grown for 16-20 hrs at 35 degrees Celsius. Bacterial growth was quantified by turbidity measurements at 600 nm. Biofilm was detected by staining with crystal violet when sufficiently robust. Photographs were taken for qualitative assessment, followed by quantitative assessment of solubilized crystal violet-stained biofilm by measuring absorbance at 590 nm.

Results: Several naturally-occurring or synthetic compounds that we recently discovered had activity against a patient-derived MRSA sample were screened for activity against the most prominent community-acquired and hospital-acquired variants of MRSA, as well as a panel of other standard bacterial strains, including Staphylococcus epidermidis, Enterococcus faecalis, Streptococcus agalactiae, Cellulophaga lytica, and Escherichia coli. A few compounds significantly inhibited growth and biofilm formation of two genera of streptococci, but little or no effect upon gram-negative bacillus growth or biofilm formation.

Conclusions: Compounds derived from natural and synthetic sources and bearing the same unique chemical scaffold inhibited staphylococci and streptococci growth as well as biofilm in those strains prone to producing a robust biofilm. Our profiling studies of standardized, clinically significant bacterial strains indicated that our compounds have antimicrobial activity against gram-positive, but not gram-negative bacteria.

Sponsor: Funded in part G67673 (JAS), G67722 (JAS) and ONR grant N00014-08-1-0094 (JAS)

## 1001 (Poster)

#### First Author/Presenter: Asia Quarterman

#### Classification: GSBS Student

Asia Quarterman, Byung-Jin Kim, Kay Kayembe, Ester Ma and Harlan Jones, Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, Texas 76107

### DETERMINATION OF ALPHA- AND BETA-ADRENERGIC RECEPTOR ANTAGONISTS ON J774 MACROPHAGE CYTOKINE ACTIVATION

Purpose: The purpose of the current study was to investigate the specificity of adrenergic receptor activation on cytokine gene expression by J774 cells. We hypothesize that selective adrenergic receptor activation can induce diverse cytokine responses by macrophages and dictate how they induce adaptive immunity.

Methods: J774 macrophage cells were placed in culture (2 x 105 cells per well). Following overnight adherence, cells were pretreated with LPS (2ug) for two hours, and then treated with EP (10-3M) and/or alpha- and beta-adrenergic receptor antagonists (10 -3, 10 -3.5, 10 -4, 10 -4.5, 10 -5) for an additional three hours. Following incubation, total RNA was extracted and optimization experiments were performed to establish a protocol for the determination of cytokine gene expression using quantitative real-time RT-PCR (qRTPCR).

Results: A concentration dependent yield in Total RNA was observed. The results demonstrate that the lowest yield of Total RNA by J774 cells was in response to 10-3 M of butoxamne. Whereas, treatment with 10-4.5 M demonstrated the highest yield of Total RNA as compared to untreated cells or cell exposed to LPS only. Optimization of qRTPCR conditions will be performed to evaluate TNF-alpha, IL-1-beta and IL-6 cytokine mRNA expression in future studies.

Conclusions: We anticipate that our results will demonstrate the selectivity of adrenergic receptor activation that corresponds with the type of cytokines expressed by J774 cells. Future studies will be conducted to determine how manipulation of adrenergic receptors can influence macrophage s ability to modulate adaptive immune cell function.

## MICROBIOLOGY/INFECTIOUS DISEASE

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## 1002 (Poster)

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First Author/Presenter: Nancy Aguwa

### Classification: GSBS Student

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ALPHA-TOXIN EXPRESSION AND HOST IMMUNITY IMPACT DISEASE SEVERITY IN A MOUSE SUBCUTANEOUS ABSCESS MODEL INFECTED WITH STAPHYLOCOCCUS AUREUS.

Purpose: To evaluate the combined effects of alpha-toxin expression & immune functioning on the pathology of murine subcutaneque pbscess infections caused by Staphylococcus aureus.

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Methods: S. aureus strains used in this model included the alpha-toxin positive strains, RN6202 UNT019-4 & DU1090. Alpha-toxin mutants were generated by genetically reading frame of the alpha-toxin gene (hla). Rabbit blood cells wa & in vitro growth curves were generated for all 4 strains m to infecting mice subcutaneously with bf ov gh

ne in Resi es reve 🕯 no si at strain er a 24-hr period. Hemolytic titers were 5re to 7-1 muta s com d to alp rain infinune suppressed animals subcutaneously infected with alpha produc absces that severe & 27% larger than those infected with the alpha-toxin mutants. tra re Additi of abs ested from immune suppressed animals was not significantly different for alpha-toxin **b**10 U cou es H positiv ains e abs s in immune competent mice infected with alpha-toxin positive strains were only slight more severe & It larger cted the alpha-toxin mutants. However, mean log10 CFU counts of abscesses harvested from immune competent mice 105 were si cantly higher (p < 0.05) for the alpha-toxin positive strains.

Conclusions: A clear correlation between abscess severity & alpha-toxin (hemolytic) expression was demonstrated in this model. Additionally, abscess severity was also influenced by the immune response of the host.

Sponsor: N/A

## 1003 (Poster)

### First Author/Presenter: David Ho

Classification: TCOM DO Student

David Ho (1), Tasneem Putliwala (2), Arvind Nana (3,4) and S. Dan Dimitrijevich (2,3) 1. Texas College of Osteopathic Medicine, Fort Worth, TX, 76107 2. Graduate School of Biomedical Sciences, Fort Worth, TX, 76107 3. Department of Orthopedic Surgery, UNTHSC, Fort Worth, TX, 76107 4. Department of Orthopedic Surgery, JPS Health, Fort Worth, TX, 76116

### PREVENTION OF BIOFILM FORMATION ON ORTHOPEDIC FIXATION DEVICES

Purpose: Biofilm development is a change in bacterial growth from the planktonic to an attached sessile state. They produce a protective film that protects them from the host s immune system and allow for the development of antibiotic resistance. This causes biofilm formation to be a major global surgical complication. Generally bacteria adhere poorly to smooth surfaces, but implantable metal devices have an oxidized etched surface that prevent leeching of metal ions from the devices and provide an attachment site for biofilms. Collagen films reestablish a smooth surface that will inhibit bacterial attachment while still preventing leeching of ions. We thus hypothesize that coating implantable devices with collagen type I film containing vancomycin will prevent attachment of GFP-expressing S. aureus to implanted devices within the body. The fluorescent bacteria will be visualized using fluorescence microscopy.

Methods: Stock solution of planktonically grown S. aureus made in a stock solution in brain heart infusion medium (BHI) was inoculated (1:1000 dilution) and cultured on six different substrates. These were glass, frosted glass, metal implants, collagen type I gels, collagen type I coated metal implants and vancomycin containing collagen type I gel coated metal implants. The adherence and proliferative nature of the organism was then determined using fluorescent microscopy.

Results: The coating of the experimental target surfaces was optimized and the inoculum for GFP S, aureus was determined to be at 1:1000 dilution. Observation of colony formation showed initial attachment of bacteria on all the surfaces but varied in size of the attached colonies. Survival and growth was observed to be high on frosted glass when compared with polished glass, collagen gel and the metal implants surfaces. Weak attachment was visualized for collagen gel or collagen coated metal implant surfaces. No growth was observed on the vancomycin loaded collagen coated implants. A vancomycin MEC for S. aureus was established at 160mcg/ml.

Conclusions: Collagen gel film and vancomycin loaded collagen gel films appeared to be effective protection barriers against S. aureus when applied to various surgically relevant surfaces. Strain RN6930 of S. aureus constitutively expressing GFP is a useful bacterial strain for biofilm formation studies. Labeling of other bacteria with GFP expression provides a fast and efficient method for studying a variety bacterial organisms and their tendency to form biofilms.

## NEUROSCIENCE

## 1100 (Poster)

## First Author/Presenter: A.N. de Oliveira-Pierce

Classification: GSBS Student

A.N. de Oliveira-Pierce, Pharmacology and Neuroscience Dpt., UNTHSC, Fort Worth, TX 76107 Tina K. Machu, Pharmacology and Neuroscience Dpt., UNTHSC, Fort Worth, TX 76107

### COLCHICINE MODULATION OF THE 5-HT3A RECEPTOR

Purpose: To investigate the actions of colchicine at the mouse and human 5-HT3A receptors.

Methods: Oocyte Injection: oocytes were injected with mouse or human wild-type 5-HT3A receptor cRNAs or point mutant or chimeric cRNAs transcribed in vitro. Two-electrode Voltage Clamp Electrophysiology: oocytes were recorded from days 1 7 following injection in a 100 µl recording chamber. Mutant and Chimera Construction: mutant cDNAs were made with the Transformer Site Directed Mutagenesis Kit, Clontech, Palo Alto, CA. Binding assays: for Kd determinations, homogenate was incubated at 37°C for 2 hours with various concentrations of [3H]-BRL-43694. For Ki determinations, homogenate was incubated at 37°C for 2 hours with various of serotonin and/or colchicine and [3H]-BRL-43694. Non-specific binding was measured using MDL-7222. Data Analysis: Graphpad Prism was used to calculate EC50s, IC50s and Hill coefficients as well as One-way ANOVA.

**Results:** Colchicine inhibited 5-HT evoked currents in oocytes expressing mouse 5-HT3ARs, with an IC50 of 59.5 ± 3 uM, however, coapplication of colchicine with 5-HT (< 1 mM) strongly enhanced 5-HT-evoked currents in oocytes expressing human 5-HT3ARs. Colchicine applied alone did not induce detectable currents in other mouse or human receptors. In binding studies of oocyte membranes expressing mouse or human 5-HT3A receptors, colchicine (25 nM 1 mM) revealed no displacement of [3H]- BRL-43694 at their respective Kds. Functional effects of colchicine occurred in the presence and absence of cold temperature incubation. Studies with interspecies chimeric receptors demonstrated that the distal one-third of the N-terminus is responsible for the bi-directional modulation by colchicine.

Conclusions: 1) Colchicine inhibits 5-HT-evoked currents in Xenopus oocytes expressing mouse 5-HT3ARs, however it potentiates currents evoked by low concentrations of 5-HT and inhibits function at higher concentrations of 5-HT in human 5-HT3A receptors. 2) Modulatory actions of colchicine at mouse and human 5-HT3A receptors occur independent of microtubule depolymerization. 4) The distal one-third of the N-termini of the human 5-HT3ARs confers colchicine s stimulatory and inhibitory effects. 5) Results suggest actions of colchicine at the 5-HT3A receptor are due to binding at an allosteric site.

Sponsor: NINDS

## 1101 (Poster)

### First Author/Presenter: Michael Gatch

#### Classification: Faculty

Michael B. Gatch, Theresa Carbonaro, Margaret Rutledge, Carla Elsken, and Michael J. Forster Pharmacology & Neuroscience University of North Texas Health Science Center

#### DISCRIMINATIVE STIMULUS EFFECTS OF THE HALLUCINOGEN 5-METHOXY-N-ISOPROPYL-METHYLTRYPTAMINE

Purpose: 5-Methoxy-N-isopropyl-N-methyltryptamine (5-MeO-MIPT) is a recreationally used hallucinogenic compound structurally related to other tryptamine hallucinogens. Behavioral and pharmacological effects of 5-MeO-MIPT have not been characterized in laboratory studies.

Methods: The effects of 5-MeO-MIPT on locomotor activity was tested in mice. 5-MeO-MIPT was tested in rats trained to discriminate hallucinogenic and psychostimulant compounds, including cocaine, methamphetamine, 3,4-methylenedioxymethylamphetamine (MDMA), lysergic acid diethylamine (LSD), (-)-2,5-dimethoxy-4-methylamphetamine (DOM), and dimethyltryptamine (DMT).

Results: 5-Meo-MIPT produced both stimulation and depression of locomotor activity. Depressant effects occurred within 10 minutes following 30 mg/kg and lasted 30 to 80 minutes. Stimulant effects occurred within 50 minutes following 10 mg/kg and lasted 110 minutes. Because of these two different effects on locomotor activity, 5-MeO-MIPT was tested at 15 and 60 minutes in the drug discrimination task. 5-Meo-MIPT fully substituted for DOM (ED50= 0.61 mg/kg) when tested 60 min after administration. 5-Meo-MIPT partially substituted for LSD, DMT, and MDMA at both time points, and for DOM at 15 min after administration. 5-Meo-MIPT failed to substitute for cocaine and methamphetamine. Substantial rate suppression was observed at 15 min following 2.5 and 5 mg/kg 5-MeO-MIPT. Higher doses were necessary to produce substantial rate depression at 60 min. These doses produced adverse effects, including tremors and rear leg paralysis.

Conclusions: Because 5-MeO-MIPT mostly produced only modest hallucinogenic effects and no psychostimulant effects, but produced substantial adverse effects, it may have limited abuse liability. However, because human users report that it is a very long-acting compound, testing at longer pretreatment times may be necessary to find peak effects. Alternatively, 5-MeO-MIPT may be qualitatively different from other hallucinogens.

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#### First Author/Presenter: Theresa Carbonaro

Classification: GSBS Student

Theresa M. Carbonaro, A.N. de Oliveira-Pierce, Tina Machu and Michael B. Gatch Pharmacology & Neuroscience, UNT Health Science Center, Fort Worth, TX, USA.

#### BEHAVIORAL AND MECHANISTIC STUDIES OF THE HALLUCINOGENS DIPT AND 4-OH-DIPT

Purpose: Commonly abused synthetic hallucinogens N,N-diisopropyltryptamine (DiPT) and 4-hydroxy-N,N-diisopropyltryptamine (4-OH-DiPT) produce different subjective effects (e.g., auditory hallucinations) than other well-known abused hallucinogens. Little is known of these compounds, except that both compounds bind to the 5-HT2A receptor, which is the site of action for most classical hallucinogens.

Methods: ): Drug discrimination and electrophysiology were used to investigate potential mechanisms of action. Adult male rats were trained to discriminate between commonly abused compounds and saline using a FR10 schedule of reinforcement. DOM, LSD, and DMT represented the three major classes of hallucinogens, whereas cocaine, methamphetamine, and MDMA represented the psychostimulants. DiPT and 4-OH-DiPT were tested for substitution for each of these drugs. The electrophysiology assay tested for percent inhibition of the mouse wild-type 5-HT3 receptor in frog oocyte cells.

**Results:** DiPT fully substituted for DMT and DOM and partially substituted for LSD. DiPT did not substitute for methamphetamine, cocaine or MDMA. 4-OH-DiPT fully substituted for LSD and DOM, and partially substituted for cocaine, methamphetamine, MDMA, and DMT. In the electrophysiology assay, both DiPT and 4-OH-DiPT produced significant inhibition of the 5-HT3 receptor.

**Conclusions:** DIPT and 4-OH-DIPT have discriminative stimulus effects similar to other abused hallucinogens. 4-OH-DIPT may also have some psychostimulant-like effects. Both drugs inhibited the 5-HT3 receptor, which may contribute to their other subjective effects.

Sponsor: NIDA N01DA-7-8872

## 1103 (Poster)

### First Author/Presenter: HAI QIAN

#### Classification: Postdoctoral Fellow

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### A NOVEL EMBOLIC STROKE MODEL IN RATS

Purpose: Try to make a more consistent embolic stroke model in rats.

Methods: Male Sprague Dawley rats (225-250g). Clots preparation: Blood (0.4 ml) was withdrawn from jugular vein with or without mixed with fibrinogen (5mg/ml) and thrombin (50u/ml). The blood was inject the blood into PE-50 tube and incubate at 37? for 2hr and stored at 4? over night. Then, the clots were pushed out from tube and cut into 3mm long pieces before use. Embolic MCAO: Rats were anesthetized with ketamine (60mg/kg i.p.) and xylazine (10mg/kg i.p.). The left ECA was cannulated with a PE-50 tube and the prepared clots were injected into ICA. Group I: 12 clots made from pure blood. Group II: 6 clots made from blood, fibrinogen and thrombin. Group III: 12 clots made from blood, fibrinogen and thrombin.

Results: There were significant differences in the clots' diameter (P <0.0001) and the infarction volume (P<0.01) between different groups. The lodging position and micro-structure are different between different groups.

Conclusions: Clot Preparation is the key to a successful surgery. Embolic MCAO with clots prepared from whole blood mixed with thrombin and fibrinogen is a reproducible embolic stroke model.

Sponsor: NIH

## NEUROSCIENCE

## 1104 (Poster)

First Author/Presenter: Margaret Rutledge

Classification: Postdoctoral Fellow

Margaret A. Rutledge, Kelly Wagner, Nathalie Sumien, & Michael J. Forster University of N. Texas Health Science Center, Fort Worth, TX 76107

### EFFECTS OF AGE ON VISUAL ACUITY AND WATER MAZE PERFORMANCE OF MALE C57BL/6J MICE

Purpose: There is a significant visual component to several of the behavioral tests widely employed to measure cognition in rodents. Old mice frequently perform more poorly on these than do their younger counterparts. In spatial learning/memory tasks such as the Morris water maze, mice that are able to swim directly to a visible platform are assumed to possess adequate visual ability, and any deficits in old mice are attributed to the effects of age on spatial learning/memory capacity. In the present study, we measured visual function separately from the Morris water maze by testing male C57BL/6J mice (divided into 4 groups, aged 6 to 29-mos) in a virtual optomotor apparatus (OptoMotry, CerebralMechanics, Inc.). The purpose was to assess the degree of age-related visual impairment in these mice and then to determine its potential role in subsequent deficits of spatial performance in the Morris water maze task.

Methods: Rotating vertical sine-wave gratings of various widths were projected on the chamber walls, and mice indicated by head-tracking behavior if they detected the moving stimuli. An acuity threshold for each eye was determined by the highest spatial frequency to which the animal responded.

Results: Visual acuity of the oldest mice (25 to 29-mos) was significantly less than that of the other age groups. Subsets of younger (7 to 12-mos) and of older mice (27 to 29-mos) were also tested in the Morris water maze, where older mice traveled longer distances to find the platform. The relative contribution of vision to water maze performance was examined by analyzing the correlation between acuity threshold and water maze path length.

Conclusions: When the age of the mouse was not taken into account, visual acuity had a modest predictive relationship to spatial maze performance. However, the correlation was no longer significant if only the older (or only the younger) mice were considered. Age had a negative effect on both vision and water maze performance, but the weak association between the two measures in older mice suggests that age-related deficits in visual acuity and spatial learning/memory occur independently.

Sponsor: N/A

### - An atom to fight

## 1105 (Poster)

First Author/Presenter: Ethan Poteet

Classification: GSBS Student

Ethan Poteet - student, Fort Worth, Tx. 76107 Shaohua Yang - PI, Fort Worth, Tx. 76107

### EFFECT OF NEURONALLY DERIVED STEM CELLS ON BRAIN REPAIR AFTER MIDDLE CEREBRAL ARTERY OCCLUSION

Purpose: This study will determine long term effects of stem cells derived from postnatal brain on neural repair and functional recovery after ischemic stroke, as well as stem cell localization in other body tissues.

Methods: We will use the Middle Cerebral Artery Occlusion (MCAO) model to induce a focal ischemia in mice. Stem cells will be obtained in advance from postnatal Green Fluorescent Protein (GFP) expressing mice and grown in culture for 2 to 3 weeks. Stem cells will be delivered by intra-arterial injection post ischemia. Stem cell distribution will be characterized with immunohistochemistry, western blot, and flow cytometry. Behavior will be examined using rotorod and the Morris water maze to asses changes in motor learning and spatial learning respectively

Results: We have successfully harvested neural stem cells from postnatal C57BL/6 mouse pups. These have been grown for 2-3 weeks where they formed neurospheres. The cells have been characterized with flow cytometry, western blots, and immunofluorescence using the neural stem cell marker nestin (intermediate filament) and the undifferentiated embryonic stem cell marker, sox2 (transcription factor).

Conclusions: N/A

## NEUROSCIENCE

## 1106 (Poster)

First Author/Presenter: Ran Liu

Classification: Staff

Ran LIU1, Xiaofei WANG1, Evelyn PEREZ1, Yi WEN1, Jie SUN2, Robert MALLET2, Shaohua YANG1

THE EFFECTS OF PYRUVATE ON APOPTOSIS AND BLOOD BRAIN BARRIER BREAKDOWN FOLLOWING TRANSIENT CEREBRAL ISCHEMIA IN RATS

Purpose: Our previous data show that pyruvate protects neuronal cells through its antioxidant actions on mitochondria in a murine hippocampal cell line. In the present study we investigated the effect of pyruvate on ischemic lesion volume, blood-brain barrier (BBB) integrity, and apoptosis following transient cerebral ischemia in rats.

Methods: Ovariectomized female Sprague-Dawley rats were subjected to 2 hours of transient focal cerebral ischemia followed by 24hours of reperfusion using a suture middle cerebral artery occlusion (MCAO) model under isoflurane anesthesia. Pyruvate or sodium chloride was administered through intravenous perfusion at the rate of 0.05mmol/min/kg with a syringe pump immediately after MCAO until 1 hour after reperfusion, respectively. Ischemic lesion volume was determined by 2, 3, 5-triphenyltetrazolium chloride staining. Blood-brain barrier integrity was assessed by IgG immunoreactivity. Apoptosis was examined by analyzing DNA fragmentation with TUNEL assay.

**Results:** Treatment of pyruvate significantly reduced the infarct volume by 84% compared to control group. The immunostaining for immunoglobulin (IgG) was dramatically increased in the ischemic cortex and subcortex of the sodium chloride treated group. Pyruvate treatment significantly decreased the IgG extravasation in the ischemic area. In sodium chloride treated control group, TUNEL positive cell represented 75% of all cells in the ischemic area, which was reduced to 14% upon pyruvate treatment. There was a strong positive correlation between ischemic lesion volume assessed by TTC stains and the number of TUNEL positive cells counted in these brains.

Conclusions: Collectively, these data indicated that pyruvate protects against transient cerebral ischemia when administered immediately after stroke at least in part by reduces BBB damage and neuronal cell loss. Therefore, pyruvate can be a potential candidate for the treatment of ischemic stroke.

Sponsor: American Heart Association, Inc. Texas Affiliate; NIH NIH R01 NS054687; NIH R01 NS054651;

## 1107 (Poster)

First Author/Presenter: Zhang Zhang

### Classification: GSBS Student

ZHANG ZHANG and JAMES W. SIMPKINS. DEPARTMENT OF PHARMACOLOGY AND NEUROSCIENCE, UNTHSC, FORT WORTH, TX 76107

OKDAIC ACID INDUCED TAU PHOSPHORYLATION AND TAU PROTEIN KINASES IN AN ESTROGEN REVERSIBLE MANNER

Purpose: The imbalance between tau protein kinase and phosphatase leads to tauopathy in Alzheimer's Disease (AD) and estrogens may exert their neuroprotective effects by reestablishing the balance between tau protein kinase and phosphatase.

Methods: Ovariectomized female rats were used to produce an AD model by microinfusion of Okadaic acid (OA) into the dorsal hippocampus unilaterally. Also, SH-SY5Y cells were used to test the neuroprotective potency and mechanisms of estrogen effects on tau phosphorylation.

Results: Our previous data showed that infusion of OA into the dorsal hippocampus can induce cognitive deficiency in rats. The present data showed that OA can induce tau phosphorylation (T205) in cortex and hippocampus with minor change of non-phospho-tau protein. Our results also showed that high dose OA can induce an increase of certain tau protein kinases, including cdk5 and GSK3ß, in both hippocampus and cortex. These results were consistent with our in vitro data that OA induces tau phosphorylation and increase of cdk5 and GSK3ß in a SH-SY5Y cell line. We also observed that 17ß-estrodial inhibits tau phosphorylation (T205) and increase of cdk5 and GSK3ß in vitro.

Conclusions: We conclude that the inhibition of phosphatase leads to tauopathy and estrogen exerts its neuroprotective effects by reestablishing the balance between tau protein kinases and phosphatase.
## NEUROSCIENCE

### 1108 (Poster)

First Author/Presenter: Akiko Dohi

Classification: GSBS Student

Akiko Dohi, Cathy L. Bell-Horner, Zhen-lan Chen, Quynh Nguyen, Glenn H. Dillon, Meharvan Singh University of North Texas Health Science Center

ERK-MEDIATED REGULATION OF GABA-A RECEPTOR FUNCTION AND INVESTIGATION OF DIRECT PHOSPHORYLATION SITE WITHIN THE ALPHA1 SUBUNIT

Purpose: Our laboratory has established that progesterone elicits the phosphorylation of ERK, a key effector of the ERK/MAPK pathway. Recently, we found that inhibition of the ERK/MAPK pathway enhanced the function of GABA-A receptor, leading us to postulate that activation of the ERK/MAPK pathway (and possibly, progesterone) inhibits the GABA-A receptor. Since the a1 subunit contains a minimal consensus ERK1/2 phosphorylation site, we hypothesized that the effects of ERK on GABA-A receptor function were associated with the direct phosphorylation of the a1 subunit of the GABA-A receptor.

Methods: Using HEK-t cells that were transiently transfected with FLAG tagged-a1 (or its mutated counterpart, where the putative ERK phosphorylation site (T375) is mutated to an alanine), ß2, and ?2 subunits of GABA-A receptor, we evaluated whether HGF, an activator of the ERK pathway in these cells resulted in an inhibition of GABA-gated currents as well as a concomitant phosphorylation of the a1 subunit.

Results: Patch clamp electrophysiology confirmed that the wild type and mutant GABA-A receptor was expressed and functional. We found that mutation of the putative ERK phosphorylation site did prevent the enhancement in GABA-gated currents elicited by the ERK/MAPK inhibitor, U0126. HGF, on the other hand, while eliciting a robust increase in ERK1/2 phosphorylation, did not elicit an increase the phosphorylation of the a1 subunit.

Conclusions: Our results do not support the hypothesis that the effect of the ERK/MAPK pathway on GABA-A receptor function is mediated by direct phosphorylation of the a1 subunit.

Sponsor: N/A

## 1109 (Poster)

#### First Author/Presenter: Anne Ngobia

#### Classification: TCOM DO Student

Anne Ngobia, Kun Don Yi, James W. Simpkins. University of North Texas Health Science Center, Department of Pharmacology and Neuroscience, Fort Worth, TX 76107

#### ESTROGEN ANALOGUES PROTECTS CELLS AGAINST IODOACETIC ACID INDUCED CELL TOXICITY IN HT-22 CELLS

Purpose: Questions concerning the use of estrogen replacement therapy for women in menopause has come under fire in the last few years due to the results of the Women s Health Initiative studies which found that women on estrogen alone or with progesterone were at greater risk of breast and ovarian cancers, cardiovascular events, and neurodegeneration. Therefore, development of estrogen analogues, which retains the neuroprotective effects but has minimal interaction with the estrogen receptors thought to be involved in the detrimental effects of estrogens, will be beneficial for women and men. Therefore, estrogen analogues with substituted groups on the estrogen backbone that show little binding to either estrogen receptors were tested for neuroprotective properties against cytotoxicity in an in vitro model of oxidative stress.

Methods: HT-22 cells (immortalized mouse hippocampal neuronal cell line) were exposed simultaneously to different concentrations of ZYC and iodoacetic acid (IAA). Cell viability was measured by Calcein AM, a non-fluorescent, electrically neutral nonpolar analog of fluorescein diacetate, which passively crosses cell membranes and is cleaved to a fluorescent derivative by nonspecific intracellular esterases. Once cleaved in viable cells, the resultant fluorescent salts are retained by intact cell membranes.

Results: IAA caused a dose-dependent decrease in cell viability. Simultaneous 17beta-estradiol treatment showed significant protection against IAA induced cell death. Three different estrogens analogues, ZYC 10, ZYC 26, and ZYC 58, also antagonized the cell death inducing effects of IAA in a dose-dependent manner when treated simultaneously.

Conclusions: The neuroprotective effects of estrogens are receptor-independent mediated events since estrogen analogues that do not bind to the estrogen receptor are as effective as 17beta-estradiol in protecting neurons against IAA-induced cytotoxicity.

Sponsor: AG 10465 and AG 22550

#### First Author/Presenter: Kathryn Kaiser

Classification: GSBS Student

Kathryn A. Kaiser1, Susan F. Franks1, Adam B. Smith21. Psychiatry, University of North Texas Health Science Center, Fort Worth, TX, 76107.2. Fort Worth Lap Band, Fort Worth, TX, 76102.

#### SUPPORT GROUP ATTENDANCE IMPROVES POST-OPERATIVE WEIGHT LOSS

Purpose: Modification of behavioral factors following bariatric surgery is critical for the long-term weight loss necessary for optimal health improvement. To achieve this goal, aftercare programs typically offer optional participation in a post-surgical support group. Yet, there is little information available regarding the impact of the frequency of support group attendance on outcomes in laparoscopic banding patients (LAGB). The purpose of this study was to investigate the relationship between support group attendance and weight loss in LAGB.

Methods: A retrospective review of 1132 LAGB patients was conducted from a single practice where a no-cost, weekly, professionally-led support group was offered. Patients with follow-up data for one year (N=104) were divided into 3 groups based on support group participation: None, n=73; Occasional (1-4 times), n=22; and Frequent (5-17 times), n=9. Percent excess weight loss (%EWL) was compared between groups using one-way ANOVA.

**Results:** There were no significant pre-operative differences in weight parameters between groups. The overall difference in %EWL at 12 months was significant, F(103) = 3.403, p = .037. See table for between groups ANOVA.

Conclusions: Results indicate that patients who regularly attend support group have improved rates of %EWL one-year post-LAGB. Post-surgical support group participation should be strongly encouraged to help optimize surgical outcomes. Future studies should examine patient motivational characteristics relative to timing of attendance to determine the independent influence of support group participation.

Sponsor: N/A

### 1201 (Poster)

First Author/Presenter: Kathryn Kaiser

Classification: GSBS Student

Kathryn Kaiser(1), Susan Franks(1), Joan Carroll(1), Adam Smith(2) 1. University of North Texas Health Science Center, Fort Worth, Texas, 76107 2. Fort Worth LAP-BAND, Fort Worth, Texas, 76102

#### EFFECTS OF BARIATRIC SURGERY ON THE RELATIONSHIP BETWEEN GLUCAGON, INSULIN AND HUNGER

Purpose: Bariatric surgery candidates are frequently insulin-resistant if not frankly diabetic. Associated with this is disruption in the interplay between insulin and glucagon in the regulation of blood glucose. This study examined the relationship between insulin, glucagon and self-reported hunger and disinhibition as measured by the Eating Inventory after laparoscopic adjustable gastric banding (LAGB).

Methods: 30 obese (19 women, group BMI M=42.8 kg/m2, SD=5.0) LAGB patients were evaluated prior to surgery (T1) and 6 months later (T2). 30 age-matched, normal weight controls (NWC, 21 women, group BMI M=22.2, SD=1.9 kg/m2) were evaluated using the same measures. The Eating Inventory was used to assess Disinhibition (D) and Hunger (H). Glucose, insulin and glucagon were measured at fasting (F) and 30 minutes PP using a mixed-macronutrient, liquid meal. Hormone absolute change (AC), and change ratios (CR) were calculated at T1 and T2 based on F and PP values. Fasting HOMA scores were calculated for between-group and within LAGB group post-surgical comparison. LAGB and NWC were compared using ANOVA and t-tests. Correlations between EWL, H, D, hormone AC, and hormone CR at T2 were examined.

**Results:** HOMA scores improved for LAGB, t(28) = 5.17, p <.001, yet were significantly higher than NWC at six months post-surgery, t(58) = 5.497, p <.001. HOMA changes 6 months after LAGB were not significantly correlated with %EWL (r = .108, p = .289). At T2, %EWL was significantly and negatively correlated with H (r = -.313, p = .05, one-tailed) as well as insulin CR (r = .36, p = .028, one-tailed) in LAGB. For LAGB at T2, %EWL approached having a significant correlation with fasting glucagon (r = -.26, p=.08, one-tailed) and post-prandial glucagon (r = -.25, p = .09, one-tailed), but not the glucagon AC or CR. No other correlations were significant. While H and D dropped significantly from T1 to T2 in LAGB, D remained higher at T2 in LAGB than in NWC, F(1,59) = 6.29, p = .015.

Conclusions: The post-surgical changes in glucagon and insulin interplay merit further investigation using meal challenges of a more ecologically valid composition and with persons of a higher degree of dysfunctional eating behavior, e.g. Binge Eating Disorder. Longer evaluations of these measures are warranted to see how quickly/to what degree insulin sensitivity improves post-LAGB and if changes in glycemic control correspond to changes in eating behavior and/or %EWL. (Funding H75/CCH224064, CDC-UNTHSC DREAMS)

Sponsor: H75/CCH224064, CDC, Div. of Diabetes Translation, UNTHSC DREAMS Project

## PSYCHOLOGY

## 1202 (Poster)

First Author/Presenter: Praveen Penagaluri

Classification: SPH Student

Rif El-Mallakh, M.D., Univ of Louisville, KY Praveen Penagaluri, M.D., Univ of Louisville, KY Kristin L Walker, B.A., Univ. of Louisville, KY

HALLUCINATIONS, PSEUDOHALLUCINATIONS, AND SEVERITY OF SUICIDAL IDEATION AMONG EMERGENCY PSYCHIATRY PATIENTS: A PILOT STUDY

Purpose: This study investigated relative relationships between auditory hallucinations and non psychotic hallucinations (pseudohallucinations), and suicidal risk

Methods: A sample of 206 consecutive patients seen in an emergency psychiatric service was evaluated for the presence and intensity of hallucinatory experiences (the hallucination item of the Positive and Negative Symptoms Scale), suicidal intensity (the suicide item of the Montgomery Asberg Depression Rating Scale), and cumulative suicide risk (the total number of risk factors).

Results: Individuals with non psychotic hallucinations experienced greater intensity of suicidal ideation versus subjects with no hallucinations or subjects with psychotic hallucinations (P = 0.0001).

Conclusions: Pseudohallucinosis is associated with higher intensity of suicidal ideation compared psychotic hallucinations or no hallucinations Sponsor: N/A

Clade/Boation: CSRS Student

Variation Katheyn Kalaer

lik Alatan Franksti), Joan Carnali (1), Adam Smith(2) 1: Unkternity of North Taxas Health Schriete Clenter, Fort Wards, Tenne little (144-84MD, Fort Wards, Tenne, 78102

MATRIC SUNCERY ON THE RELATIONSHIP SETWEEN GLUDDAGON, INSULIN AND HUNGER

An end of supery conditions are frequently insulta-metateric if not framidy diabetic. Associated with this is duruption in the frampley and grid glucagon in the regulation of blood glucase. This study eramined the relationship between insulin, glucagon and selfrest and distribution as measured by the Eating Inventory after locameccyle adjustable gratitic beneficy (LAGB).

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A sense improved for UAGE, 1(38) = 5, 17, p < 001, yet vaste significantly telefor (tash NWC at alk months post-surgery, 1(38) = 4. Accustively consisted with 16 (\* - -313, o = -05, one-tailed) as well as insuln CR (\* - 36, p = -365, one-tailed) in UAGB. For UAGB and accustively consisted with 16 (\* - -313, o = -05, one-tailed) as well as insuln CR (\* - 36, p = -365, one-tailed) in UAGB. For UAGB and accustively consisted with 16 (\* - -313, o = -05, one-tailed) as well as insuln CR (\* - 36, p = -365, one-tailed) in UAGB. For UAGB and the set works a significant completion with fabring (subspon (\* + -26, p = 05, one-tailed) and post-prevails globagen (\* - -25, p and be not the glucopen AC or CR. No other consistence were confident. While H and D dropped significantly from 15 to 72 in and tailed at 12 in UAGB than to NWC, F(1,56) = 0.25, p = .053.

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Republic COC. Div. of Disbetts Translation, UNTHSC DREAMS President

First Author/Presenter: Jamie Huff

#### Classification: Dual Degree Student: DO/PhD

Jamie Huff, BS, OMS-III, PDF1, Xin Zhang2, Hollis H King, DO, PhD1, and Lisa M Hodge, PhD1,2. Department of Osteopathic Manipulative Medicine, 2 Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, TX.

LYMPHATIC PUMP REDUCES PULMONARY BACTERIAL LOAD AND INCREASES LEUKOCYTES IN AN EXPERIMENTAL PNEUMONIA MODEL

Purpose: The lymphatic system transports the fluid component of blood that seeps out into tissues back to circulation, as well as lymphocytes and antigen from tissue to organized lymphoid tissue for recognition and activation. Osteopathic physicians utilize manipulative medicine techniques to enhance the body s natural immune defenses. One such technique, the lymphatic pump technique (LPT), has been shown to enhance lymph flow and increase the leukocyte output in the thoracic and intestinal duct in an animal model. Clinical studies suggest that these techniques can increase delivery of antibiotics, increase vaccine response, and decrease the length of hospital stay and need for antibiotics in patients with pneumonia; however, there is very little scientific evidence to support its clinical use. In this study, we wanted to determine 1) if a single application of LPT could increase blood leukocytes in healthy animals and 2) if the daily application of LPT during acute Mycoplasma pulmonis infection could decrease the severity of disease or influence leukocyte redistribution.

Methods: In order to determine the effects of a single application of LPT, blood samples were collected before, immediately following LPT or sham treatment, and up to 2 hours after treatment. In a separate set of experiments, Lewis rats were infected intra nasally with 5 x 105 bacterial colony forming units (CFU) of M. pulmonis. On days 1-5 post infection, rats received either LPT (4 minutes LPT under anesthesia), sham (4 minutes light touch under anesthesia), or control (infected untreated no anesthesia). Cardiac blood and lung leukocytes were enumerated, pulmonary CFU were determined, and serum was analyzed for M. pulmonis specific antigen by enzyme linked immunoabsorbant assay (ELISA).

Results: In healthy rats, at 45 minutes following LPT, blood leukocytes were significantly increased as compared to sham (p < 0.05) bacterial numbers compared to sham and increased the number of pulmonary leukocytes and M. pulmonis specific IgG in the serum.

Conclusions: These findings may be responsible for reducing the impairment of bacterial clearance seen with anesthesia, but further studies need to be completed. Overall, these studies suggest a clinical benefit for the use of LPT and begin to elucidate a possible mechanism for this benefit.

Sponsor: American Osteopathic Association Grant #06-11-542

## 1301 (Poster)

#### First Author/Presenter: Artur Schander

#### Classification: Dual Degree Student: DO/PhD

Principle Investigator: Lisa M. Hodge, Ph.D CO-Investigator: H. Fred Downey, Ph.D. Primary Student investigator: Artur Schander, M.S.; D.O./Ph.D student Clinical support: Hollis H. King, D.O. Ph.D. Student investigators contributed: Melissa K. Bearden, M.S., Jamie B. Huff, D.O./Ph.D. student Research Associate: Arthur Williams, Jr. University of North Texas Health Science Center, Fort Worth, TX 76107

#### LYMPHATIC PUMP TECHNIQUE ENHANCED LEUKOCYTE RELEASE FROM ABDOMINAL ORGANS: A NOVEL IMMUNOTHERAPY.

Purpose: A group of osteopathic manipulations known collectively as the lymphatic pump techniques (LPT) are designed to enhance lymph return from specific areas of the body. These treatments are thought to aid the removal of cellular wastes, toxins, and bacteria from the interstitial fluid in addition to reducing edema. Further, LPT has been reported to enhance immune function. Previously, we demonstrated that LPT increased leukocyte counts in thoracic duct lymph; however, the tissue source of these mobilized leukocytes was unknown. Earlier studies indicated the gastrointestinal lymphoid tissue (GALT) as a possible source. LPT, specifically abdominal LPT, most likely compress organs and tissues and releases pooled leukocytes into the lymph and blood circulation. This leads to an accelerated transit of leukocytes through lymphatic and blood circulation and thus can possibly be used as an adjunct immunotherapy by physicians. The purpose of this study was to determine if LPT would immediately increase the release of leukocytes from the gastrointestinal lymphoid tissue, mesenteric lymph nodes (MLN), and the spleen into lymph and blood circulation.

Methods: To determine the acute effect of LPT on thoracic and intestinal lymph, a catheter was inserted into either the thoracic or the large intestinal lymph ducts or the veins of above mentioned organs. In addition, the MLN were fluorescently labeled in situ. Lymph samples from the abdominal and thoracic duct, as well as blood samples from the splenic vein and other peripheral veins were collected during 4 min of baseline, 4 min of LPT, and 10 min following cessation of LPT.

Results: LPT accelerated leukocyte flux in the thoracic duct and intestinal lymph respectively from a baseline of  $8.88 \pm 2.0 \times 106$  to a peak value of  $153 \pm 67 \times 106$  cells/min and  $2.1 \pm 0.25$  cells/min to a peak of  $25.0 \pm 6.2$  cells/min at 2 min LPT(P < 0.01, vs baseline). LPT also increased flux of CD4+ T cells, CD8+ T cells, and IgA+ and IgG+ B cells in intestinal lymph. Furthermore, LPT increased the release of leukocytes, and specifically lymphocytes, from the spleen by approximately 4-fold.

Conclusions: LPT facilitates the release of leukocytes from abdominal organs and tissues. The enhanced release of leukocytes during LPT may provide scientific rationale for the clinical use of LPT to enhance immunity and treat infection.

Sponsor: NIH-NCCAM; AOA

#### 1400 (Poster)

First Author/Presenter: Pabak Sarkar

#### Classification: GSBS Student

Pabak Sarkar, Zygmunt Gryczynski, Rafal Luchowski, Ignacy Gryczynski. Center For Commercialization of Fluorescence Technologies, Department of Molecular Biology and Immunology, Department of Cell Biology and Genetics, UNTHSC. Fort Worth, TX - 76107

CHARACTERIZATION OF NOVEL GROUP OF FLUOROPHORE TO IDENTIFY SUITABLE 'DONOR' FOR LONG-WAVELENGTH FORSTER RESONANCE ENERGY TRANSFER STUDIES IN CELL CULTURES

Purpose: To identify a fluorophore, from a set of newly developed dyes suitable, to be a donor in Forster Resonance Energy Transfer (FRET) experiments that use change in fluorescence lifetime to measure the molecular distance. Using fluorophores with fluorescence in long wavelengths for FRET experiments we can safely neglect the conventional autofluorescence background which introduces noise in measured data.

Methods: We used absorption and steady-state fluorescence measurements to calculate the relative quantum yields of the new dyes. We measured the fluorescence decay and calculated average fluorescence lifetimes of those dyes. Also, photostability of these dyes were measured using direct illumination from a 7W white light source.

Results: DyLight 594 conjugated with immunoglobin has a broad excitation range and a significant average fluorescence lifetime of 4.12 nsec and shows moderate stability when continuosly illuminated to white light source. It is also not sensitive to temperature between 5C to 55C

Conclusions: DyLight 594 conjugated with immunoglobin is a better donor at long wavelength range. It is brighter than the conventional conjugated dyes in this region, has a significant lifetime and is not easily photobleached during the course of measurements. As it fluoresces at long wavelength, its signal-to noise ratio is better in cytochemical experiments where auto-fluorescence can introduce significant amount of noise in shorter wavelengths.

Sponsor: N/A

## 1401 (Poster)

#### First Author/Presenter: Christian Ramirez

Classification: McNair/SMART Participant

RAMIREZ C.E. AND ALVAREZ-GONZALEZ, R. Graduate School of Biomedical Sciences, The University of North Texas Health Science Center at Fort Worth.

# CHARACTERIZATION OF POLY(ADP-RIBOSE), (AN EUKARYOTIC NUCLEIC ACID), BY ELECTROHORESIS AND SILVER STAINING USING THE PHASTSYSTEM

Purpose: The purpose of this experiment is to modify the PhastSystem (an automated electrophoretic system), and the process of separating proteins to run gels, with nucleic acid samples as well as the verification of the presence of a specific nucleic acid. For this experiment, the nucleic acid known as poly (ADP- ribose) was utilized.

Methods: 1) Enzyme Assay. Rat liver chromatin was incubated with NAD+, and Type XV Calf Thymus DNA, at 37° C for 30 min to enzymatically produce protein-bound poly(ADP-ribose. After obtaining the maximum amount of poly(ADP-ribose), precipitation was done in 20% Trichloracetic acid to form a pellet with proteins and nucleic acids. Finally, EDTA and KOH were added to break down proteins leaving the nucleic acid intact. 2) Purification of Poly(ADP)ribose: Purification was carried by Affinity Chromatography with a boronate resin made specifically to bind moecules with at least two free ribose rings. 3) Lyophilization: Purified poly (ADP- ribose) was lyophilized (Labconco lyophilizer) to obtain a dry solid. 4) The PhastSystem: After lyophilization, the sample was ready for electrophoresis. Native buffer strips were treated with a (Tris Borate EDTA), with a pH appropriate for nucleic acids. The gels utilized here were 20% homogenous polyacrylamide gels. 5. The Staining Process: We used 0.4% Silver nitrate to stain gels with DNA-containing chromatin samples or boronate purified poly(ADP-ribose), separately.

Results: Before running the sample containing pure poly (ADP- ribose), controls proved that our final sample was a nucleic acid. The controls involved running both, protein and nucleic acid samples, in our case, either pure core histones or chromatin DNA, respectively. Two different types of staining were used (Comassie blue and Silver staining). The results observed for all control samples were positive which confirmed the notion that poly (ADP- ribose) would be visible through the PhastSystem, after silver staining.

**Conclusions:** The control experiments that were performed proved that, indeed nucleic acids from mammalian chromatin can be resolved through a 20% gel on the PhastSystem. In fact, pure DNA fragments and DNA were visible (figure 2), thus showing that nucleic acids can run through the PhastSystem gel and can be stained with silver. The same was observed for chromatographically purified poly(ADP-ribose) samples.

## 1402 (Poster)

#### First Author/Presenter: Jia Guo

### Classification: GSBS Student

Jia Guo, Katalin Prokai-Tatrai2, Laszlo Prokai1. 1 Department of Molecular Biology and Immunology, 2 Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, 3500 Camp Bowie Blvd, Fort Worth, Texas 76107

### SELECTIVE ENRICHMENT OF NITRATED PEPTIDES FOR THE SURVEY OF THE NITROPROTEOME

Purpose: In this study, we identified nitration sites of bovine serum albumin under chemical and biological nitration conditions to create a set of reference peptides for method development. We have developed a method for the enrichment of nitrotyrosine-containing peptides by using carbon tagging followed by solid-phase hydrazine chemistry.

Methods: We employed tetranitromethane and sodium peroxynitrite treatments for chemical and in vitro biological nitration, respectively. The nitration sites were identified by liquid chromatography tandem mass spectrometry (LC MS/MS). For the enrichment of nitrotyrosine-containing peptides by LC MS/MS, the nitrotyrosines in the peptides were converted first to the corresponding amino-tyrosines followed by aldimine formations using a formyl succinate. Then carbolylated peptides were enriched by solid-phase hydrazide chemistry using hydrazone beads on glass.

Results: The nitration sites of bovine serum albumin were different under conditions mimicking biological nitration, when compared to products of chemical nitration. The nitrotyrosines in a model peptide could be converted to the carbonylated tyrosines for capture by solid-phase hydrazide chemistry.

**Conclusions:** Protein nitration is dependent on the conditions employed. Therefore, effects of this posttranslational modification on protein activities may be different under various conditions of nitrosative stress. The nitrotyrosine-containing peptides can be enriched by solid-phase hydrazide beads after specific derivatization. This enrichment method has a potential to enable the exploration of the nitroproteome from organelles, cells or tissues.

Sponsor: N/A

## 1403 (Poster)

#### First Author/Presenter: Navin Rauniyar

Classification: GSBS Student

Navin Rauniyar, Katalin Prokai-Tatrai, Laszlo Prokai; University of North Texas Health Science Center, Fort Worth, TX-76107

#### TARGETS FOR COVALENT MITOCHONDRIAL PROTEIN MODIFICATION BY REACTIVE CARBONYL STRESS MEDIATED BY 4-HYDROXY-2-NONENAL, AN END-PRODUCT OF LIPID PEROXIDATION

Purpose: ROS generated during oxidative stress can lead to unfavorable cellular consequences, predominantly due to production of HNE during lipid peroxidation that subsequently causes RCS on the cellular proteome. The objective of this study is to identify and characterize selectivity of HNE modifications to rat brain proteins.

Methods: Mitochondrial proteins from rat brain were treated with HNE in vitro and subsequently digested with trypsin. HNE modified tryptic peptides were enriched by a solid-phase reversible hydrazide chemistry to capture and, then, release HNE-modified peptides from complex mixtures. The released peptides were analyzed by data-dependent liquid chromatography tandem mass spectrometry (LC-MS/MS). The collected tandem mass spectra were extracted by BioWorks version 3.3 and searched against the IPI rat protein sequence database using the Mascot search algorithm. Additionally, bioinformatics (Ingenuity Pathway Analysis) was used to identify biological pathways, networks, and functions significantly altered by such modifications.

Results: The use of solid-phase hydrazide enrichment strategy and mass spectrometry-based approach enabled identification of HNE-modified peptides in rat brain mitochondria. The modification primarily comprised of Michael addition on histidine residues as the increase in mass was by 156 Da with each HNE adduct. Several tryptic peptides of rat brain mitochondrial proteins were found to be HNE-modified in the eluted fraction of solid-phase hydrazide beads including ATP synthase subunit beta, aconitate hydratase, creatine kinase (Ckb and Ckmt1), glutamate dehydrogenase 1, isoform IA of synapsin-1, isoform 1 of syntaxin-binding protein 1 and others.

Conclusions: Identification and characterization of site of HNE modification in proteins is challenging because of the substoichiometric nature of such modifications. The front-end enrichment of HNE-modified peptides from complex mixtures of tryptic peptides by solid-phase hydrazide strategy facilitated identification of HNE modification sites on various mitochondrial proteins of the brain. When searched in the Ingenuity Pathway Analysis Database, oxidative stress was found to be the top toxic event associated with these proteins. Therefore, proteins HNE-modified mitochondrial proteins due to RCS can be promising biomarkers of oxidative stress. This work was supported by the grant AG025384 from the National Institutes of Health.

Sponsor: NIH

## 1404 (Poster)

First Author/Presenter: Tatjana Talamantes

Classification: GSBS Student

Tatjana Talamantes, Navin Rauniyar, Laszlo Prokai; University of North Texas Health Science Center, Fort Worth, TX-76107

DETECTION OF OXIDATION-ASSOCIATED IN VIVO CARBONYLATION OF BIOLOGICALLY SIGNIFICANT PROTEINS DURING EARLY DEVELOPMENT OF ZEBRA FISH EMBRYOS

Purpose: The focus of this study is to determine and identify oxidation-associated in vivo carbonylation of specific proteins under HNE treatment using the zebra fish vertebrate model. Zebra fish are a major model organism that is widely utilized for studying development due to its annotated and sequenced genome and many beneficial innate qualities and biological similarity to humans.

Methods: Embryos of Danio rerio were separated for viability and incubated at 27°C in embryo media. Forty eight hours post fertilization; half of the sorted embryos were treated with HNE in vivo and proteins were extracted from embryos, reduced, alkylated and subsequently digested with trypsin. HNE modified tryptic peptides were reacted overnight with a solid-phase reversible hydrazide reagent to capture and then release HNE-modified peptides from the peptide mixture. Validation of peptide-based protein identification, sequencing, and PTMs were analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). Tandem mass spectra were extracted by BioWorks version 3.3 and searched against the IPI zebra fish protein sequence database using the Mascot search algorithm. Data was integrated into bioinformatics (Ingenuity Pathway Analysis) to identify biological pathways, networks, and functions significantly altered by such modifications.

Results: Utilization of mass spectrometry-based techniques along with the solid-phase hydrazide reagent, allowed for identification of HNEmodified peptides in zebra fish embryos. Identified proteins were modified on histidine residues these included but not limited to ATP synthase subunit beta, an important mitochondrial protein.

Conclusions: HNE is known to alter protein function and disrupt cellular mechanisms. It has also been associated with aging and involved in the onset and progression of various diseases including neurodegenerative diseases and cancer. Identification of PTMs involving this highly cytotoxic, reactive aldehyde to proteins will aid in understanding its impact on protein function, activity, and effects on downstream targets that could potentially change cellular function and pathologies of associated diseases. (Supported by the National Institutes of Health, grant number AG025384)

Sponsor: NIH

## 1405 (Poster)

First Author/Presenter: Rui Branca

#### Classification: Postdoctoral Fellow

RMM Branca, Dept. of Molecular Biology and Immunology, Health Science Center, University of North Texas at Fort Worth, Texas 76107 VP Pearce, Dept. of Pharmacology and Neuroscience, Health Science Center, University of North Texas at Fort Worth, Texas 76107 L Prokai, Dept. of Molecular Biology and Immunology, Health Science Center, University of North Texas at Fort Worth, Texas 76107

#### IMMORTALIZATION OF HUMAN BREAST EPITHELIAL CELLS: A BROAD PROTEOMICS SURVEY BY MASS SPECTROMETRY.

Purpose: To characterize the major changes in protein composition occurring in cells undergoing immortalization.

Methods: Human Li-Fraumeni syndrome-derived breast epithelial cells were studied. The control group consisted of two different lines of mortal parental cells, and the immortal group consisted of two different lines of cells expressing telomerase and high levels of hTERT. After protein isolation, and adjustment of total protein concentration to the same level in all samples, digestion was carried out by trypsin overnight. Online reversed-phase liquid chromatography tandem mass spectrometry (LC-MS/MS) of the protein digests was performed using a hybrid linear ion trap Fourier transform ion cyclotron resonance mass spectrometer. Label-free quantitation was done by spectral counting via the SEQUEST algorithm on the Proteome Discoverer software platform.

Results: We have identified profound changes in protein levels occurring upon immortalization. We found a general decrease of cytokeratins (CKs), with the exception of CKs 8 and 18 that maintained their levels. On the other hand, we have identified a cluster of actin and actin-binding proteins and a number of histones that have increased in abundance during transformation.

Conclusions: The trend revealed by the results concerning CK composition is indicative that the cells undergoing immortalization were of the luminal type. The cluster of proteins showing increased levels suggested augmented cell motility and proliferation in the immortalized cells. With our rapid and straightforward label-free MS-based method, we can potentially characterize any type of transformation process occurring in cells that implies major alteration of the proteome.

### 1406 (Poster)

First Author/Presenter: Marilyne Kpetemey

Classification: GSBS Student

Marilyne kpetemey & Andras Lacko Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, Texas 76107

LARGE SCALE ISOLATION OF APOLIPOPROTEIN A-I, A CONSTITUENT OF RHDL DRUG DELIVERY SYSTEM

Purpose: To Achieve a Rapid Isolation of apo A-I in High Yield

Methods: Recombinant Apo A-I was obtained via the process described by Ryan et. al. The E.coli cells were recovered from the cultures in the usual manner and lysed using a commercial lysis buffer. After removal of the cell debris by centrifugation (3,000RPMI), the supernatant was treated with (NH4)2SO4, to achieve a 30% saturation. The supernatant was once again recovered by centrifugation (3,000RPMI) and applied to the Octyl-Sepharose column (2.5 X 16 cm). A step wise gradient elution protocol was applied using three eluants 1) PBS buffer 2) deionized water and 3) 30% ethylene glycol, 4M guanidine.HCI, 10 mM NaOH. Upon collection of the fractions, protein determinations and SDS-Page gel electrophoresis were carried out.

**Results:** Recombinant Apolipoprotein A-I was successfully obtained using the Octyl-Sepharose hydrophobic Interaction column upon analysis by SDS-Page gel electrophoresis. Data obtained from protein determinations suggest that higher yields may be obtained by modification of the elution system used on octyl-sepharose. Work is currently under way to explore these options to improve the apo A-I isolation procedure

Conclusions: The Octyl-Sepharose hydrophobic Interaction column shows promise to obtain larger quantities of apo A-I via a rapid isolation procedure.

Sponsor: N/A

## 1407 (Poster)

First Author/Presenter: Yalla Vara Prasad Mettikolla

Classification: GSBS Student

Mettikolla P 1, Luchowski R 1, Calander N 1, Muthu P 1, Borejodo J 1 1. University of North Texas Health Science Center, Fort Worth, Texas

ON AND OFF TIMES OF A SINGLE CROSS-BRIDGE DURING CONTRACTION OF SKELETAL MUSCLE

Purpose: The overall goal is to understand the molecular basis of contraction of muscle and efficiency of ATP utilization. Determination of the efficiency of ATP utilization in contracting muscle may aid in understanding diseases like familial hypertrophic cardiomyopathy, muscular dystrophy.

Methods: Fluorescent anisotropy and lifetime measurements were used to study ATP utilization. The experiments were done using Micro Time 200 and ISS-Alba-FCS confocal systems coupled to Olympus IX 71 microscopes.

Results: The frequency of impulses is one order of magnitude smaller than the observed ATPase activity, suggesting that most of the hydrolysis events do not lead to a cross-bridge cycle and are wasted as heat.

Conclusions: The average value of duty cycle in isometrically working muscle was ~34%. The present results were consistent with other recent results which suggested that close to 1/3 cross-bridges were active during isometric contraction.

## **GENERAL PUBLIC HEALTH**

### 1500 (Poster)

#### First Author/Presenter: Katandria Johnson

#### Classification: SPH Student

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#### ACCULTURATION AND SELF-REPORTED HEALTH AMONG HISPANICS USING A SOCIO-BEHAVIORAL MODEL:

Purpose: Acculturation is defined as continuous, firsthand contact with other cultures functioning at both group and individual levels (Castro 2007). It is reflected in our culturally diverse society, calling for a greater understanding of the environmental and cultural impact on health (Castro 2007). Self-reported health (SRH), a robust and well validated predictor of future mortality for all racial/ethnic groups, has been differentially reported by Hispanics compared to whites, especially based on their acculturation status (Idler and Benyamini 1997; McGee et al. 1999; Sudano and Baker 2005). This study investigated the relationship between acculturation and self-rated health (SRH) among Hispanics.

Methods: Hispanic participants (n=135) were assessed on acculturation, various psychosocial factors, and a self-reported single item general health status measure. Participants underwent a comprehensive interview utilizing a standardized questionnaire on acculturation, various psychosocial factors, and a self-reported single item health indicator. Health status was ascertained by the question, In general, would you say your health is: excellent, very good, good, fair, or poor (Cohen, Kamarck, and Mermelstein, 1983). In addition, physiological measurements and demographic characteristics including age, gender, body mass index (BMI), medical history, and socioeconomic status were also obtained.

Results: Univariate analyses found Mexican-oriented participants 3.16 times more likely to report fair/poor SRH (95% CI 1.37, 7.25) compared to Anglo-oriented Hispanics. Acculturation was also associated with SRH in multiple regression models controlling for enabling or need factors, but not predisposing factors.

Conclusions: Acculturation status is a powerful determinant of SRH, even after accounting for other underlying factors. Medical and public health professionals should promote the use of acculturation measures in order to better understand the role of acculturation in Hispanic behaviors, health outcomes and health care use. Such research findings will contribute to the design of culturally sensitive prevention and treatment strategies for racially/ethnically diverse and immigrant populations.

Sponsor: Grant Number P20MD001633 from the National Center on Minority Health and Health Disparities

## 1501 (Oral)

#### First Author/Presenter: Katandria Johnson

#### Classification: SPH Student

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### LEAD EFFECT'S ON PEDIATRIC DEVELOPMENT

Purpose: Lead is a poison by which serious health effects occurs, requiring school-age children receive special education services. Children can be exposed to lead orally by sucking or ingesting lead contaminated objects; by inhalation; and through skin contact with lead containing products. Children are also exposed by drinking water from leaded pipes and the use of stain-glassed windows. Since children s bodies are not fully developed, gastrointestinal absorption of lead in children is higher than in adults, causing adverse reactions in their neurological system.

Methods: A qualitative systematic review of the literature was conducted from 1950-2008. A keyword and subject search terms were combined using the Boolean AND : lead, prevention, developmental delay, and pediatric. Articles were included and discussed if they directly addressed one of the three aims: the causes of lead exposure; the mental and socio-educational effects post-exposure; and solutions to reduce the number of school-aged children exposed to lead. Findings were described in a qualitative format with implications discussed in the conclusions section.

Results: The CDC has found that minority populations are disproportionately susceptible to lead poisoning, specifically African-American children that are almost three times as likely to be exposed to lead compared to Non-Hispanic whites. Findings from 23 articles show that lead exposure should be reported to public health departments, which can inform its communities through prevention programs. Chinese-made toys have been recalled and many more toys have been found tainted with lead. State and local programs should encourage legislation to fund blood lead screenings as part of the vision and hearing screening programs conducted at the school district level.

Conclusions: At the clinical practice level, healthcare professionals should utilize their case history form to inquire about a child s potential exposure to lead. As members within our environmental network, public health and allied health professions must find ways to involve the community as they strive to protect our children from the health threat of lead poisoning. Once responsibilities shift and alternatives are generated through public participation, public health entities at federal, state and local levels can continue to collaborate with community based facilities to educate and train families on how to identify and reduce the exposure of lead among pediatric populations in the U.S. and abroad.

## 1502 (Poster)

First Author/Presenter: Sue Lurie

Classification: Faculty

Sue G. Lurie, Ph.D. and Alex Appah, Department of Social and Behavioral Sciences, School of Public Health, UNT Health Science Center

SENIOR HEALTH AND SOCIAL SERVICES ASSESSMENT IN A SURBURBAN COMMUNITY

Purpose: The senior health and social services assessment was conducted to evaluate and determine the need for changes in senior center services provided in a suburban community, to adapt to changing determine need for change in services in a suburban community.

Methods: Rapid Assessment methods combined analysis of public use demographic data with analysis of qualitative interviews conducted with planners, service providers. local retirement community director, and a focus group conducted with senior center representatives.

Results: Results found current health and social services meet the basic needs of seniors in the community. However, providers and seniors concurred that additional health, mental health and educational services, transportation, activities for men and women, as well as identification and outreach to new residents are needed.

Conclusions: Expanded health, mental health and social services, senior center facilities, a greater range of activities for both men and women, and outreach to new residents are recommended for seniors in this community. Future needs assessments should be designed for comprehensive service planning.

Sponsor: N/A

### 1503 (Poster)

First Author/Presenter: Damon Schranz

#### Classification: Faculty

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HELP ESTABLISH ACCESS TO LOCAL TIMELY HEALTHCARE FOR YOUR VETS (HEALTH VETS) ACT OF 2007 H. R. 315

Purpose: To evaluate the Help Establish Access to Local Timely Healthcare for Your Vets (Health Vets) Act of 2007/H.R. 315 bill which has been proposed to aid those veterans located in rural areas whose access to the VA health care system is limited.

Methods: The HEALTHY Vets Acts of 2007 would amend Title 38, United States Code, to require the Secretary of Veterans Affairs to enter into contracts with community health care providers to improve access to health care for veterans in highly rural areas, and for other purposes. The Bill sets forth four criteria to determine the geographical inaccessibility of rural veterans to VA Healthcare systems. The criteria are as follows: The residence is in a county with a population density of less than 7.0 people per square mile and is more than 75 miles from the nearest department health care facility, in a county with a population density of more than 7.0 and less than 8.0 people per square mile and is more than 100 miles from the nearest VA health care facility, in a county with a population density of more than 1.0 miles from the nearest VA health care facility, in a county with a population density of more than 1.0 miles from the nearest VA health care facility, in a county with a population density of more than 1.0 miles from the nearest VA health care facility, in a county with a population density of more than 1.0 miles from the nearest VA health care facility, in a county with a population density of more than 1.0 miles from the nearest VA health care facility.

Results: Stakeholders have noted both benefits and limitations to H. R. 315. The American Legion believes it is in the best interest of veterans residing in highly rural areas that local care be made available to them. Veterans of Foreign Wars (VFW) has concern about contracting, but their concerns are outweighed by the potential benefits to rural veterans. Adversely, The US Department of Veterans Affairs believes the bill would create obstacles to further expansion of VA strategic plans. Paralyzed Veterans of America (PVA) is concerned the bill would threaten the long-term viability of the VA health care system. Vietnam Veterans of America state the bill would add bureaucratic clutter.

**Conclusions:** H.R. 315 addresses the issue of accessibility; however, unintended consequences are probable if this legislation is passed. H.R. 315 will increase costs to the Veterans Administration causing funding priorities to be reorganized to accommodate the influx of new veterans in the VA healthcare system further endangering the quality of care veterans receive. Additionally, the administrative task of negotiating contracts with individuals and hospitals throughout the US will burden the already overwhelmed bureaucratic arm of the VA health care system.

## **GENERAL PUBLIC HEALTH**

## 1505 (Poster)

First Author/Presenter: NIRUPAMA SABNIS

Classification: SPH Student

NIRUPAMA SABNIS SALIMA DHANJI ANGELINA STRICKLER PARNA PRAJAPATI

EXAMINING THE HEALTH KNOWLEDGE AND HEALTHY LIFESTYLE PRACTICES OF UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER STUDENTS

Purpose: The hypothesis of the present study was Health knowledge is correlated with healthy lifestyles among UNTHSC students. This study is significant in the sense that the UNTHSC students who are the future health professionals are expected to know and act according to healthy lifestyle guidelines. There actions could be improved by be proper training and awareness so that they could spread the healthy habits in the community. The results of this study could be used to asses on campus health education or used to compare to other health professional schools.

Methods: A group survey was administered to 240 current UNTHSC students in School of Public Health (SPH), Texas School of Osteopathic Medicine (TCOM), Physicians Assistant (PA) and Graduate School of Biomedical Sciences (GSBS) classes. The survey questions asked students about health knowledge, physical activity and nutritional practices. The data was analyzed using frequency, odds ratio and chi square statistics

Results: Data showed that there was a significant difference observed between the knowledge levels, nutritional practice levels and physical activity levels between all schools, with TCOM and PA schools being the highest and GSBS being the lowest. We did not reject the null Hypothesis for nutritional practice, i.e. health knowledge is not correlated with nutritional practices. We rejected the null Hypothesis for physical activity reactivity, i.e. health knowledge is correlated with physical activity practices.

Conclusions: This study demonstrated that our research question, Is health knowledge correlated with healthy lifestyles among UNTHSC students? was proven correct only for physical activity being correlated with health knowledge, but not for nutritional practices. It was also shown that health knowledge and healthy lifestyles is different across all schools.

Sponsor: N/A

## 1506 (Poster)

#### First Author/Presenter: Christina Mathews

Classification: School of Health Professions MPAS Student

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#### IDENTIFICATION OF OVERWEIGHT CHILDREN BY FAMILY MEDICINE PRACTITIONERS

Purpose: The purpose of this study was to examine at what frequency overweight or at risk for overweight children were identified and intervention provided by family medicine practitioners.

Methods: The data was collected by a retrospective chart review of well child visits in a North Texas Family Medicine clinic that sees mostly minority, Medicaid patients. After receiving IRB approval, the researchers used the ICD-9 well check code and age range of 5-19 as chart selection criteria. Potential charts were dated from September 1, 2005 to April 30, 2008. A total of 783 charts were eligible to review. After exclusion criteria were applied, including that the BMI-for-age could not be less than the 85th percentile, 257 charts remained for data collection. Major variables included demographic information and documentation of: patient identification as overweight or at risk for overweight, patient s current diet and exercise habits, patient education, referral, or follow up. The data was analyzed using SPSS for chi-square and logistic regression.

Results: Of the 257 reviewed charts that met the inclusion criteria, 62.6% were overweight and 37.4% were at risk for overweight. Among them, the majority was Hispanic (75.9%) and had Medicaid or Chips as their payer source (99.6%). BMI-for-age percentile was only documented in 4 out of the 257 reviewed charts by the family medicine practitioners. Furthermore, they accurately identified children as overweight or at risk for overweight 36.2% of the time. The most frequent intervention documented was patient education (41%). The data supported a significant association between BMI category and the practitioner identifying the patient as overweight or at risk for overweight. Significant predictors of active practitioner identification were age (OR=1.17; 95% CI= 1.06-1.28) and BMI-for-age percentile (OR=1.43; 95% CI = 1.28-1.61).

Conclusions: This study highlights that identification and intervention of at risk for overweight and overweight children are being documented by family medicine practitioners at an unsatisfactory level. However, this problem is not specific to family medicine. The trend of low level of documentation is noted in a previous study of a pediatric clinic, which found that children were identified as overweight or at risk for overweight only 24.2% of the time, as compared to the 36.2% found in this study. A resolution to this problem is to add more specific prompts on the Well Child Check forms; particularly BMI-for-age percentile.

## 1507 (Poster)

#### First Author/Presenter: Christine Moranetz

Classification: Faculty

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THE IMPACT OF A UNIQUE HUMAN IMMUNODEFICIENCY VIRUS PREVENTION PROGRAM THAT MERGES MEDICINE AND THEATER ON ADOLESCENTS

Purpose: The purpose of this study was to determine if an innovative HIV/AIDS prevention program impacted adolescents with regard to knowledge, attitudes and perceptions of risk for Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS) and other sexually-transmitted infections (STIs). This post-program evaluation of the Dramatic AIDS Education Project (DAEP) assessed both typical-risk and high-risk youth who received the culturally-sensitive, developmentally-appropriate program.

Methods: A cross-sectional study was conducted using 443 pre-adolescent and adolescent males and females ages 12-18 from two middle schools and two high schools within the Kansas City metropolitan area in April 2008. A voluntary, anonymous, self-reported, post evaluation survey derived from the AIDS Survey for School-Aged Youth (ASSAY) was administered immediately after the presentation of DAEP. This study protocol was approved by the KU Human Subjects Committee (The University of Kansas Medical Center, March 2008).

Results: Data indicated that of those surveyed, 92% (n=407) felt they learned something new as a result of this program. The majority (78%) felt HIV and AIDS were important health issues in their lives, and 92% felt they would be supportive of a friend who was diagnosed with HIV/AIDS. With regard to behavioral intentions, 30% indicated that they would change their sexual behavior after seeing DAEP. Developmental differences were observed, with high school students being more likely to perceive HIV/AIDS as an important health issue in their life (p<0.05). With regard to gender, females were more likely than males to believe that teens were putting themselves at risk for contracting HIV/STIs (p<0.05). African Americans were most likely to report they had learned something new when compared to other categories of race/ethnicity (p<0.05).

Conclusions: This post-evaluation study reflects that the DAEP is an effective program in positively impacting knowledge, attitudes and perceptions of risk related to HIV/AIDS and other STIs in this population.

Sponsor: N/A

## 1508 (Poster)

#### First Author/Presenter: Vamsi Kanumuri

#### Classification: SPH Student

Vamsi Kanumuri, MPH Environmental & Occupational health UNTHSC. Dr. Lilly Ramphal MD, MPH, FACOEM Associate professor Environmental & Occupational health UNTHSC.

#### RETROSPECTIVE ANALYSIS OF ASBESTOS EXPOSURE AND LUNG DISEASE IN A GROUP OFSHEET METAL WORKERS

Purpose: Asbestos is a naturally occurring silicate mineral which has been implicated in a number of diseases including asbestosis, lung cancer and mesothelioma. Sheet metal workers specialize in installation and service of heating, ventilation and air conditioning systems. Our main hypothesis was to assess the various factors of asbestos exposure by work category and duration in sheet metal workers for any associations of increased parenchymal disease and pleural disease on B-reader chest x-rays and abnormalities in pulmonary function tests

Methods: The Sheet Metal Occupational health institute trust established in 1986 was contracted to offer a standardized screening program for sheet metal workers who had been employed in the industry for at least 20 years in the United States and Canada. About 18,211 individuals were examined and asked to answer a standardized questionnaire. We had access to 144 such questionnaires which have information regarding age, No. of years worked, specific job categories and duties, time worked in each department, clinical symptoms, cigarette smoking, pulmonary function tests results and B-reader chest x-rays results.

**Results:** Among the 144 individuals, the mean age was 60.92 and the median age was 60 years. The participants had worked for a mean duration of 34.22 years in the sheet metal trade. Among the entire group 5(3.5%) had parenchymal abnormalities and a total of 12 (8.3%) had pleural scarring on B-reader chest x-rays. All the workers who had pleural scarring were above 60 years of age. Obstructive pattern of pulmonary function tests were observed in 21(15.6%) workers, 11(7.6%) had restrictive pattern, 5(3.5%) had combined obstructive and restrictive patterns while 97(67.4%) had normal lung function

Conclusions: Based on the above results we found that the presence of parenchymal and pleural abnormalities was dependent on both the year in which the worker first worked and the duration of work. Older workers started working earlier which explains the increase in parenchymal and pleural abnormalities in them. The reduced asbestos exposure through strengthened Occupational Safety and Health Administration (OSHA) regulations and improved personal protective equipment such as respirators may have had a protective effect on the younger workers as compared to the older workers. Another factor to consider is the long latency of asbestosis. Due to this latency we may still see an increasing prevalence of asbestos related disease in the future even in the young workers

## **GENERAL PUBLIC HEALTH**

### 1509 (Poster)

#### First Author/Presenter: Carlos Reyes-Ortiz

Classification: Faculty

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#### NEIGHBORHOOD ETHNIC COMPOSITION AND INFECTIOUS BIOMARKERS AMONG MEXICAN AMERICANS

Purpose: To determine the association between neighborhood ethnic concentration and seroprevalence of infections among Mexican American men and women aged 17 years and over.

Methods: Data were the NHANES III (1988-94), linked to the US Census data (1990). Outcomes were seroprevalence of infectious biomarkers including herpes virus I and II, Helicobacter pylori, Hepatitis virus A, B and C. Percent of Hispanics at the census tract level was used as a proxy for neighborhood ethnic concentration. Control variables were age, gender and census tract percent poor.

Results: Mexican Americans living in high concentrated Hispanic neighborhoods (less acculturated or Latino barrios) were significantly more likely to have a positive seroprevalence for herpes I, Helicobacter pylori, and Hepatitis A compared to Mexican Americans living in low concentrated Hispanic neighborhoods. However, poverty explained the associations of the barrio with herpes I and Helicobacter pylori but the association with hepatitis A remained (OR= 3.97, 95% CI 1.87-8.45).

Conclusions: Because these infections have oral -person to person- or enteric waterborne-transmissions, our results suggest that the environment of the Latino barrio may facilitate the existence of infections due to deprived socioeconomic conditions.

Sponsor: DOD-Army W81XWH-06-1-0290

## 1510 (Oral)

#### First Author/Presenter: Damilola Funmilayo

Classification: SPH Student

Damilola Funmilayo MPH\*; Titilola Jolaosho MHS\*\*, Kim Seechuk MPH!; Fang Fang Zhang MD PhD§; \*Department of Epidemiology; \*\*Washington DC Bureau of Surveillance and Epidemiology; \*!Washington DC Tuberculosis Control Unit; §Department of Epidemiology, University of North Texas Health Science Center, Fort Worth, TX

DESCRIPTIVE ANALYSIS OF TUBERCULOSIS INFECTED PEOPLE IN DISTRICT OF COLUMBIA, 1992-2007

Purpose: The purpose of this study was to assess racial/ethnic distributions of tuberculosis and the concurrence of TB and HIV Infection among District of Columbia residents between 1992 and 2007.

Methods: Data from TIMS and HARS were extracted using Electronic Record Linkage using Link Plus and MS Access. Statistical analysis was conducted using SAS

Results: In 2007, 66% of TB cases were African American. The incidence of TB among African Americans have about 3 times the incidence of TB compared to all other races combined. The total number of TB cases is higher in males than in females in each age group and is highest among those between ages 45 and 64 years In 2007, 71% of TB cases were males and 42% of all the cases were between the ages of 45-65 years old. In the DC population, the number of TB cases peaked in 1993 and has been decreasing gradually since then . The number of TB cases is increasing among foreign born persons. 23% of the foreign born cases are from Ethiopia. Between 1992 and 2007, 28.9% of the all TB cases were HIV positive

Conclusions: Our results indicate racial/ethnic differences in TB occurrence with the highest burden on African American population. Although the total number of TB cases has been decreasing during the past 16 years, the percentage of TB cases among the foreign born people has been increasing. Also, the number of HIV infection cases is increasing as well, we suggest that additional measures need to be put in place to help reduce these occurrences within the DC population.

#### First Author/Presenter: O. Mayowa Ijagbemi

Classification: SPH Student

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HEALTH LITERACY AS A MEDIATOR BETWEEN SENSE OF CONTROL AND HEALTH LITERACY: DOES THE RELATIONSHIP EXIST?

Purpose: It is necessary for clinicians to promote medication adherence in diseased persons for wellness to occur. Previous studies show that two predictors of adherence are sense of control (SOC) and health literacy. This study tested the hypothesis that health literacy acts as a mediator between SOC and medication adherence among persons with HIV.

Methods: SOC and medication adherence were derived from cross-sectional surveys of 123 HIV participants recruited from Tarrant County Public Health Preventive Medicine Clinic. Health literacy was determined by taking the absolute value of the difference between patients self-reported CD4 count and actual lab-reported CD4 count. Participants with absolute values less than 50 were categorized as health literate greater than 50 were not health literate. Simple and multiple linear regression was performed. The independent, mediating, and dependent variables were SOC, health literacy, and medication adherence respectively. We used three regression equations to test for mediation: SOC predicting health literacy; SOC predicting medication adherence; and both SOC and health literacy predicting medication adherence. Multiple linear regression, stress, and social support.

Results: Most participants were adherent (69%; N=86) and not health literate (58.5%; N=72), while the mean SOC score was 0.8 (SD= 0.5). No significant effects or interactions were observed between the three main variables either before or after controlling for confounders. The role of SOC as a predictor of health literacy was inconclusive, as the unadjusted model showed that higher levels of SOC yielded higher levels of health literacy (OR=1.342; 95% CI=0.653-2.759), while the adjusted model showed the opposite (OR=0.766; 95% CI=0.301-1.949). Though not significant, participants with high SOC had an 82% higher likelihood of being adherent (OR=1.821; 95% CI =0.834-3.979). These odds were reduced to 46% after controlling for confounders (OR=1.467; 95% CI =0.529-4.071). Introducing health literacy into the equation did not produce a significant change in the effect of sense of control on medication adherence (OR=1.446; 95% CI=0.521-4.011).

Conclusions: Health literacy did not act as a mediator between SOC and medication adherence. Further investigation with a larger sample size is needed to determine the true relationship between these three variables.

Sponsor: N/A

## 1512 (Poster)

First Author/Presenter: Michael Meador

Classification: School of Health Professions MPAS Student

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THE PREVALENCE OF COMMUNITY ACQUIRED METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS AMONG PEDIATRIC PATIENTS PRESENTING WITH DERMAL INFECTION AT THE UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER PATIENT CARE CENTER (UNT-PCC) AND BLUEBONNET CLINIC

Purpose: The purpose of this study is to provide new information on the prevalence of CA-MRSA to providers. An analysis of patient assessments, laboratory findings, culture sensitivities, prescribing habits, and associated demographic data can offer predictive value to positively influence patient outcomes. If relevant, data acquired from this study can be implemented to change the overall treatment policies among pediatric providers at local clinics.

Methods: A non-randomized purposive retrospective chart review of pediatric patients treated at local clinics was used to collect data. 276 charts were chosen from ICD-9-CM codes that include skin and soft tissue infections (SSTI's)consisting of: dermal cellulitis, abscess, folliculitis, impetigo, infected insect bites, and boils. Patients who were treated up to 18 months prior to the beginning of the study and had not been hospitalized within six-weeks of being seen at either UNT clinic were included in the study.

Results: The prevalence of CA-MRSA from reviewed charts was 2.9% of patients who presented with SSTI's overall. Providers cultured wounds 16.3% of the time. Analysis of charts that were cultured indicates a MRSA prevalence of 17.8%. Patients who were female, black or Hispanic, received government subsidized insurance, were under the age of three, and were diagnosed with impetigo were more likely to test positive for MRSA. Empirical treatment choices included mupiricin 49%, cephalosporins 13.8%, clindamycin 10.5%, or no prescription drugs offered 13.4% of the time. Definitive treatments for MRSA infections were found to be clindamycin 87.5% and TMP-SMX 12.5%. Patients diagnosed with impetigo had the greatest opportunity (9.8%) to have their wounds cultured due to suspected MRSA. Analysis indicates that patients diagnosed with folliculitis were 3.3 times more likely to receive sensitivity cultures than those diagnosed with impetigo.

**Conclusions:** The percentage of SSTI wounds that cultured positive for CA-MRSA was far from negligible (17.8%), but the overall number of providers that elect to culture wounds was quite small (16.3%). Given the reported prevalence of MRSA and its relationship to skin and soft tissue infections, healthcare providers should culture wounds more frequently. Data analysis revealed statistical associations between whether wounds were cultured and other aspects of treatment, however, the predictive value of the study was limited due to small sample size.

## 1513 (Poster)

First Author/Presenter: Ashton Tassin

Classification: SPH Student

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### SLEEP AND LEISURE ACTIVITY AMONG UNTHSC STUDENTS

Purpose: HYPOTHESIS: Graduate students, including medical students, are an at-risk population for sleep impairments. Current research suggests that active leisure activity can be protective against both professional burn out as well as sleep dysfunction. We hypothesize that students at UNTHSC who participate in increased amounts of leisure activity have better sleep quality than those students who have decreased leisure activity. We created and implemented a 23 item self-administered survey. The campus mail box and drop off were utilized for both distribution and collection of completed surveys. The purpose of this study was to :1) Establish prevalence of poor sleep quality among students. 2) Measure levels of leisure activities in the student population. 3) Assess the association between quality of sleep and active leisure activity in the graduate student population. Address research question, Do Students who engage in more leisure activity experience better sleep quality?

Methods: A cross sectional study was conducted with a 23-item survey instrument to assess the relationship between sleep quality and leisure time activity among the UNTHSC student population. Through convenient sampling, a sample size of nearly 200 was obtained using mail and drop off survey modes. Pearson correlation coefficient was used to assess correlation while Cochran-Mantel Haenszel test was used to measure the association between sleep quality and leisure time activity. SAS 9.1 was used for both the calculations.

Results: Among our UNTHSC sample, 38.22% of students reported poor sleep quality. The proportion of students reporting high activity 28.71 while that of students reporting lower amounts of leisure activity was 48.89. After removing outliers, the Pearson Correlation Coefficient (r) between sleep quality score and leisure activity was -0.3 with p-value <0.01. The Cochran-Mantel-Haenszel test with dependent and independent variable produced an odds ratio of 2.36 (95% C.I.= 1.32-4.23.)?

Conclusions: Students who reported high levels of activity were 2.37 times more likely to report good sleep quality compared to those with low levels of activity. The study results clearly supported the hypothesis that as duration of leisure time activity increases, the reported quality of sleep increases from poor to good.

Sponsor: N/A

## 1514 (Poster)

First Author/Presenter: Benjamin Cruz

Classification: SPH Student

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SEASONAL VARIATION OF WATER QUALITY INDICATORS AND THEIR ASSOCIATION WITH CLIMATE FACTORS IN NORTH CENTRAL TEXAS

Purpose: Water quality is an important aspect of overall public health safety. Water quality varies with space and time. To maintain high quality of drinking and recreational water quality, understanding of factors that modify water quality is necessary. The purpose of this study is to document seasonal variation of water quality indicators in a North Central Texas area and to investigate a relationship between climate factors and those indicators.

Methods: The water quality monitoring data from 2001 to 2005 were obtained from City of Denton, Texas and the three water quality indicators were chosen to study the association with climate factors. The indicators were coliform bacteria count, nitrate concentration, and phosphate concentration. Climate factors were temperature and precipitation. The association was investigated with the analysis of Variance.

Results: Coliform bacteria levels show a peak concentration during the months of June and July, and appear to have an association with precipitation but not with temperature. Nitrate levels over a twelve-month period peak in the spring months and its concentration varies with precipitation, not by temperature. Orthophosphate levels show higher levels during the late summer through the winter months and their fluctuations were associated with precipitation but not by temperature.

Conclusions: Precipitation influences the concentration of coliform bacteria in the water as well as season. However, further analysis is needed to sufficiently show evidence of relationship

## 1515 (Poster)

First Author/Presenter: Harrison Ndetan

Classification: SPH Student

Harrison Ndetan MSc, MPH, SPH Marion W. Evans Jr. DC, PhD, CHES, Dean Graduate Programmes, Cleveland College of Chiropratic, Kansas Ronald Rupert MS, DC, Dean of Research Parker College of Chiropractic, Dallas

SHOULD DOCTORS OF MANIPULATIVE THERAPY BE CONCERNED ABOUT METHICILLIN RESISTANCE STAPHILOCOCCUS AUREUS ON TREATMENT TABLES?

Purpose: To assess the presence of microbes and other allergens or pathogens on cloth-covered chiropractic treatment tables.

Methods: Cloth-covered tables in a chiropractic college teaching clinic were selected. Samples were taken from the facial piece and hand rests with RODAC plates containing nutrient agar, followed by confirmatory testing when indicated.

Results: Numerous microbacteria strains were found, including Staphylococcus aureus and Propionibacterium. Allergen-producing molds, including Candida, were also found.

Conclusions: Cloth tables were shown to contain pathogenic microbacteria and allergens. The chiropractic profession should establish an infection control protocol relevant to treatment tables and discard use of cloth-covered treatment tables in this process.

Sponsor: N/A

#### 1516 (Poster)

First Author/Presenter: Afshan Kamrudin

Classification: McNair/SMART Participant

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NOI DUOC TIENG ANH?: LANGUAGE AND BARRIERS TO ACCESSING HEALTHCARE AMONG VIETNAMESE IMMIGRANTS

Purpose: Using the Behavioral Model for Vulnerable Populations, ability to speak English was studied among Vietnamese Immigrants and compared to their experiences of accessing healthcare. It was hypothesized that immigrants that spoke English would encounter less barriers when accessing healthcare services.

Methods: Thirty-six Vietnamese patients in a tax-supported, saftey-net healthcare system in a large urban county in north Texas, were interviewed by phone in the fall of 2000. This data is a secondary analysis of the data collected in 2000.

Results: Non-english speakers were significantly less likely to be U.S. citizens or applicants for citizenship or to work, and more likely to need an interpreter during visits, need someone to go with them to the doctor, and have problems transportation, and report overall report to be less healthy.

Conclusions: It is important to brea in mind that this study included patients in only one safety-net healthcare system. There were few Asians in the overall sample and only one third met the criteria for the participants studied in this paper. There was not qualitative study available and future research should assess the experience of healthcare among this population qualitatively.

## 1517 (Poster)

First Author/Presenter: Gabriela Cantu

Classification: SPH Student

Gabriela Cantu-UNTHSC Lindsey Brown-UNTHSC Dr. Martha Felini-UNTHSC

## DALLAS POLICE DEPARTMENT S PROSTITUTE DIVERSION INITIATIVE: ONE-YEAR EVALUATION

Purpose: To perform a one year evaluation of the PDI using information collected by participating organizations from October 2007 through September 2008 initiatives.

Methods: Data was received from PDI organizations in real-time on the night of each monthly. Evaluation consisted of quantifying PDI outcomes, defined as (1) characterization of demographic, behavioral profile, and physical and mental health, (2) success rate of PDI participants opting to enter the program, and (3) cost benefit in terms of time and money.

Results: Within the first year of the PDI, 175 prostitutes were contacted. The average PDI participant was African American (67%), female (91%), and 37 years of age. Half reported completing at least a high school education and 68% were caretakers with a mental health condition and addicted to one or more drugs. Results suggest that the prevalent drugs abuse (>95%) is self-medication to co-exist with multiple mental health conditions and cope with risky behaviors. Many indicated they needed help, as observed by the high proportion choosing to go into treatment (68%). Of these, nine (17%) have left prostitution and are in recovery. Preliminary evaluation of the overall project indicated that inter-agency communication needs to be improved in order to become more efficient on-site.

Conclusions: Findings demonstrate the feasibility of community organizations partnering with law enforcement agencies to bring needed resources directly to the streets where vulnerable populations often experience barriers to care. Moreover, the PDI provides a means to identify health priorities so that interventions and research can be responsive to the needs of prostitutes and the communities surrounding these neighborhoods. Future research will focus on examining outcomes related to drug abuse, mental health, and distributions of HPV types.

Sponsor: N/A

22.

## **RECEPTOR PHARMACOLOGY & DRUG DELIVERY**

## 1600 (Poster)

First Author/Presenter: Aleksa Jovanovic

Classification: HealthPoint

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THE EFFECT OF METAL IONS ON ENZYMATIC ACTIVITY OF CLOSTRIDIUM COLLAGENASE

Purpose: The healing of wounds is a complex process, which is often further complicated by the presence of non-viable, necrotic tissue in the wound area. Debridement is the process of removing the non-viable tissue from a wound to prevent or diminish infection and to promote healing. Proteolytic debriding enzymes, such as collagenase, have been used for the wound debridement for decades. Clostridium collagenase (C. collagenase) is a metalloproteinase, which can specifically attack collagen debris in necrotic tissues.

Methods: The Collagenase activity was measured using the FALGPA substrate assay in the presence of various metal salts.

Results: The authors have found that certain metal ions, in the form of water-soluble salts can enhance the enzymatic activity of C. collagenase in vitro. The examples of metals that had a positive influene on enzyme activity are : Sodium (Na), Magnesium (Mg) and Potassium (K).

Conclusions: These results could help clinicians better understand how C. collagenase can be used most effectively in combination with therapies containing metal salts.

Sponsor: N/A

## 1601 (Poster)

#### First Author/Presenter: Anindita Mukerjee

#### Classification: Postdoctoral Fellow

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## CURCUMIN LOADED PLGA NANOSPHERES AS THERAPEUTICS AGAINST PROSTATE CANCER

Purpose: Among the potent anti-cancer agents, curcumin has been found to be very efficacious against many cancer cells. However, the major disadvantage associated with curcumin is its low systemic bioavailability when administered orally due to its poor aqueous solubility. Many established pharmaceutical industries are gearing-up their efforts towards developing more effective and performance-based new drug delivery systems. The growing need for biodegradable polymers for use in the emerging technologies like gene therapy, novel drug delivery systems, implantable devices and nanotechnology have resulted in the development of a range of biodegradable polymers for drug delivery. Based on these aspects, our present work investigates the method for the efficient encapsulation of curcumin in PLGA nanospheres.

Methods: The nanospheres were formulated using a unique solid/oil/water emulsion solvent evaporation method and then characterized for percent yield, encapsulation efficiency, surface morphology, particle size, drug distribution within nanospheres and drug polymer interaction. The in vitro drug release profiles were performed to determine the sustained release behavior of the drug from the nanospheres.

Results: Our studies showed the successful formation of smooth and spherical curcumin loaded PLGA nanospheres with a high percent yield of about 92.01±0.13% and an encapsulation efficiency of 90.88±0.14%. The mean particle size of the nanospheres was found to be 45nm. Results showed robust intra-cellular uptake of the nanospheres in the cells. Cell viability studies revealed that these curcumin loaded nanospheres resulted in less cell viability for the cancer cells (LNCaP, PC3) as compared to normal cell line (PWR1E). Further, the observed effect was more pronounced with curcumin loaded nanospheres than with free curcumin.

Conclusions: Our studies show the successful formulation of curcumin loaded PLGA nanospheres which released curcumin in a sustained manner over a prolonged period of time. Intracellular uptake and cell viability assays demonstrated efficient uptake and action of curcumin nanospheres in prostate cancer cell lines. Therefore, curcumin loaded nanospheres have high potential as an anti-cancer therapeutic for clinical application. Further studies in mouse model system will be designed in future wherein the curcumin loaded nanospheres will be administered via intraperitoneal injections and the tumor regression will be monitored along with immunohistochemical analysis.

Sponsor: Supported by grants- DOD Breast Cancer Research Program (BC075097) and NIH (R21CA109593) to JKV

## **RECEPTOR PHARMACOLOGY & DRUG DELIVERY**

## 1602 (Poster)

#### First Author/Presenter: Vien Nguyen

Classification: Postdoctoral Fellow

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PHARMACOKINETICS OF ORAL CARISOPRODOL IN THE BRAIN: INFLUENCE OF CIMETIDINE ON THE METABOLIC CONVERSION OF THE DRUG TO MEPROBAMATE

Purpose: The long-term goal of the project has been to investigate whether liabilities for carisoprodol abuse due to its own intrinsic activity or is associated with its metabolism to meprobamate. To enable neuropharmacological studies addressing this question, we evaluated cimetidine as an inhibitor of the cytochrome P 450 (CYP2C19) isozyme thought to be responsible for the metabolism of carisoprodol to meprobamate. We measured both drugs in situ in the brain (nucleus accumbens, the site of action) using cerebral microdialysis in freely moving rats.

Methods: Animal preparation: A guide cannula was implanted 5-7 days before the microdialysis experiments into the nucleus accumbens of two male Sprague-Dawley rats using a stereotaxic micromanipulator. One rat was treated with 100 mg/kg cimetidine (2 ml/kg in 0.9% saline) and the other rat was treated with saline for control once daily for 4 days. Brain concentrations of carisoprodol and meprobamate were determined by in vivo microdialysis after a single dose of carisoprodol (100 mg/kg, p.o., by gavage) on the fourth day of treatment. In Vivo Microdialysis : To obtain test samples, microdialyzates were collected in freely moving rats by perfusing probes (CMA/12, CMA Microdialysis, Acton, MA, USA) introduced through the guide cannula into the nucleus accumbens of the brain. Samples were collected every 5 min in the first hour after carisoprodol administration, then every 20 min for up to 5 h. The microdialysates were then analyzed by liquid chromatography tandem mass spectrometry (LC MS/MS) using atmospheric-pressure chemical ionization.

Results: Compared to saline control, pretreatment with cimetidine afforded a considerable increase in the carisoprodol to meprobamate ratios in the nucleus accumbens for 40-50 min (and peaking around 20-25 min) after the oral administration of the drug. The decrease in meprobamate levels was especially profound, when data were projected to drug concentrations reached in the cellular membrane compartment of the tissue.

**Conclusions:** We have shown that carisoprodol metabolism to meprobamate can be inhibited through cimetidine administration allowing for the study of the differential roles of these molecules in carisoprodol abuse.

Sponsor: N/A

## 1603 (Poster)

### First Author/Presenter: David Cummings

Classification: Dual Degree Student: DO/MS

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#### SERINES IN TRANSMEMBRANE HELIX FIVE ARE KEY SITES OF AGONIST INTERACTION WITH THE D4 DOPAMINE RECEPTOR

Purpose: The D4 subtype of dopamine receptor is located in the eye and other brain regions. It plays a critical role in photoactive circadian rhythms, as well as attention and libido. The D4 receptor has the unique ability to be stimulated by physiological concentrations of norepinephrine, which mediate attentional states. Interest in D4-selective agonists has surged recently because D4 receptor agonism promotes penile erection. Surprisingly little is know about the molecular interactions of drugs with this receptor subtype. Consequently, we investigated the contributions of the conserved serines of transmembrane segment five (TM5) as they have been shown to be critical for the interactions of the endogenous agonist dopamine with the related D2 and D3 subtypes of dopamine receptor.

Methods: D4 receptors containing serine to alanine mutations at positions 5.42, 5.43, and 5.46 of TM5 were stably expressed in CHO10001 cells. These cells were assayed by radioligand competition for the ability to bind various ligands. Ligand function by determined by cAMP accumulation. All results were compared to the D4 wild type receptor.

Results: Dopamine had drastically reduced affinity (>100-fold) for the S5.42A and the S5.46A mutants, while the affinity for norepinephrine was drastically reduced at all three mutants (>250-fold). The potency of dopamine s functional response was significantly decreased for the S5.42A and S5.43A mutants (>41-fold), but dopamine was unable to activate the S5.46A mutant. Even at an extremely high concentration (250  $\mu$ M), norephinephrine lost its ability to activate any of the TM5 serine to alanine mutant receptors. However, a structurally different agonist, quinpirole, was able to activate the D4 wild type and the mutant receptors with similar efficacy and potency. An experimental antagonist gained agonist properties at S5.43 mutant receptor.

Conclusions: To our knowledge this is the first report where a single point mutation in a biogenic amine receptor is able to convert the functional properties of a subtype-selective antagonist to an agonist. We also discovered that, in contrast to D2 and D3 receptors, dopamine has significant interactions with both S5.42 and S5.46 in the D4 receptor. Further, all three conserved serines are critical for the binding and function of norepinephrine at the D4 subtype of dopamine receptor. These findings suggest that the D4 receptor contains a unique serine-mediated hydrogen-bonding network that is important for agonist interactions.

Sponsor: NIH R01 MH063162 (JAS)

## **RECEPTOR PHARMACOLOGY & DRUG DELIVERY**

## 1604 (Poster)

#### First Author/Presenter: Theresa Carbonaro

#### Classification: GSBS Student

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### RECEPTOR PROFILING OF NOVEL HALLUCINOGENS

Purpose: While many drugs of abuse have been extensively investigated, hallucinogens, in general, have not been as well characterized with respect to the brain targets that might account for their specific sensory effects. The 5-HT2A receptor has been reported to be a target for some of the better characterized hallucinogens, such as lysergic acid (LSD) and dimethyltryptamine (DMT), but their sensory effects are different, as are those of many other hallucinogenic compounds, suggesting that other receptor targets may be involved. Here a panel of five cloned receptors was screened against the known hallucinogen DMT, two novel hallucinogens with structural similarities to DMT, Diisopropyltryptamine (DiPT) and 4-hydroxy-DiPT (4-OH-DiPT), and two marine natural products intermediates named CJL-4 and CJL-5.

Methods: Stable cells lines were created that express one of a panel of five different cloned receptors. These included three serotonin receptor subtypes, 5-HT1A, 5-HT2A, 5-HT2C, a dopamine receptor and a sigma receptor. Radioligand competition binding assays were utilized to assess the ability of the test compounds to interact with the different receptors. A two-stage displacement, corresponding to moderate and strong interactions, was used as a cut-off for the purpose of profiling.

Results: DMT, DiPT, 4-OH-DiPT, CJL-4 and CJL-5 all had strong interactions with the 5-HT2A receptor. However, the interaction profiles with respect to the other receptors were different for each compound.

Conclusions: DMT, DiPT and 4-OH-DiPT have hallucinogenic activity and bind to the 5-HT2A receptor, a common site of action for hallucinogens. The variability in the profiles of these drugs for the other receptors screened may provide further insight with respect to their reported differences in sensory distortion experiences. The two natural product intermediates CJL-4 and CJL-5 also bound the 5-HT2A receptor suggesting that they have hallucinogenic potential or that they might be able to block hallucinations.

#### First Author/Presenter: Patrick Wright

#### Classification: Resident

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#### FIBERWIRE IS SUPERIOR TO STAINLESS STEEL FOR TENSION BAND FIXATION OF TRANSVERSE PATELLA FRACTURES

Purpose: Internal fixation using metal implants in configurations based on the tension band principle remains the mainstay of treatment for operative transverse patella fractures. Heavy suture, however, is easier to place accurately in the soft tissues, conforms more readily to bony structures, is less likely to fragment over time, and appears to be associated with greater patient satisfaction and decreased re-operation rates. The present study aims to (1) evaluate differences in stiffness and failure strength between No. 5 FiberWire with an without a surgical knot, and 18-guage stainless steel wire with and without a compression twist; and (2) evaluate the effectiveness of FiberWire as a tension band construct using a three-point-bend model.

Methods: The two materials were used for tension band fixation of a custom three-point-bend model. To mimic the Lötke figure-of-eight anterior tension band technique, two parallel longitudinal tunnels were drilled in the model to allow the passage of the FiberWire or stainless steel wire. After the suture or wire was secured, the model was loaded in three-point-bending. The four constructs tested were: (1) single stainless steel wire with two (bilateral) compression twists; (2) single strand FiberWire tied with a sliding knot; (3) double strand FiberWire tied with individual sliding knots; and (4) double strand FiberWire tied with a Wagoner's Hitch.

Results: An extremely statistically significant difference (P<0.0001) was found when the failure load of the stainless steel wire (636.0 [N]) was compared to that for the single strand (343.4 [N]) and Wagoner's Hitch FiberWire (1337.4 [N]) constructs.

Conclusions: Mechanical tests were performed to compare FiberWire to the current standard of treatment employing stainless steel wire. Results indicate that the double strand FiberWire requires a similar load as the 18-guage stainless steel wire for construct failure. The load required for construct failure however, was increased substantially when the FiberWire was tied with a Wagoner's Hitch. In summary, the results from this study suggest that FiberWire is mechanically superior to stainless steel for tension band fixation of patella fractures. Furthermore, clinically, the use of FiberWire may decrease the incidence of implant related pain, decrease re-operation rates, and increase patient satisfaction. This study clearly demonstrates that FiberWire may be a possible alternative to stainless steel wire in patella fracture fixation justifying further study.

Sponsor: N/A

## 1701 (Poster)

#### First Author/Presenter: Joan Carroll

#### Classification: Faculty

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# RECREATIONAL ACTIVITY PARTICIPATION IN AFRICAN AMERICAN, HISPANIC, AND WHITE ADULTS (NORTH TEXAS HEALTHY HEART STUDY)

Purpose: To determine if there were disparities in self-reported recreational activity participation in middle-aged and older African American, Hispanic and White adults.

Methods: 200 men and women (75 African American, 75 Hispanic, 50 White) who enrolled in the North Texas Healthy Heart Study (NTHHS) completed the Modifiable Activity Questionnaire (MAQ). The average number of self-reported recreational activities and the estimated caloric expenditure for overall recreational activity were compared among groups with a one-way ANOVA and a Scheffe post-hoc test. Racial/ethnic differences in percentages of respondents participating in individual activities were compared overall and by sex with a chi-square test.

Results: Overall, 89% of all respondents reported participating in at least one recreational activity, with no differences among racial/ethnic groups. However, Whites reported a significantly greater number of activities (3.2±2.0) than African Americans (2.2±1.7) or Hispanics (2.1±1.8) (p=0.001). Estimates of overall caloric expenditure indicated that Whites also expended more kcal per week in recreational activities (2521±2742) compared with Hispanics (1058±1314) or African Americans (1462±1837) (p=0.001). Walking was the most popular activity reported (65%); jogging was also reported by 21% of respondents. There were no racial/ethnic differences in the percentages of individuals reporting participation in walking or jogging. However, African Americans expended 837±1025 kcal per week walking compared with 653±1215 and 277±282 kcal per week for Whites and Hispanics, respectively (p=0.02). More Whites reported gardening/yard work (66%) than did Hispanics (25%) or African Americans (24%) (p=0.05). More Whites (18%) and Hispanics (17%) reported swimming than did African Americans (5%) (p=0.05).

Conclusions: Whites in the NTHHS reported participating in a greater number of recreational activities than African Americans and Hispanics. Estimated caloric expenditure in recreational activities was also greater for Whites. There was no racial/ethnic difference in the percentage of participants who reported walking, the most popular activity. There were racial/ethnic differences in the percentage of participants in other activities such a gardening and swimming. A larger sample size is needed to fully evaluate other noted trends in recreational activity participation. This information will prove important for activity-programming decisions in this population.

Sponsor: NIH P20 MD001633

## 1702 (Oral)

#### First Author/Presenter: Lauren Currie

Classification: GSBS Student

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EFFECT OF OBESITY ON COGNITIVE FUNCTION IN YOUNG MALE AND FEMALE OB/OB MICE.

Purpose: A leptin-deficient model of obesity (ob/ob) has been used to determine the effects of obesity on cognitive function. While a relationship between obesity and cognitive impairment has been suggested in epidemiological studies, an acceptable animal model to study this relationship not been established. The purpose of this study was to determine if leptin-deficient mice are an acceptable model for the study of effects of obesity on cognition. Further, we would like to determine the effect of gender on obesity-related cognitive decline. We hypothesize that obesity will impair cognitive function in ob/ob mice, regardless of gender.

Methods: Six-month old male and female ob/ob (n=30) and C57BL/6 (n=30) mice were assessed for cognitive ability. Prior to behavioral testing, weight and food intake was measured. Spontaneous locomotor activity, spatial learning and memory (swim maze performance) and frontal cortical function (T-maze) was assessed.

Results: As expected, male and female ob/ob mice were less active, weighed and ate more than controls. While the obese animals swam significantly slower than controls, their capacity to learn the location of the platform was not impaired. Overall, T-maze performance was impaired in obese mice; however, obese females performed worse than obese males.

**Conclusions:** Obesity seemed to affect cortical but not hippocampal function at an early age in mice and affected males and females differently. More studies are needed to determine possible mechanisms of obesity-induced cognitive declines.

Sponsor: N/A

## 1703 (Poster)

First Author/Presenter: Randy Moore

Classification: School of Health Professions MPAS Student

Randy Moore, PA-S; Christopher Cooper MPAS, PA-C; Olive Chen PhD

DOES A SEMINAR INCREASE MINORITY STUDENT INTEREST IN PURSUING A CAREER IN THE PHYSICIAN ASSISTANT PROFESSION?

Purpose: According to American Academy of Physician Assistants, there are over 70,000 Physician Assistants (PA s) practicing in the United States and 6.1% of them are Black. As of 2000, Blacks represented 12.3% of the US population and were projected to constitute 13.4% by 2006. It is unknown why Blacks are underrepresented in the PA profession. This study examined the role of an educational seminar in increasing Black student interest in the PA profession.

Methods: After IRB approval, the seminar was presented to Black college students from three Texas colleges in the summer of 2008. This seminar had three goals: (1) educate students about the PA profession, (2) provide a role model for Black college students, and (3) present the college prerequisites needed to apply to most PA programs. A pre and post survey was administrated to see if there were differences in the number of students interested in a career as a PA. Also measured were differences in familiarity with and knowledge about the PA profession and an understanding of the prerequisites needed to apply to PA school. Paired samples t-test was utilized to analyze the data.

**Results:** Forty-four students participated and 40 surveys were eligible for inclusion. Three areas were surveyed: (1) respondent s familiarity with the PA profession, (2) their understanding of the prerequisites for admission to PA school, and (3) their willingness to apply to a PA school. Statistical differences were found between pre and post scores. Following the seminar, participants demonstrated significant increases in the following areas: familiarity with the PA profession (t= 8.52; P<.001).

**Conclusions:** The results indicate that a seminar is effective in increasing familiarity with and knowledge about the PA profession. Further, participants demonstrated increased understanding about the general prerequisites needed for PA school and were more willing to apply to PA school. We conclude that seminars should be utilized by PA programs who are interested in recruiting Black students. Further studies are needed to determine if the presenter s ethnicity affects respondent s answers.

First Author/Presenter: Cortney Hanson

Classification: School of Health Professions MPAS Student

Cortney Hanson, PA-S, UNTHSC, Fort Worth, TX 76107 Brenda Wallace, PA-S, UNTHSC, Fort Worth, TX 76107

ASSESSING THE HEALTH LITERACY LEVEL OF CAREGIVERS OF THE PEDIATRIC PATIENT UTILIZING THE NEWEST VITAL SIGN

Purpose: Studies show that low literacy levels of pediatric caregivers correlate with higher incidences of health care problems in children. This study aimed to assess the health literacy level of caregivers by utilizing The Newest Vital Sign (NVS) Questionnaire in the pediatric setting.

Methods: This was a cross-sectional study utilizing the NVS Questionnaire and a Demographic Questionnaire in a pediatric clinic of North Texas. After gaining IRB approval, the researchers recruited 100 participants to participate in this study. The NVS has six questions and participants gained points based upon how many questions they answered correctly. Scores of 0-1 suggests high likelihood of limited health literacy, 2-3 indicates the possibility of limited health literacy, and 4-6 indicates adequate health literacy. A Demographic Questionnaire was utilized to collect information regarding the participant s age, gender, ethnicity, education level, their perceived health literacy confidence level, and their child s health insurance information. Pearson Chi square was used to test the relationship of the participant s perceived confidence level and their score on the NVS. Logistic regression was used to analyze the relationship between the participant s demographic variables and their NVS score.

Results: The majority of the participants were English speaking females between 26-35 years old with some college education. Majority of the children were insured by Medicaid. The data showed 40% of the participants have limited health literacy as they scored less than 4 on the NVS and 60% had adequate health literacy with a score greater than 4.Education level as well as ethnicity showed to have a relationship with the level of health literacy of the participants. As one increases their education, they are more likely to have adequate health literacy (OR = 2.749). When compared to Caucasians, Hispanics and African Americans showed a (76% and 84%) reduction in odds of having adequate health literacy (OR = 0.244 and OR = 0.156 respectively).

Conclusions: Forty percent of participants had limited health literacy which means that they may not understand the instructions or information provided to them by their providers. In order to avoid these misunderstandings or lack of communication, clinicians should encourage the caregiver to ask questions during/after the visit and utilize a teach back method.

Sponsor: N/A

## 1705 (Poster)

First Author/Presenter: Michael Hellman

Classification: TCOM DO Student

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### COMPARING FATIGUE BETWEEN FIBERWIRE AND STAINLESS STEEL FOR THE REPAIR OF TRANSVERSE PATELLA FRACTURES

Purpose: Transverse patella fractures (TPF) have historically been repaired via internal fixation with stainless steel (SS) wire based on the tension band principle. However, heavy suture has been shown to be a viable and promising alternative to SS in such procedures. Double strand FiberWire® (FW) tied with a Wagoner s Hitch has been previously shown to have greater strength in tension band fixation than 18-guage SS wire. However, fatigue testing of FW has yet to be investigated for the treatment of TPF. This study aims to compare the fatigue strength of double strand FW tied with a Wagoner s Hitch, to the current gold standard of treatment using SS wire with two (bilateral) compression twists.

Methods: A novel 3-point-bending patella model, designed to simulate a worse case loading scenario, was used for the fatigue testing of the two different wire constructs. The patella model has a convex surface, similar to a human patella, and has two parallel holes drilled along its length to allow for reproducibility of the surgical technique. Each wire was used to bind the halves of the simulated TPF together prior to fatigue testing. The FW was tied using a Wagoner's Hitch, while the SS wire was bound with two compression twists, each having seven twists. Once bound, each of the patella constructs was subjected to cyclical three-point-bending at 90%, 60% and 30% of the maximum strength reported for the SS wire. Furthermore, a 100N pre-load force was applied to maintain the wire in constant tension during fatigue testing. Based on published findings, fixation failure was defined as a 3mm gap at the apex of the convexity.

Results: With each loading cycle, fatigue damage in the SS wire accumulates leading to gradual increases in permanent deformation. In contrast, the FW is able to withstand damage, returning closer to its original length, for many more loading cycles. Furthermore, comparing the forcedeformation curves between the SS wire and FW constructs, a softening occurs for the SS while a hardening behavior is exhibited by the FW.

Conclusions: The FW construct is superior to the SS construct in fatigue, withstanding a greater number of cycles before failure. The combination of increased strength, previously reported, and the current findings, suggests FW to be superior to SS for the fixation of TPF.

#### First Author/Presenter: Katie Krueger

#### Classification: School of Health Professions MPAS Student

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## SCREENING FOR SUICIDALITY IN ADOLESCENTS BY PEDIATRIC PROVIDERS

Purpose: The purpose of this project was to identify whether pediatric providers were screening for suicidality in their practice based on the American Academy of Pediatrics (AAP) guidelines. In September of 2007, the AAP issued an updated statement calling for providers to screen for risk factors in four different categories (fixed, mental health, social/ environmental and immediate) as well as interview the adolescent separate from the care-giver and directly question the teen about current suicidal thoughts.

Methods: Institutional Review Board approval was obtained prior to initiating data collection. A retrospective chart review was conducted at two North Texas pediatric clinics. All charts meeting the inclusion criteria (new, well-child/sports physical visit; between the ages of 13-17; seen between September 2007 and July 2008) were included. Eleven risk factors were evaluated to determine how many and which risk factors were being screened by the clinicians. Other factors evaluated per the AAP guidelines included how the teens were being interviewed, if they were being directly questioned about suicidality, and if the potential for suicide was addressed in the treatment plan when indicated.

Results: A total of 54 charts were reviewed. The data revealed that an average of 4.56 out of 11 risk factors was being assessed per visit, 3.7% of teens were interviewed without care-givers present and 40.7% were directly questioned about current suicidal ideation. Nine of the 11 risk factors evaluated in this study were present on the intake forms utilized by these clinicians. Additionally, the potential for suicide was addressed in the treatment plan in only two of nine charts where positive risk factors were identified.

Conclusions: The results of this study indicated that, while clinicians were asking questions about suicidality, they were under screening based on AAP guidelines. While the intake forms were generally comprehensive and thorough, only two questions would need to be added in order to meet all of the AAP screening criteria. The divided responsibility of interviewing patients posed some difficulty in collecting all the data included on the intake forms. Minor adjustments in the organization of the intake forms and personnel training could result in full adherence with AAP guidelines.

Sponsor: N/A

## 1707 (Poster)

#### First Author/Presenter: Rafal Luchowski

#### Classification: Postdoctoral Fellow

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FLUORESCENCE LIFETIME IMAGING MICROSCOPY STUDIED MOLECULAR ORGANIZATION OF ANTIFUNGAL ANTIBIOTIC AMPHOTERICIN B IN LIPID MONOLAYERS

Purpose: Amphotericin B (AmB) is a life-saving polyene antibiotic used to treat deep-seated mycotic infections. Both the mode of therapeutic action as well as toxic side effects are directly dependent on molecular organization of the drug. Binding of AmB to lipid monolayers formed with dipalmitoylphosphatidylcholine, pure and containing 40 mol% cholesterol or ergosterol, the sterol of fungi, has been examined by means of Fluorescence Lifetime Imaging Microscopy.

Methods: Fluorescence Lifetime Imaging Microscopy measurements were performed on MicroTime200 Picoquant, GmbH Berlin, Germany. As excitation source was 375 nm laser diode working with repetition rate 20 MHz and resolution 16 ps. Images were taken on the OLYMPUS Microscope IX71 and gathered by means of the Perkin Elmer APD detectors.

Results: AmB emits fluorescence with the characteristic lifetimes dependent on actual molecular organization: tM2=5 ps and tM1=0.35 ns in the monomeric state, the emission from the S2 and the S1 states respectively and tD=14 ns and tA=3.5 ns in the form of a dimer and associated dimers respectively.

**Conclusions:** Analysis of the Langmuir-Blodgett films reveals that AmB binds to the lipid membranes and to the cholesterol-containing lipid membranes preferentially in the form of associated dimers. The same form of AmB appears in the membranes containing ergosterol but additionally the monomers and dimers of the drug can be observed, which can severely affect molecular organization of the lipid membrane. The results are discussed in terms of selectivity of AmB towards the ergosterol-containing biomembranes of fungi.

#### First Author/Presenter: Jonathan Piotrowski

Classification: School of Health Professions MPAS Student

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INTERACTIONS OF PHARMACEUTICAL REPRESENTATIVES AND PHYSICIAN ASSISTANTS AND ASSOCIATED INFLUENCES ON PRESCRIBING PRACTICE

Purpose: The medical community continues to debate the proper boundaries of its relationship with the pharmaceutical industry. To contribute to this debate, this study collected data about the frequency and types of interactions between physician assistants (PAs) and pharmaceutical industry representatives (PRs) and what influence these interactions may have on PA prescribing practice.

Methods: This research was a multi-state, cross sectional study. Twenty American Academy of Physician Assistants (AAPA) state chapters were randomly selected and invited to participate with 8 chapters agreeing to participate. Surveys from respondents who do not provide direct patient care and/or do not have prescriptive authority were excluded from the study. The survey contained questions pertaining to demographics, types and frequency of interaction, and level of influence these interactions may have had. In addition to descriptive statistics, the data was analyzed using the Kruskill-Wallis, Kendall s tau and Spearman s rho tests. This study has been approved by the UNTHSC IRB.

Results: There were 147 respondents to the survey of which 134 met inclusion criteria. Nearly half of the respondents (49%) indicated interaction with pharmaceutical representatives one or more times a week. Also, approximately one third of the respondents (29%) indicated receiving gifts of food and/or other items one or more times a week. Interactions differed depending on a PA s medical specialty (X2 = 15.9, P = .001) and practice site (X2 = 26.0, P < .001). Fifty-seven percent of respondents agreed or somewhat agreed that pharmaceutical representatives influence the prescribing practices of most PAs. Correlations were found between the frequency of food and beverage received in the workplace and PR influence on respondent s prescribing practices (t=.155, p = 0.048), as well as between the frequency of PA-PR interactions and the importance of pharmaceutical representatives in the PA s understanding of new medications (t=.176, p = .020).

Conclusions:<sup>2</sup> Our results indicate that PAs are interacting with pharmaceutical representatives and that those interactions often influence the prescribing practices of PAs. As such, PAs must be aware that their interactions with pharmaceutical representatives could influence their prescribing practices. PAs should also be included in discussion about ethical guidelines governing the relationship between healthcare providers and the pharmaceutical industry.

Sponsor: N/A

## 1709 (Poster)

#### First Author/Presenter: Mariusz Szabelski

#### Classification: Postdoctoral Fellow

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#### POTENTIAL REFERENCE PROBES FOR IMPULSE RESPONSE EVALUATION FOR TIME-RESOLVED FLUORESCENCE MICROSCOPY

Purpose: The reference pulses, necessary for accurate lifetime measurements, are usually taken from the excitation scattering or reflection, which is at shorter wavelengths than observed fluorescence emission. Commonly used detectors, photomultipliers and photodiodes respond differently to different color of the pulsed light, which is known as a color effect of photodetectors. This problem can be solved by using known standard probes as a reference, preferably with very short lifetimes.

Methods: Fluorescence decays were collected by time domain technique using a FluoTime 200 lifetime spectrometer (PicoQuant GmbH) equipped with R3809U-50 microchannel plate PMT (Hamamatsu) and PicoHarp300 TCSPC module. The MicroTime 200 fluorescence lifetime microscope system with two types of detectors Perkin-Elmer and MPD single photon sensitive APDs was used to obtain the time-resolved information. The excitation source was an LDH470 pulsed laser diode.

Results: In presented work we showed a few standards which have ultrashort fluorescence lifetimes (16 25 ps) and can be used to measure instrument response functions of single photon detectors. We demonstrated that instrument response functions for commonly used detectors are practically the same for scattering as for our fluorescence standards. We also analyzed a complex fluorescence decay using both elastic scattering and probes as a response function.

Conclusions: Fluorescence probes with a picosecond lifetime are an ideal reference for IRFs evaluation of photodetectors used in spectroscopy/microscopy. We demonstrated that the use of proposed references as IRF results in the absence systematic error in lifetime measurements and analysis.

First Author/Presenter: Xiangle Sun

Classification: Staff

Xiangle Sun, Ph.D., M.D. Rance Berg, Ph.D. Jerry Simecka, Ph.D.

FLOW CYTOMETRY AND LASER CAPTURE MICRODISSECTION CORE FACILITY

Purpose: The Flow Cytometry and Laser Capture Microdissection Core Facility provides cutting-edge technologies to advance research. Faculty, students, staff and any research groups are welcome to visit our facility in order to explore the possibility of taking advantage of these powerful technologies.

Methods: You are encouraged to contact core facility manager Xiangle Sun at 817-735-0117, room 2-438 or 2-442. Dr. Jerry Simecka (core director) and Rance Berg (principle investigator) are also available to discuss your projects. You can obtain valuable information and references from core website: www.hsc.unt.edu/fcf.

Results: More impressive results will be produced to strengthen your publications or grant submissions.

**Conclusions:** The Flow Cytometry and Laser Capture Microdissection Core Facility is a supportive unit to help achieve your research goals. We welcome any suggestion and thoughts to improve our service, establish new methods and explore new applications.

Sponsor: N/A

## 1711 (Poster)

First Author/Presenter: Irina Akopova

Classification: Postdoctoral Fellow

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#### METALLIC NANOSTRUCTURES FOR ENHANCED FLUORESCENCE

Purpose: Fluorescence emission can be significantly enhanced near silver nanostructures due to plasmonic fluorophores particle interactions. Plasmons are density waves of electrons, created when light hits the surface of a metal under precise circumstances. Because these density waves are generated at optical frequencies, very small and rapid waves, they can theoretically encode a lot of information. This phenomenon is being used for the ultrasensitive detection of fluorescent indicators, such as cardiac or cancer markers.

Methods: Here, we present several silver nano-structures studied by Atomic Force Microscopy (AFM). Silver nano-structures are known to significantly increase the fluorescence signal. Our observations in a Confocal Time-Resolved Microscope revealed the results that fluorescence on silver coated slides can be enhanced by 2 to 10 times. The question is, why such a big range of enhancement?

Results: One of the possible explanations is difference in silver nano-structures formed on the glass. To check this hypothesis we use AFM to resolve the surface structures formed by silver particles.

Conclusions: Our results demonstrate that it is a dependence of fluorescence enhancement on size, shape and density of silver nano-structures formed on the surface of the glass slide.

#### First Author/Presenter: Nolan Malthesen

Classification: Resident

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## THE EFFECT OF FLEXOR TENDON SHEATH EXPANSION ON TOTAL RANGE OF MOTION OF THE FINGER

Purpose: This study aims to prove the null hypothesis that reconstruction of the flexor tendon sheath with extensor retinaculum does not create a bowstringing effect, and does not decrease the total range of motion of the finger.

Methods: Nine fresh cadaveric fingers were used to test the hypothesis. Each finger was removed from the hand at the base of the metacarpal. The skin was removed to expose the flexor tendon and pulley system. The fingers were then marked on either the radial or ulnar side at the proximal and distal metaphysis in each phalanx. Each finger was flexed by pulling the flexor tendon in a controlled manner until the distal tip of the finger was 2 cm from the volar surface of the metacarpal. High resolution digital photographs were then taken and used to measure the angular motion of each finger. Finger motion was then re-measured after the pulley system was released starting at the distal end of A4 and incised proximally a distance equal to that finger s individual excursion. The pulley system was then reconstructed using fascial tissue from the extensor retinaculum and total range of motion was again re-measured.

Results: When each finger s sheath was incised, the distance involved included the distal end of A4 to the distal end of A2 in almost all of the fingers. The average loss in finger total range of motion (TRM) from an intact sheath to an incised sheath was 17.3 degrees. When the sheath was repaired with a graft from the extensor retinaculum, the average improvement in TRM was 15.6 degrees. The repaired sheath averaged a loss in TRM of 1.7 degrees as compared to the intact sheath prior to release.

Conclusions: After repair of a flexor tendon it may be necessary to incise the sheath in order to facilitate repair or allow for free gliding of the repair. Studies have shown that incision of too great a distance of the flexor tendon sheath can create bowstringing and result in loss of flexion. The results from this study suggest that repairing the sheath with a graft from the extensor retinaculum does not lead to a loss in total range of motion of the finger.

Sponsor: N/A

## 1713 (Poster)

#### First Author/Presenter: Hsueh-Fen Chen

#### Classification: Faculty

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## HOSPITAL FINANCIAL CONDITION AND THE PROVISION OF UNPROFITABLE SERVICES

Purpose: The purpose of this study is to examine the effects of hospital financial condition on the provision of unprofitable services hospitals deliver.

Methods: Economic theory and a longitudinal empirical study design are applied to address study objectives. The dependent variable is the logged total volume of unprofitable services for each study hospital. Unprofitable services were defined based on prior work of Darrell Gaskin and Jill Horowitz and included maternity care, newborns with complications, substance abuse, psychiatric care, trauma, and burn services. Discharges for these unprofitable services were extracted from the HCUP-SID and aggregated to the hospital level separately for insured and uninsured patients. The primary independent variables of interest were financial performance measures, including the ratio of cashflow to total revenues and operating margin. These were obtained from Medicare hospital cost reports. Control variables included health policy, hospital, and market factors from several data sources including the AHA annual survey, Area Resource File, Interstudy, Census Bureau, and Medicaid Statistical Information System. First difference models with instrumental variables were used to control for latent hospital-specific effects and endogeneity of hospital financial condition. Models were estimated separately for not-for-profit (NFP), public, and for-profit (FP) hospitals.

Results: NFP hospitals with strong financial performance provided more unprofitable services for both insured and uninsured patients than did those NFP hospitals with worse financial condition. Financial performance did not influence public and FP hospitals provision of these services.

Conclusions: The results are consistent with the utility maximizing behavior of NFP hospitals in that they use their profits to expand services that may meet community need but are not adding to their profits. FP hospital s behavior is consistent with profit maximization in that they provide these services as a business cost to attract and maintain consumers, especially insured patients.

Sponsor: National Heart, Lung, and Blood Institute

## 1714 (Oral)

#### First Author/Presenter: Sarah Brown

#### Classification: SPH Student

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## PROFILES OF PATIENTS WITH MULTIPLE VISITS TO A PSYCHIATRIC EMERGENCY CENTER

Purpose: John Peter Smith (JPS) Health Network of Tarrant County Psychiatric Emergency Center (PEC) utilization patterns were examined to develop a greater understanding about how these services are used by the community. The PEC serves patients in crisis, is often a gateway to mental health services, and many patients return multiple times. Identifying and characterizing patients who use the PEC multiple times and investigating how these patients differ from those with only one admission is of specific interest.

Methods: Existing data from an internal intake and discharge database provided a record of consecutive visits to the PEC from January 1, 2000 through November 30, 2007. This database captures demographic characteristics, admission status, presenting problems, diagnosis and treatment, and discharge. For this analysis patients were categorized by number of visits to the PEC during the study time period: one visit, two visits, three or four visits, and five or more visits. Demographic and clinical characteristics were examined for each of these groups.

Results: During this nearly eight year period, 42,306 patients were seen in the PEC for a total of 79,320 visits. Of the total visits to the PEC, 36.5% of visits were by patients seen only one time, while the remaining visits were by patients admitted more than once. While the overall number of patients who made five or more visits appeared relatively low (2,721), these patients accounted for 63.5% of the total admissions during the study period. These groups of patients had identifiable differences in demographic and clinical characteristics. Compared to those who make a single visit, patients with five or more visits are more likely to have a diagnosis of schizophrenia (26.6% vs. 11.1%). On the other hand, single visit patients are more likely than multiple visit patients to have depressive disorders (36.4% vs. 28.2%) or adjustment disorders (9.3% vs. 2.3%).

Conclusions: A disproportionally large number of the total visits to the PEC were made by a small number of patients. Differences in characteristics, such as demographics and diagnostic categories can be used to create profiles that will help clarify what characteristics are related to likelihood of multiple visits. Identifying differences that exist between patients who make single visits versus those with multiple visits to the PEC will prove useful in understanding the role of the PEC and how it is used by patients.

Sponsor: N/A

## 1715 (Poster)

#### First Author/Presenter: Kia Brown

#### Classification: GSBS Student

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#### IMPLICATIONS OF CLUSTERING ON SAMPLE SIZE CALCULATIONS OF RANDOMIZED CONTROLLED TRIALS

Purpose: The main goal of this project was to educate investigators and clinical researchers about the intricate details related to sample size calculations for cluster randomized controlled trials. These include the impact of the intracluster correlation coefficient (ICC), the design effect (DE), and the effective sample size (ESS).

Methods: A literature review on relevant topics was conducted using PubMed and print resources from the UNTHSC library. Sample size calculations were conducted with and without accounting for the clustering effect for a cluster randomized controlled trial currently being conducted by the North Texas Primary Care Practice-Based Research Network (NorTex). Sampsize Software was used to determine the unadjusted sample size without clustering effects based on a specified power, significance level, standard deviation and minimum difference. The software was also used to determine the adjusted sample size for a range of ICC values and differences in power. Separate calculations were done to determine the ESS and DE values for a range of ICC s.

Results: The sample size calculated for a clustered randomized controlled trial was found to be 4 times the sample size needed for a simple randomized trial at the same significance level and power. A 0.1 increase in the ICC almost doubled the total sample size needed for a clustered trial. Inflation of the sample size increased as the ICC increased. The ESS decreased as the ICC increased. The DE increased as the ICC increased as well. A 5% increase in power of a clustered trial required a 20% increase in the sample size and was best accomplished by keeping the cluster size the same and increasing the number of clusters.

Conclusions: Due to the loss of statistical efficiency caused by clustering, a larger sample size is needed for these trials. It is important to estimate this value carefully because even a small change in the ICC can drastically change the sample size. In order for a cluster randomized trial to achieve the equivalent power of a simple randomized trial, the standard sample size must be inflated by the DE. The DE should be kept low by increasing the number of clusters and keeping the cluster size small. This will create an adequately powered study and keep the ESS large. Without knowing the implications of clustering effects on sample size calculations, studies may produce results with no true value to the investigator or to the medical community.

### First Author/Presenter: William Effinger

#### Classification: Dual Degree Student: DO/MS

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#### THE MENTAL HEALTH SCREENING AND TREATMENT INITIATIVE FOR THE TARRANT COUNTY PROBATIONER POPULATION

Purpose: To enable Licensed Chemical Dependency Counselors (LCDCs) to perform routine standardized mental health screenings for over 300 probationers at the Tarrant County Treatment Alternatives to Incarceration Program (TC-TAIP) facility in downtown Fort Worth every month.

Methods: The TC-TAIP serves probationers experiencing substance abuse problems. LCDCs provide crucial services such as chemical dependency screening and placement into treatment programs. Probationers with substance use disorders are at an increased risk for having comorbid untreated psychiatric disorders, yet probationers are not currently being screened for other mental illnesses or co-occurring disorders. There are many barriers to providing routine mental health screening services for all TC-TAIP probationers. Hiring psychiatrists to screen TC-TAIP probationers is not feasible, but screening for psychiatric disorders is beyond a LCDC s training level. Currently, there is no validated mental health screening instrument that has been customized for efficient, effective clinical use for LCDCs in the TC-TAIP.

Results: A novel solution has been developed by the Mental Health Screening and Treatment Initiative (MHSTI) team. The project model utilizes innovative new technology in the form of a computer-assisted Mental Health Screening Tool to enable non-psychiatrist LCDCs to perform standardized mental health screenings and decide which probationers need to be referred for a more comprehensive psychiatric assessment. This technology system should allow all non-psychiatrist LCDCs at the downtown Fort Worth location TC-TAIP to effectively and efficiently provide mental health screening services for all the probationers they interview.

Conclusions: The implementation of this model mental health screening program will be a key step towards the development of a comprehensive mental health screening and treatment program for this underserved probation population. This program will have significant community and public health implications by reducing recidivism, and making a safer and more productive Texas. The barrier to efficiently and effectively screening for mental health disorders is a problem for the criminal justice system nation-wide. Innovations developed in building this model program may have implications beyond the criminal justice system as well.

Sponsor: N/A

## 1717 (Oral)

### First Author/Presenter: Gloria Mendoza

#### **Classification: SPH Student**

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#### BIOTERRORISM: AWARENESS AND PREPAREDNESS OF DENTON COUNTY MEDICAL RESERVE CORPS (MRC) VOLUNTEERS

Purpose: 1. Assess the prevalence and recency of bioterrorism training among Denton County MRC volunteers. 2a. Assess MRC volunteers awareness in regards to bioterrorism and bioterrorist agents. 2b. Assess MRC volunteers preparedness to respond to a bioterrorist event. 3. Analyze the relationship between bioterrorism training and awareness/preparedness.

Methods: Investigators developed a web-based survey of 30 questions and offered it to MRC volunteers. After 1 month they collected 115 responses and following data cleaning, were left with a total of 109 responses. Respondents were reached via a list-serve provided by the Denton County MRC personnel. Survey was opened for response on November 3, 2008 and closed temporarily on December 1, 2008.

Results: Results showed that 61% of the MRC volunteers had received bioterrorism training. In assessing for bioterrorism awareness, ¬ 73% were categorized as aware. However, 53% were found to be prepared and 47% were found to be not prepared for a bioterrorist event.

Conclusions: Volunteers that have received bioterrorism training are 4.29 times more likely to be aware than those who have not received any bioterrorism training. In addition, volunteers that have received bioterrorism training are 7.19 times more likely to be better prepared than those with no bioterrorism training. Hence, the results of this pilot study are directed at first responders who form part of the Denton County MRC and have therefore been provided training to respond to a health emergency in order to analyze their readiness and preparedness. Investigators concluded it is essential to train first responders.

#### First Author/Presenter: Kristen Morton

Classification: School of Health Professions MPAS Student

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## THE PREVALENCE OF MALE OSTEOPOROSIS SCREENING

Purpose: This study aimed to investigate the osteoporosis screening frequency for men who possess certain risk factors. Secondarily, the research explored whether race, insurance status, or type of department correlates with osteoporosis screening frequency.

Methods: A retrospective chart review was conducted at a North Texas Family Medicine clinic and an Internal Medicine clinic. The reviewed charts had one or more of the following osteoporosis risk factors: the age of 70 years or older, rheumatoid arthritis, glucocorticoid steroid use, osteopenia, hypogonadism, hyperparathyroidism, and/or alcoholism. To identify age risk factor, seventy simple random charts were selected. A purposive sampling method was utilized to identify remaining risk factors. Chi Square and Fischer s Exact Tests were used to examine relationships demographics had with male osteoporosis screening. Additionally, a logic regression model was developed for both screening and osteoporosis prevalence to examine the effect of all risk factors as a whole. Statistical significance was based on a p value being < 0.100 since this was a preliminary study of a small sample size.

Results: The frequency of Bone Mineral Density scans performed ranged from 20.0% to 22.6% depending on the recommendations or guidelines applied. Out of the 35 patients who were screened, 34% were diagnosed with osteoporosis. Patients with government insurance were about 5 times more likely to be screened, compared to patients with only private insurance (P = 0.056). Osteoporosis screening occurrence had a statistically significant relation with patients 70 years of age or older regardless of additional risk factors (P = 0.005), patients with osteopenia (P = <.001), patients taking oral glucocorticoid steroids (P value = 0.08), and patients with more than one risk factor (P = < 0.001). None of the 15 African American patients at risk received screening. Internal Medicine providers were statistically more likely to screen their at risk male patients for osteoporosis than Family Medicine providers (P = 0.095).

Conclusions: The results of this study indicate that the male patient sample at risk for osteoporosis is inadequately screened. Most healthcare providers recognized advanced age as a risk factor for male osteoporosis but did not pay attention to other risk factors, especially hypogonadism. More education should be provided to primary care healthcare professionals regarding this disease, risk factors, and current recommendations and guidelines.

Sponsor: N/A

## 1719 (Poster)

#### First Author/Presenter: William Effinger

#### Classification: Dual Degree Student: DO/MS

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PREVALENCE AND SOCIETAL COSTS OF MENTAL ILLNESSES IN THE TARRANT COUNTY TREATMENT ALTERNATIVES TO INCARCERATION PROGRAM

Purpose: The primary objective of this study was to highlight the magnitude and severity of mental health pathology in this population of probationers as well as its significant associations with substance abuse and probationer criminality.

Methods: 302 probationers in the Tarrant County Treatment Alternatives to Incarceration Program (TC-TAIP) were asked to take this study s 72question Mental Health Screening Tool (MHST) prior to their scheduled interview with with a Licenced Chemical Dependency Counselor (LCDC). 241 completed surveys were used for data analysis. All statistical tests were performed using SPSS version 15.0.

**Results:** The prevalence rates of current, symptomatic disorders were: 27.4% (21.7%-33.0%) for Internalizing disorders, 8.3% (4%-.11%) for Externalizing disorders, 22% (17%-27%) for Substance use disorders, 14.9% (10.4%-19.4%) for Co-occurring disorders, 8.3% (4.8%-11.8%) for adult ADHD, 21.6% (16%-27%) for Depression, 17.4% (13%-22%) for Anxiety disorders, and 19.5% (14%-25%) for Bipolar disorder. There was a significantly larger percentage of probationers identified as suffering from current internalizing disorders (p<.001), externalizing disorders(p<.001), current adult ADHD(p=.001), current Depression(p<.001), current Anxiety disorders(p=.001), and current Bipolar disorder(p<.001) in current substance abusing vs. non-substance abusing probationers.

Conclusions: Untreated mental health pathology decreases probationers treatment success rates in a substance abuse treatment program such as the TC-TAIP, and this in turn is associated with increased criminal recidivism. There is a heavy presence of mental health pathology in this population, especially in substance abusers. The Primary Care Research Institute (PCRI) is preparing to implement a novel Mental Health Screening Program utilizing technology to enable non-psychiatrist LCDCs to efficiently provide mental health screening services for this entire population.

#### First Author/Presenter: RIT VATSYAYAN

#### Classification: Postdoctoral Fellow

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#### PROTECTIVE ROLE OF RLIP76 AGAINST CCL4 INDUCED HEPATOTOXICITY

Purpose: Present studies were designed to investigate the protective role of RLIP76 against CCl4 induced hepatotoxicity in a mouse model.

Methods: Twenty C57BL/6 mice (age 8-12 weeks) were randomly divided into 4 groups (5 mice in each group). Group 1 was control, receiving corn oil as vehicle, where as groups 2-4 received 1:1 (v/v) mixture of CCl4 and corn oil (1 ml/kg body weight i. p.). Groups 3 and 4 received empty liposomes and RLIP76 proteoliposomes (200µg/mice i. p.), respectively, 2 h post exposure of CCl4. MDA and 4-HNE levels were measured by a colorimetric method using a lipid peroxidation kit obtained from Oxford Biomedical Research, Oxford, MI. Tissues were processed for light microscopy and stained with hematoxylin and eosin, Tissue sections were observed and photographed on an Olympus Provis AX 70 microscope with DP70 digital camera.

Results: Our results show that the lipid peroxidation and 4-HNE levels in the liver of CCl4 treated mice were induced by approximately 2 fold over the control mice treated with vehicle only. However the 4-HNE levels were attenuated in mice delivered with RLIP76 proteoliposomes 2 h post CCl4 exposure. Histopathological examination of liver tissues from CCl4 exposed mice showed signs of hepatotoxicity which included cellular swelling, disarray and vacuolization, but the mice treated with RLIP76 liposomes showed minimal hepatotoxicity.

Conclusions: These findings suggest that post administration of a single dose of RLIP76 proteoliposomes protects mice from chemical induced hepatotoxicity. These studies also support our previous in vitro findings that RLIP76 protects cells from chemical toxicity by limiting the accumulation of LPO products.

Sponsor: N/A

## 1721 (Poster)

#### First Author/Presenter: Nicole Phillips

#### Classification: GSBS Student

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# THE CHILEAN POPULATION DATABASE PROJECT: A HIGH THROUGHPUT APPROACH FOR DNA PROFILING OF 1000 CHILEAN POPULATION SAMPLES

Purpose: The UNT Center for Human Identification R&D Laboratory (UNTCHI R&D) has been contracted to generate a Chilean population database. Three genetic profiles are to be obtained from each of the 1000 male population samples: (1) an autosomal short tandem repeat (STR) profile; (2) a Y chromosomal STR profile; and (3) a mitochondrial DNA (mtDNA) profile. Demonstrated herein are a number of the methods and tools employed for high throughput sample and data processing of the Chilean population database. The project s workflow/design is highly focused on automation, minimizing the opportunity for human error while maximizing efficiency.

Methods: Male buccal swabs were collected from each of five Chilean regions, totaling approximately 1000 population samples. The Freedom EVO® 100 is the robotic platform employed for DNA extraction using DNA IQ" system chemistry. The PCR reactions are simultaneously setup using another robotic platform, the MiniPrep. Excel worksheets were developed to automate sample management, DNA extract normalization, reaction volume calculations and concordance verifications. GeneMapper® v3.2 was validated as an expert system for autosomal and Y-STR data analyses of the 1000 population samples.

Results: The extraction and amplification setup procedures are laborious and time-consuming processes when executed manually. Using liquid handling robotics to automate these two processes allows the analysts to initiate a series of robotic commands and then proceed to other tasks while it is operating. Excel spreadsheets expedite processing and decrease the likelihood of human error in sample entry, calculations, and profile verification. Auto-populating spreadsheets allow for electronic upload of sample sheets to the various software programs, are pre-programmed to perform the required calculations for reaction component volumes and extract normalization values, and verify concordance between data interpretations of the two analysts. The use of expert systems for STR data analysis of single source samples decreases the amount of time required to assign and verify genetic profiles. When properly optimized, the analyst is only required to review the genotypes of questionable quality, greatly decreasing the number of loci to be reviewed, and thus the required amount of time.

Conclusions: We have implemented many methods and tools which increase automation. In doing so, the overall efficiency is maximized and the likelihood of human error is significantly decreased.

#### First Author/Presenter: Helvia Abdelfattah

Classification: GSBS Student

Helvia Abdelfattah, B.S.; Lena Abraham, B.S.; Holly Cherian, B.S.; Elizabeth Feller, B.S.; Cheryl Lowe, B.S.; Ally Newman, B.S.; Pam Musslewhite, B.S.; Nicole Phillips, B.S.; Lakshmi Reddy, B.E.; Rhonda K. Roby, Ph.D, M.P.H. University of North Texas Health Science Center, Fort Worth, TX 76107

#### FACTORS AFFECTING PCR AND FRAGMENT ANALYSIS FOR FORENSIC DNA PROFILING

Purpose: In forensic genetics, commercial chemistry kits are available for fragment analysis. We demonstrate various factors that affect PCR of human DNA for forensic DNA profiling.

Methods: The following amplifications were performed using the Identifiler® kit using the 310 Genetic Analyzer. To demonstrate the effect of adding various quantities of template DNA to amplification reactions, a range of DNA was amplified. The manufacturer s recommended cycling parameters were used. To demonstrate the effect of annealing temperature variation, the PCR parameters were altered. To demonstrate the effect of incomplete non-template adenylation, samples were removed at specific times during the final extension phase of amplification. To demonstrate the effect of charged ions on electrokinetic injection, formamide was purposely degraded.

Results: Template DNA addition of 2.5ng to 10ng resulted in spectral pull-up, increased stutter and shouldering. Below 500pg of template DNA, peak height imbalance and allele dropout were observed. Full, well-balanced profiles were obtained from amplification of 0.5ng to 1.0ng of template DNA. Samples exhibiting high degree of peak height imbalance may indicate a primer-binding site mutation. To evaluate this possibility, the annealing temperature experiment was performed. By lowering the temperature stringency, heterozygote peak balance was improved. When extension time was eliminated, split peaks, shouldering, and broad peaks were observed. Many alleles were incorrectly called as off-ladder due to poor peak morphology. As extension time increased, these artifacts became less prevalent. After 96 hours of formamide degradation, the overall signal intensity significantly decreased and only partial profiles were obtained.

Conclusions: Optimal template DNA for PCR amplification is in the range of 500pg to 1ng; outside this range, data becomes more difficult to interpret. As the annealing temperature deviates from the recommended temperature, the signal strength decreases across some loci due to the primers binding less specifically, generating non-specific PCR product. Incomplete non-template adenylation results in poor peak morphology such as shouldering and split peaks. Prolonged exposure of formamide to moisture causes the generation of formate ions which compete with PCR products for electrokinetic injection into the capillary. The result is an overall decrease in signal intensity which can lead to allele dropout and, therefore, partial profiles.

Sponsor: N/A

## 1723 (Poster)

First Author/Presenter: Vicki Neitek

#### Classification: Faculty

Vicki Nejtke, Ph.D. Matthew Avila, Ph.D. Kathryn Kaiser, Doctoral Candidate Jemila Lea, B.S. Alan Podawiltz, D.O. J.K. Vishwanatah, Ph.D.

#### ETHNIC DISPARITIES IN CO-OCCURRING DISORDERS

Purpose: Mental and physical health disparities in our disadvantaged minority populations are often associated with increased stress-induced alcohol and/or drug use. Left unrecognized and untreated, mental illness and substance abuse can negatively impact physical health outcomes overall. We found that Non-Hispanic Blacks preferred cocaine as their drug of choice while about half of the Non-Hispanic Whites and Hispanics prefer cocaine and methamphetamines equally. Drug use may influence the onset and/or aggravation of chronic and life-threatening medical illnesses such as hepatic and cardiovascular diseases, hypertension and HIV/AIDS. Thus, examining health disparities among treatment-seeking minority persons with co-occurring mental illness, chronic medical diseases and substance use disorders is clinically and culturally significant.

Methods: Sociodemographic data and drug preferences were analyzed using Chi-square and ANOVA tests between groups. Subjective drug effects for methamphetamine and cocaine were factored analyzed and factor scores compared among ethnic groups.

**Results:** There were no differences in the percentages of Blacks, Hispanics, and Whites trying cocaine (95%, 96%, and 94% respectively). Blacks (n=61; 3.9 + 1.4) liked using cocaine significantly more than Whites (n=48; 3.4 + 1.7) or Hispanics (n=24; 3.4 + 1.7). Significantly fewer Blacks (31%) ever used methamphetamine compared to Hispanics (76%) and Whites (90%); ?2(2) = 44.33, p < 0.0005. Blacks who tried methamphetamine (n=20) liked it significantly less than Whites (W) (n=46) or Hispanics (H) (n=19); F(2,82) = 13.28, p < 0.0005. Whites rated methamphetamine drug effects as significantly better than Blacks (p = 0.001) or Hispanics (p = 0.03). Blacks and Hispanics had significantly lower bad effect factor scores with cocaine use than Whites or Hispanics (p = 0.05 and p = 0.04, respectively).

Conclusions: This is the first study to explore ethnic group differences in subjective physiological differences for drug preferences. Blacks significantly preferred cocaine over methamphetamine. Recognizing these ethnic drug preference disparities have shed light on the onset of secondary drug-related medical illnesses such as HIV/ AIDS and Hepatitis C. Whites and Hispanics had intravenous drug use while Blacks did not. Identifying these differences should promote culturally sensitive treatment of co-occurring disorders.

Sponsor: EXPORT

#### First Author/Presenter: Jason Kennedy

#### Classification: Resident

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# RECOMMENDATIONS FOR TEMPORIZING EXTERNAL FIXATION LOWER EXTREMITY: A SURVEY OF THE ORTHOPAEDIC TRAUMA ASSOCIATION (OTA) MEMBERSHIP

Purpose: The use of temporary external fixation of intra-articular and periarticular fractures of the lower extremity has been successfully employed in staged protocols over the last decade. Temporary external fixation allows time for the patient to be resuscitated, the soft tissue of the injured extremity to recover sufficiently for safe reconstruction, and the surgeon to prepare a preoperative plan. The aim of our study was to survey experts in orthopaedic surgery, the membership of the Orthopaedic Trauma Association (OTA), who definitively treat these injuries, in an attempt to optimize care.

Methods: A web-based survey was design to assess preferences of the OTA membership regarding the knee and ankle spanning external fixators and also treatment of lower extremity periarticular trauma. The total was then subdivided into those who perform >21 of knee spanning or ankle spanning fixators.

Results: The estimated time to definitive fixation after the placement of temporary external fixator of fractures to the distal femur were 1-7 days in 68.6% of the responses, 8-14 days in 71.3%. In tibial pilon fractures, 57.7% reported 8-14 days and 38.7% at 15-21 days. 82.5% believe that overlap of the pin sites and the definitive plate fixation should be avoided. 72.6% surgeons agree that the accuracy of the reduction in the external fixator is important, while 93.9% believe that length is the most critical aspect of the reduction. 94% believe that CT scans are helpful in planning reconstruction and should be performed after stabilization by external fixation. 76.3% disagree with the plating of the fibula at the time of external fixation by the referring surgeon. 48.5% prefer to delay fibular plating for a combined repair of the plafond. 80.7% agree with the placement of the delta frame on the ankle. 64.9% agree with the anterior placement of femoral pins while 39.1% advocate lateral pin placement. Among high volume ankle surgeons, there was a clearer agreement that the plating of the fibula in plafond fractures should be left to the discretion of the definitive surgeon.

Conclusions: Our study reports on the responses of 202 of 396 active OTA members, who provide definitive treatment of periarticular lower extremity trauma. This information can be shared with community orthopedic surgeons who may provide more optimal care whether the injury ends up being treated by them or referred to a tertiary center, and between tertiary care centers, to generate ongoing discussions.

## WOMEN'S HEALTH

## 1900 (Poster)

#### First Author/Presenter: Kimberly Brown

Classification: Staff

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## ROLE OF ETHNICITY IN THE EXPRESSION OF FEATURES OF HOT FLASHES

Purpose: The overall goal of this study was to determine the effects of ethnicity on features of hot flashes (HFs) in a population of menopausal women in North Central Texas.

Methods: A total of 397 ethnically diverse menopausal women from North Central Texas were administered our Menopausal Vasomotor Symptoms (MVS) survey to ascertain accurate information about number, length, intensity and behaviorally disruptive effects of hot flash episodes for subsequent analysis for effects of ethnicity in the occurrence of hot flashes. The mean (SD) age for participants was 50.2 (5.3) years; 40.3% were White,37.8% were Black, and 21.9% were Hispanic. To evaluate and identify potential association and predictors of the hot flash (HF) features in women and race, and other independent variables, ordinal/multinomial/binary logistic regression models were used to calculate crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs).

Results: The analysis demonstrates strong associations with race and the Number of HF s/day, Length of each HF episode, Intensity of HFs, and Interruption of Activities. Race was important in the crude and adjusted model describing the association between number of HFs per day and race. Blacks were 2.22 (95% CI, 1.38-3.56) time more likely to experience more frequent HFs per day than white. Similarly, Hispanics were 1.85 (1.08-3.18) time more likely to experience more frequent HFs per day than white.

Conclusions: Collectively, our results show more frequent, more intense and more bothersome hot flashes in Non-Caucasian women in comparison to Caucasian women. These observations contribute to our understanding of health disparities in middle-aged women and foster additional studies to determine the contributing factors to this increase severity of the menopausal experience in Non-Caucasian women. Knowledge of these factors (e.g., genetics, diet, culture, body weight, environmental stressors or socioeconomic status) could contribute to the elimination of this health disparity.

Sponsor: National Center for Minority Health and Health Disparities, NIH

## 1901 (Poster)

First Author/Presenter: Nani Carter

Classification: School of Health Professions MPAS Student

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#### DO CLINICIANS FOLLOW ACOG GUIDELINES TO SCREEN FOR POSTPARTUM DEPRESSION

Purpose: The purpose was to investigate if clinicians follow American College of Obstetricians and Gynecologists (ACOG) guidelines to screen for postpartum depression (PPD). Common areas of failure in the screening process in comparison to ACOG guidelines were identified.

Methods: A retrospective chart review was performed. Adherence to ACOG guidelines was measured based on the presence or absence of documentation of initial PPD screening, third trimester education, second week follow-up, and six week follow-up. Accurate follow-up was determined by the presence of PPD screening at the second and six week follow-up visits. After gaining IRB approval, a list of patient charts who presented for obstetrical visits from January 1, 2006 to December 31, 2006 were generated. Using random sampling, 400 charts were selected, but only 241 charts were located. Eligible charts were selected by using the following criteria: 1) female patients over 18 at time of initial visit 2) patients are postpartum at time of data collection. Exclusion criteria included: 1) patients whose pregnancies ended before 24 weeks, 2) patients who transferred care to another physician s office before giving birth. A total of 84 charts met the inclusion criteria and were used for evaluation in this study. These results were analyzed using Chi-squared method and descriptive statistics.

Results: Screening behaviors of clinicians were examined based on adherence to ACOG guidelines. This study found that initial screening of depression was documented 76.2% of the time, and third trimester education was documented in 11.9% of the charts. At the two-week postpartum visit, PPD screening was documented in 34.5% of charts, and PPD screening at the six-week postpartum visit was documented in 32.1% of charts. Based on these findings, the majority of charts (98.8%) in this study did not meet the ACOG guidelines for postpartum depression screening. Accurate follow-up with PPD screening at the two and six week postpartum visits was found in 33.33% of the charts.

**Conclusions:** The results of this study indicate that clinicians in the North Texas area may not be meeting the ACOG postpartum depression screening guidelines. ACOG guidelines were completely followed and met in only 1.2% of the reviewed charts. This could be due to the fact that there is no universal screening method. During this study, it was found that clinicians were more likely to document PPD screening and education if they were provided with forms containing prompts.

## WOMEN'S HEALTH

## 1902 (Poster)

#### First Author/Presenter: Mieshia Beamon

#### Classification: Staff

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IMPROVING PERINATAL OUTCOMES AMONG AFRICAN AMERICAN WOMEN IN FORT WORTH: THE AUNTIE-TIA PROGRAM

Purpose: The objectives of this study are (1) to determine whether the provision of social support (as provided by the Aintie-Tia program) improves perinatal outcomes among African American women using a randomized trial design; (2) to determine whether experiences before or during pregnancy and social context contribute to perinatal outcomes by producing differential levels of stress; and (3) to determine the extent to which interactions between social support and social context contribute to perinatal outcomes.

Methods: This study is approved by the University of North Texas Health Science Center IRB, John Peter Smith Hospital IRB, Baylor IRB, and Texas Health Resources IRB. We are enrolling 120 African American women from the UNTHSC affiliated obstetrical clinics. We conduct a 45minute face-to-face questionnaire with the participants, who are then randomized to either the Aintie-Tia Program and their regular medical care or to their regular medical care alone, and are followed until their infants 4th month. The Aintie-Tia Program has successfully trained 8 women from the local community in over 50 hours of community-based doula curricula training in the Chicago Health Connection model. Four of these women have been recently hired to carry out the Program, and each is assigned 15 participants. Aintie-Tias are specially trained to help education women about pregnancy, childbirth, parenting and breast feeding, and they are also available as resource to women until their children are 4 months old.

Results: Upon birth, we will obtain pregnancy outcome data for all study participants from the health system sites. Two major outcomes will be assessed: birth outcomes and breastfeeding. Birth outcomes, including birth weight, gestational age at delivery, and type of delivery, will be determined from review of the participants medical record. Breastfeeding and several of the psychosocial measures from the initial questionnaire will be assessed by conducting a brief telephone survey 4 to 6 months after delivery.

**Conclusions:** The Aintie-Tia Program brings together a university and community-based organization with a strong record of improving pregnancy outcomes to create knowledgeable role models in the community. The Aintie-Tia Program has achieved a high degree of visibility in Fort Worth, particularly in the African American communities. This partnership approach to improve perinatal outcomes has the potential to reduce persistent and pervasive disparities.

Sponsor: NIH, CDC

## 1903 (Poster)

#### First Author/Presenter: Mieshia Beamon

#### Classification: Staff

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#### HPV VACCINE ACCEPTABILITY STUDY

Purpose: The HPV Vaccine Acceptability Study used focus groups to identify issues pertaining to access and barriers to health care services, knowledge of HPV and the vaccine, and attitudes and acceptability of utilizing the vaccination in the African American community. The specific aims are to explore what English-speaking women, who are primary caregivers of African American girls aged 7-18, know about the human papillomavirus (HPV) and the HPV vaccine and how they make decisions about the HPV vaccine; to explore how these women understand mainstream media messages with regard to trust believability and risk perceptions; and to explore how messages in mainstream media influence processing and acting on health information to reduce HPV and cervical cancer risk. Qualitative and quantitative methods were used in order to ascertain the degree of knowledge of HPV and participants attitudes and perceptions towards having their own daughters vaccinated.

Methods: This study is approved by the University of North Texas Health Science Center IRB. We conducted a series of six focus groups to explore these women s knowledge and risk perceptions about HPV and HPV vaccine; communication barriers, including access to and use of information about HPV and the HPV vaccine; and their media images (i.e., trust and believability) about sources of information on health and HPV, which may influence their receptiveness to messages about HPV and the vaccine. The findings will be collected in collaboration with local health departments, who will use them in strategic communication efforts to address HPV in their communities. We will also share our findings with community and clinical partners to inform their efforts to target HPV communication in other underserved communities.

Results: n/a

Conclusions: This study is probing in-depth HPV awareness and risk perceptions; information-seeking behaviors; and the reasons that primary caretakers of at-risk young women seek or do not seek information

## WOMEN'S HEALTH

## 1904 (Poster)

First Author/Presenter: Esther Han

#### Classification: TCOM DO Student

Esther Han (TCOM OMS II, Fort Worth, TX 76107) Kollier Hinkle, M.D. (UNTHSC, Fort Worth, TX 76107) Lindsay McBride, D.O. (JPS, Fort Worth, TX 76107) Joy Ebo (UNTHSC, Fort Worth, TX 76107) Peggy Smith-Barbaro, PhD (UNTHSC, Fort Worth, TX 76107)

# ASSESSMENT FOR THE NEED OF HPV, CERVICAL CANCER AND HPV VACCINE HEALTH EDUCATION BASED ON PATIENT POPULATIONS AT THREE COUNTY LEVEL HOSPITALS IN TARRANT COUNTY

Purpose: Recent data has shown women may not know enough about HPV or its link to cervical cancer to make an educated decision on whether or not to receive (or allow their daughters to receive) the HPV vaccine. Our purpose was to assess whether or not the patient population in three county hospitals in Tarrant County has been adequately informed about human papillomavirus infections, their link to cervical cancer, and the availability of a vaccine proven to prevent both.

Methods: The survey was developed with the help of our School of Public Health. Patients and clinic personnel were asked to complete the survey over a six week period. The survey encompassed demographics, Pap Smear/HPV knowledge, and HPV vaccine knowledge

Results: Out of 190 patients/employees surveyed, 129 (67.9%) replied no health care professional (Nurse Practitioner, Doctor, Nurse midwife, etc.) had ever discussed with them the HPV or the HPV vaccine. Out of those 129 responses, 109 (83.7%) replied they would get a vaccine for HPV if they knew it would prevent cervical cancer. The data when broken down by race revealed 39.4% of the Caucasian patients surveyed have had a health care provider talk to them before about HPV or the HPV vaccine compared to only 30% of the African American population surveyed and a meager 11.1% of the Hispanic/Latino population surveyed.

Conclusions: It is evident through the results of the survey that awareness about HPV and its link to cervical cancer among patients/employees in the county clinics of Tarrant County is low. Health care providers have not been proactive enough in passing along health information to their patients about HPV. Strategies to increase dialogue between clinical personnel and their patients about HPV and its link to cervical cancer is a first step to allowing patients to make an educated decision about the HPV vaccine.

Sponsor: N/A

## 1905 (Poster)

#### First Author/Presenter: Maritza Lopez

Classification: SPH Student

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#### RELIGIOSITY AND THE USE OF BREAST CANCER SCREENING METHODS AMONG OLDER LATIN WOMEN

Purpose: To examine the association between religiosity and breast cancer screening methods among Latin American and Caribbean older adults.

Methods: A sample of 6,541 women aged 60 and older from the first interview of Health, Well-Being and Aging in Latin America and the Caribbean Study (SABE), in seven cities (Buenos Aires, Bridgetown, Havana, Mexico, Montevideo, Santiago, and Sao Paulo). The outcomes were reporting a mammogram, a clinical breast examination (CBE) or breast self-examination (BSE) within the last 2 years. Independent variables were religiosity (religion being very important, religion being somewhat or not important, vs. no religious affiliation/ no response) and other socio-demographics, medical conditions, and functional status.

Results: In the combined sample, for 75% of women religion is very important, for 12% it is somewhat or not very important, and for 13% there was no religious affiliation. In multivariate analysis, women who reported religion being very important were more likely to have a mammogram (OR=1.90, 95% CI 1.53-2.35), a CBE (OR= 1.70, 95% CI 1.44-2.00) and a BSE (OR= 1.44, 95% CI 1.23-1.68) compared with women who reported no religious affiliation. Other independent predictors for having a mammogram, a CBE and a BSE were younger age (60-74 vs. 75+), being married, having higher education, higher number of medical conditions and less functional difficulties. In a sub-sample without Havana, which has universal insurance coverage, having any insurance (vs. no insurance) was associated with having a mammogram. Some variations across cities were found.

Conclusions: Older women who are more religious tend to have higher breast cancer screening rates. This suggests that religious affiliation and higher self-rated religiosity may facilitate breast cancer screening behaviors among older women in these populations, independent of other socioeconomic or health factors.
## WOMEN'S HEALTH

### 1906 (Poster)

#### First Author/Presenter: Stephen Miller

Classification: TCOM DO Student

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THE RELATIONSHIP BETWEEN BODY MASS INDEX AND MAMMOGRAPHY USE AMONG OLDER WOMEN IN LATIN AMERICAN AND CARIBBEAN CITIES

Purpose: Body mass index (BMI) may influence breast cancer screening rates. However, there are no data on how BMI affects breast cancer screening utilization among older Latinas. The objective of this study was to examine the relationship between BMI and mammography use among Latin American and Caribbean older women.

Methods: A sample of 5,222 women aged 60 and older from the first interview of Health, Well-Being and Aging in Latin America and the Caribbean Study (SABE), in six cities (Bridgetown, Havana, Mexico, Montevideo, Santiago, and Sao Paulo). Outcome was reporting a mammogram within the last 2 years. Body mass index (weight and height measured at interview; kg/m2) was categorized as underweight (<18.5), normal weight (18.5-24.9), overweight (25.0-29.9), and obesity classes I (30-34.9), II (35-39.9) and III (40+). Other independent variables were sociodemographics, medical conditions, and functional status.

Results: In the combined sample, the prevalence of mammography use across BMI categories is shown in Table (p <.0001). In multivariate analyses, women who were underweight or with extreme obesity (class III) were less likely (OR=0.51, 95% CI 0.32-0.80; and OR= 0.57, 95% CI 0.37-0.89; respectively) to have a mammogram compared with women who had normal weight. Other independent predictors for having a mammogram were younger age, being married, higher education, having history of cancer and better functional status. Some variations across cities were found.

Conclusions: Having underweight or obesity class III were associated with lower mammography use rates, suggesting that extreme measures of BMI may be barriers to screening mammography among Latin American and Caribbean older women.

Sponsor: N/A

#### 1907 (Poster)

First Author/Presenter: Alyssa Robbins

#### Classification: School of Health Professions MPAS Student

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#### PREVALENCE OF ABNORMAL PAP SMEARS AND INCIDENCE OF NOTIFICATION AND LOST TO FOLLOW-UP IN A OB/GYN CLINIC

Purpose: Annual Pap smears aid in the early detection of Cervical Cancer and are vital to preventative healthcare. About 55 Million Pap smears are performed annually and 6% detect abnormalities requiring follow-up. The purpose of this study was to identify the prevalence of abnormal Pap smears and if the current ACOG recommendations for follow-up for abnormal results were being implemented. The ultimate goal of this study was to describe how well clinicians were documenting notification of abnormal results and appropriate follow-up.

Methods: This study was a retrospective cohort chart review. The outcome variables were as follows: if the patient received notification of results of their most recent abnormal Pap smear and if they patient received the appropriate follow-up. The independent variables included: patient age and ethnicity, the classification of abnormal Pap smear, and the method by which the patient was notified. After gaining IRB approval a list of patients age 18 and older from the OB/GYN clinic who had received a Pap smear over a 24 month period was generated. The researchers manually identified patients who had an abnormal Pap smear and recorded the pertinent information from these patients charts. Seventy-nine patient charts were eligible; however, two were excluded due to disconnected phone lines.

Results: A total of 77 charts were reviewed. Patient mean age was 29.99. Seventy-two out of 77 (93.5%) patients charts had documentation of notification of abnormal Pap smear results. Fifty out of the 77 abnormal Pap smear results required follow-up. Of those 50 charts requiring follow-up, 38 (76%) of patient charts had documentation that they were scheduled for a colposcopy.

Conclusions: The results revealed that patients are being notified at a satisfactory rate. However, in order to reach the ultimate goal of 100% notification, implementation of a standard method of documentation would be necessary. Another result revealed that follow-up of abnormal Pap smears was occurring at an unsatisfactory rate. A flow sheet of abnormal test results in the front of patient charts could assist clinicians in improving follow-up rates.

## WOMEN'S HEALTH

#### 1908 (Poster)

First Author/Presenter: Lindsay McBride

Classification: Resident

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#### KNOWLEDGE AND ACCEPTANCE OF THE HUMAN PAPILLOMAVIRUS (HPV) VACCINE IN A COUNTY HOSPITAL SYSTEM

Purpose: In our hospital system, the HPV vaccine is being distributed in a limited fashion. Our purpose was to evaluate the acceptance of the HPV vaccine in our county hospital system in order increase its utilization for our patients.

Methods: The survey was developed with the help of our School of Public Health. Patients and clinic personnel were asked to complete the survey over a six week period. The survey encompassed demographics, Pap Smear/HPV knowledge, and HPV vaccine knowledge.

Results: 30 employees and 200 patients were surveyed (53.8% Spanish speaking). Patients older than 40 years were most likely to allow their child to receive the HPV vaccine and under the age of 21 were most likely to be undecided. Hispanic patients were most likely to be undecided about the vaccine encouraging sexual activity. Only 48.3% of employees strongly disagreed that the vaccine would encourage sexual activity. 34.5% of employees would not allow their child to receive the HPV vaccine. 73.9% of patients responded that no medical professional had discussed HPV or the HPV vaccine.

Conclusions: It is evident through our survey that patients and clinic personnel require more effective education about cervical dysplasia and the HPV vaccine. Levels of education, language and age have all proven to be variables in need of consideration. Our survey has given us insight that will allow us to better educate the population we are trying to help. We plan to repeat our survey next year to monitor the success of our educational programs.

Sponsor: N/A

#### 1909 (Poster)

#### First Author/Presenter: Paul Singh

Classification: Resident

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#### OSTEOPOROSIS AWARENESS AMONG HEALTH CARE PROVIDERS

Purpose: The objective of this study was to assess the existence of an awareness deficit with regard to osteoporosis among health care providers in the Greater Chicago Medical District and the Fort Worth Medical District.

Methods: During the initial stage of this project a 10 question survey was developed and distributed to health care professionals in Chicago, including nursing personnel, medical students and residents in OBGYN and Family Practice. Survey data were reviewed and analyzed for possible effects of confounding variables, including ethnicity, age, gender, income, education, and health care provider status. The survey has been completed by 129 Health Care workers in the Fort Worth Medical District.

Results: 136 surveys were completed by Health Care Professional in the Greater Chicago area. 73% of health care workers felt that public information regarding osteoporosis was inadequate while 40.6% were unfamiliar with DEXA scanning as a modality for osteoporosis screening. 61.2% of health care workers admitted not being able to interpret the results of DEXA screening and 45% stated that they were unaware of bone formation agents for treating osteoporosis. Preliminary analysis survey data has revealed consistency between Chicago and Fort Worth data.

Conclusions: Data from Chicao and Fort Worth are being compared and will be presented with appropriate comparisons. Although limited in scope, this pilot study suggests the existence of a significant awareness deficit among health care professionals regarding osteoporosis. Differential awareness exists across current medical trainees, attending physicians and nursing professionals with regard to osteoporosis awareness.

## WOMEN'S HEALTH

#### 1910 (Poster)

First Author/Presenter: Paul Singh

#### Classification: Resident

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DAVINCI AND LAPAROSCOPY COMPARATIVE STUDY

Purpose: To compare traditional laparoscopic training tasks performed on a pelvic trainer and on the robotic platform.

Methods: Residents and students were randomized and compared on four tasks using one of the two modalities. The tasks were ascending in difficulty and included grasping, object moving, passing and suturing (Simulab Corp).

Results: For all tasks, the performance on the daVinci systems showed faster times to completion, regardless of level of subject training.

**Conclusions:** Statistical significance is being determined. We plan to continue this study in order to add power for the next year. Due to the paucity of published data on robotic surgery, especially in the area of resident and student training, small studies such as this are needed to stimulate further investigation, and to determine how robotic training fits into the surgical curriculum of gynecology training programs.

Sponsor: N/A

#### 1911 (Poster)

First Author/Presenter: Joseph Pallone

#### Classification: Resident

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ROBOT-ASSISTED SURGICAL PLATFORMS IN GYNECOLOGIC SURGERY: A CASE SERIES OF THE FIRST 109 CASES PERFORMED AT JOHN PETER SMITH HOSPITAL

Purpose: Over the last 15 years, the increased utilization of minimally invasive surgery for performing general gynecologic surgeries, ranging from simple myomectomies to complex radical hysterectomies with associated lymph node dissections, have led to a significant reduction in surgical morbidity. At the same time; however, these procedures, have been shown to be similar in both clinical safety and efficacy to their open counterparts. Nevertheless, many surgeons have professed limited use of laparoscopy in gynecologic surgery because of longer operative times, lack of training and steeper learning curves. Recently; however, many reports have shown that robot-assisted surgical platforms may overcome many of these obstacles often seen in traditional laparoscopy. Unfortunately, few data series are available regarding clinical outcomes when the robot-assisted surgical platform is utilized for performing general gynecologic surgeries.

Methods: The investigators retrospectively reviewed 109 charts at John Peter Smith Hospital and at the JPS Diagnostic and Surgery Hospital recording operative time, anesthesia time, estimated blood loss, IV pain medication requirements, and length of hospital stay and other variables.

Results: Initial results indicate that operative times initially were often long for a given procedure, but were reduced as the efficiency in docking and preparing the robot improved. In addition, estimated blood loss for a given procedure was usually significantly reduced, with most cases with less than 100ml.

**Conclusions:** Based on initial data, it seems that as the experience level of the surgeon increases, the corresponding operative times are reduced. Thus, the feasibility of robotic laparoscopy in gynecologic surgery was demonstrated.

## WOUND HEALING

#### 2000 (Poster)

#### First Author/Presenter: Lei Shi

Classification: HealthPoint

Lei Shi1, Ryan Ermis1, Tasha Garcia1, Dale Telgenhoff2, and Dannis Carson1 1Healthpoint Ltd., Fort Worth, TX 2Tarleton State University, Fort Worth, TX

DEGRADATION OF HUMAN COLLAGENS BY CLOSTRIDIUM COLLAGENASE AND THEIR EFFECT ON CELL MIGRATION

Purpose: The purpose of this in vitro study was to investigate the ability of C. collagenase to digest human collagen Types I, III, IV, V, and VI (Types IV, V, and VI have not been previously examined) and to determine the effect of C. collagenase and collagen degradation products on the migration of keratinocytes and fibroblasts.

Methods: Human collagens type I, III, IV, V and VI were treated by C. collagenase. SDS-PAGE was used to examine the digestion of the collagens. The gold surface migration assay was used for human keratinocytes, while a QCM method was used for human fibroblasts.

Results: Our results confirmed the digestion of human collagen Type I and III by C. collagenase, and showed that C. collagenase could also break down human collagen Type IV and V but not VI. Among the collagens that could be degraded, the degradation products of Type I and III demonstrated promotion of keratinocyte migration, while the other collagens showed no effect when compared with untreated controls. Similar effects were seen in the fibroblast migration test, with the exception that type IV collagen degradation products also induced migration. C. collagenase itself was confirmed to have the ability to enhance cell migration in both assays.

Conclusions: The data suggest that C. collagenase is effective in digesting collagen debris in necrotic tissues, and that both C. collagenase and the degradation products of collagenolysis have the potential to promote cell migration. Therefore, collagenase treatment may provide at least two potential mechanisms to enhance cell migration.

Sponsor: N/A

#### 2001 (Poster)

First Author/Presenter. Sarah Ramsay

Classification: HealthPoint

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#### THE DB/DB MOUSE AS A MODEL OF IMPAIRED WOUND HEALING

Purpose: To evaluate the genetically diabetic db/db mouse as a model of wound healing, and to validate the model through the use of plateletderived growth factor (PDGF-BB) as a positive control.

Methods: Genetically diabetic and non-diabetic female mice were obtained from Jackson Laboratories (Bar Harbor, Me). Fur was removed and two full- thickness 6mm punch biopsy wounds were created on the backs of each animal. The wounds were traced onto glass microscope slides, treated and covered. Healing was evaluated over 21 days by tracing wound area. Area was assessed using MetaVue software.

Results: Heterozygous animals healed primarily through contraction whereas homozygous animals healed more through granulation tissue formation and epithelial migration. Wounds treated with PDGF-BB gel had greater amounts of granulation tissue formation and less scabbing. Statistical differences in wound healing ability were seen between diabetic and non-diabetic animals. Also, the use of PDGF-BB gel as a positive control indicated that statistically significant differences in wound healing can be measured between treatment groups in the same animal.

**Conclusions:** The delay in healing and histological differences between heterozygous and homozygous diabetic animals presented here support the use of the db/db mouse as a model of impaired wound healing. Furthermore, an approved agent for promoting healing of chronic human ulcers, PDGF-BB gel, was effective in this model suggesting the relevance of the model for evaluation of novel wound healing agents.

Sponsor: Healthpoint

## WOUND HEALING

#### 2002 (Poster)

#### First Author/Presenter: Paul Renick

Classification: HealthPoint

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#### A MURINE MODEL FOR BIOFILM INFECTION IN PARTIAL THICKNESS WOUNDS

Purpose: To develop a mouse model of biofilm infection in wounds. In vivo models serve a crucial role in the development of novel treatments for chronic human wounds, and the presence of biofilm is believed to be a major cause of non-healing wounds.

Methods: A partial thickness wound was generated on the back of each mouse and wounds were inoculated with a multi-drug resistant MRSA strain and covered with a bandage. The level of infection and the efficacy of treatments were determined by biopsy of wounds followed by quantitative microbiology. Two days of treatment with topical agents was initiated either prior to establishment of a mature biofilm (4 hours after inoculation) or after allowing a biofilm to form (24 hours after inoculation).

Results: The MRSA infection exhibited high bacterial levels in the tissue that were stable over the course of several days. Qualitative comparison between infected and uninfected animals suggested that the wound infection led to increased inflammation, more crust formation, and delayed healing. When treatment of wounds with topical antimicrobials was initiated 4 hours after inoculation, the tested topical agents exhibited a reduction in the bacterial load of the wound tissue. In contrast, when the infection was allowed 24 hours to establish, the effect of topical agents was greatly reduced or eliminated. Microscopic examination of stained histology samples revealed the presence of a dense staphylococcal community.

**Conclusions:** The high density of bacteria, the observed bacterial community, and the lack of drug efficacy support the biofilm nature of this model. While further development is required, the model should serve as a valuable tool for studying biofilm infection and identifying novel agents for the prevention or treatment of wound biofilms.

Sponsor: Healthpoint

#### 2003 (Poster)

#### First Author/Presenter: Anupam Sule

#### Classification: GSBS Student

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#### COLLAGEN IMPREGNATED MATRICES AS 3-D MODELS OF HARD TISSUE

Purpose: Cell monolayer cultures are the major in vitro model used in studies of variety of biological events. It is however increasingly obvious that in vivo, cells function in a three dimensional environment (3-D) and that the extra-cellular matrix (ECM) is a source of important response signals. In order to study tissue events in an in vivo relevant manner 3-D models of various tissues are required. The matrices or scaffolds with different degrees of stiffness impart different mechanical properties to the 3-D model that they support. We intend to combine the biocompatibility of collagen type I with matrices/porous scaffolds of different stiffness. To demonstrate that porous scaffolds when impregnated with neutralized and gelled collagen type I (CT-I) provide a suitable environment for survival, and differentiation of normal human cells.

Methods: Collagen type I foam, ß tricalcium phosphate (TCP- Preforms®) and tantallum metallic foam were impregnated with CT-I containing fluorescently labeled hTERT human dermal fibroblasts (DFbs) and human osteoblasts. The specimens were examined for the presence of cells using confocal microscopy. Treatment of the matrices with collagenase released the cells and allowed determination of their numbers. Collagen type I was fluorescently labeled by conjugation with Cy-5.

**Results:** After impregnation with collagen; collagen foam, BTCP, and tantalum absorbed 500%, 50%, and 10% of their weight of collagen gel respectively. Collagen and cells were present throughout the matrices examined. Long-term viability (30 days), migration of DFbs in and out of the collagen-impregnated foam and cell alignment when the matrices were stretched was also demonstrated.

Conclusions: All the matrices examined retain collagen type I within their pores as a fibrillar hydro-gel. The pores then behave as 3-D microequivalents within the scaffold. The cells were randomly distributed throughout the collagen gel making up the micro-equivalents. Long-term cell survival in the three-dimensional matrices allows time for in situ differentiation. Free migration of the cells into and out of the matrix, demonstrated its cytocompatible nature. The alignment of cells in response to external forces suggested behavior appropriate for tissues subjected to mechanical forces. Taken together these observations suggest that the strategy being tested will allow studies of multiple physiological processes like mechanosignaling, cell migration in 3-D that are in vivo like.

## **CASE PRESENTATION**

#### 2100 (Poster)

#### First Author/Presenter: Carrie Gilstrap

Classification: Resident

Carrie A. Gilstrap D.O., Rheumatology Fellow, UNTHSC, Ft. Worth, TX 76107; Rahul K. Patel M.D., Rheumatology Assistant Professor, UNTHSC, Ft. Worth, TX 76107

#### SCURVY: A MODERN DAY CASE OF AN OLD WORLD DISEASE

Purpose: Scurvy is a potentially fatal disease caused by a lack of ascorbic acid in the diet. Humans are unable to synthesize this vitamin, therefore, adequate intake from sources rich in vitamin C, such as fresh fruits and vegetables, is essential. The clinical picture of scurvy reflects the functions of ascorbic acid, which include collagen biosynthesis, iron absorption and antioxidant activity.

#### Methods: Chart review

Results: A 54 year old Caucasian male presented to the emergency department with a 2 year history of recurrent left knee pain and swelling. The patient had a large left knee effusion associated with swelling of the thigh and bruising. In addition, perifollicular petechiae and corkscrew shaped hairs were noted on the patient's lower extremities. The patient denied alcohol use, but reported a 60 pack-year history of tobacco use and stated that his diet was devoid of fresh fruits and vegetables due to financial limitations. A left knee arthrocentesis was performed on the second hospital day and fluid analysis was consistent with a hemarthrosis. An ascorbic acid level was obtained on the 12th day of hospitalization and the patient was empirically started on ascorbic acid supplementation in addition to iron, folate and vitamin B12 replacement. The ascorbic acid level was found to be low despite nearly two weeks of proper nutrition during the patient's hospitalization.

Conclusions: This case illustrates that although scurvy is often considered a diagnosis of only historical significance, malnutrition exists in the modern day and ascorbic acid deficiency should be considered with the typical clinical symptoms. Most humans consume a sufficient amount of vitamin C in their daily intake; however, diets lacking in fresh fruits and vegetables place individuals at high risk.

Sponsor: N/A

#### 2101 (Poster)

#### First Author/Presenter: Candice Flaugher

#### Classification: Resident

Candice Flaugher, D.O., Rheumatology Fellow, Plaza Medical Center, Fort Worth, TX 76104 Bernard Rubin, D.O., M.P.H, Professor of Medicine, UNTHSC, Fort Worth, TX 76107

#### A CANCER MIMIC

Purpose: Sarcoidosis is a non-caseating granulomatous disease of unknown etiology that affects the lungs in 90% of affected individuals, but is capable of affecting any organ system. Systemic sarcoidosis is more common in African-Americans and is more often associated with nonspecific constitutional symptoms. Thirty to fifty percent of individuals are asymptomatic at diagnosis while 33% demonstrate fever, fatigue, and weight loss. Early sarcoid lesions consist of accumulated activated T-cells and macrophages that secrete TNF-a.

#### Methods: Chart Review

Results: A 45 year old African-American male presented to the ED with complaint of fatigue, stiffness, progressive foreskin tightening, and a 70lb weight loss over the previous year. Bilateral testicular masses were present. Preliminary work-up included imaging of his chest and abdomen which demonstrated mediastinal and abdominal adenopathy and mixed sclerotic and lucent lesions of the spine and the iliac wings that were highly suspicious for metastatic disease. Circumcision and a radical left orchiectomy revealed a 2.4 x 3.0 x 2.0 cm mass. Pathology demonstrated granulomatous orchitis involving the testicular parenchyma and epididymis. A right iliac crest needle core biopsy demonstrated non-caseating granulomatous inflammation without evidence of infection. He presented to Rheumatology clinic for further evaluation and treatment and was found to have a normal bloodwork, SACE level and physical exam. He was placed on Adalimumab 40mg subcutaneous every other week and is currently being followed for resolution of his granulomas.

Conclusions: There have been several case reports documenting an association between testicular cancers and sarcoidosis or a sarcoid-like processes. Other case series have documented testicular sarcoidosis with associated bilateral hilar lymphadnopathy mimicking metastatic testicular cancer. While musculoskeletal sarcoidosis may be found in 25-40% of cases, axial sarcoidosis is rare. Genitourinary involvement of sacoidosis is also rare, occurring in 0.2% of clinically diagnosed cases and 5% at autopsy. Pre-existing sarcoidosis should not delay the work-up of testicular masses.

## **CASE PRESENTATION**

#### 2102 (Poster)

First Author/Presenter: Ashley Mekala

Classification: TCOM DO Student

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#### HEREDITARY SPHEROCYTOSIS IN A HISPANIC MALE

Purpose: A 28-year-old male was evaluated for one month history of weakness, fatigue, eight pound weight loss, and jaundice. He reported a four day history of cough, sore throat, subjective fever, and night sweats. He recently travelled to Puerto Vallarta, Mexico returning home 6 months prior to admission. He denies any recent sick contacts or insect bites.

Methods: Routine physical exam revealed a well nourished, well developed Hispanic male with diffuse jaundice and icteric sclerae. Splenomegaly was noted, and a CT scan of abdomen was obtained. His physical exam was otherwise unremarkable.

Results: Initial assessment for hemolytic anemia and splenomegaly were made by the emergency department. The patient was cross matched and transfused with packed RBCs. Supportive measures were started and the admitting team and hematology service were consulted.

Conclusions: Evaluation of hereditary spherocytosis (HS) is usually straightforward. In this case, however, rapid transfusion proved not to be the best decision and resulted in a normal osmotic fragility test, delaying the diagnosis of HS. This delay in diagnosis resulted in treatment delay, unnecessary invasive tests, and a prolong hospital stay. Blood transfusions are associated with many identified risks, and the decision to transfuse an anemic patient without a clear diagnosis should be undertaken with caution.

Sponsor: N/A

#### 2103 (Poster)

#### First Author/Presenter: Laura Arnold

#### Classification: TCOM DO Student

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#### PRIMARY PULMONARY LEIOMYOSARCOMA IN AN ASYMPTOMATIC MALE

Purpose: The objective of this case presentation is to present a case of a primary pulmonary leiomyosarcoma and emphasize the importance of early detection and treatment. A 56-year-old asymptomatic male was found to have a pulmonary mass on routine chest radiography. The patient was essentially asymptomatic except for a mild cough and fatigue.

Methods: A CT biopsy of the lesion revealed a 3.5 x 2.2cm bilobulated mass. Histology revealed bundles of spindle-shaped cells with small nuclei and a few large hyperchromatic nuclei. The malignant spindle cells tested strongly positive for smooth muscle actin, vimentin and S100 antigen.

Results: The patient underwent a left thoracotomy with a left lower lobectomy. Overall morphologic and histologic features favored a high grade sarcoma with evidence of smooth muscle differentiation, a leiomyosarcoma.

**Conclusions:** Primary pulmonary leiomyosarcomas are rare neoplasms of smooth muscle that account for less than 0.5% of all malignant lung tumors. This case emphasizes the importance of the primary care physician in the detection of primary leiomyosarcomas of the lung. If these are detected in the early symptomatic or asymptomatic phase, resection is essentially curative.

## **CASE PRESENTATION**

#### 2104 (Poster)

First Author/Presenter: Jessica Toler

Classification: TCOM DO Student

Jessica R. Toler, OMS III. Texas College of Osteopathic Medicine. Fort Worth, Texas 76107.

#### CHRONIC TOLUENE EXPOSURE AND THE IMPACT ON THE BODY

Purpose: The objective of this case presentation is to demonstrate that patients presenting with toluene exposure may need more extensive treatment for damaging effects of toluene such as multiple myeloma. A 39-year-old male presented with a positive history of multiple admissions for toluene exposure which the patient attributed to his employment as a painter. Multiple lab values for this patient presented as abnormal, including a high alkaline phosphatase, total protein, and low bicarbonate and sodium. Multiple myeloma was suspected in this patient and thus required further assessment.

Methods: The patient s electrolytes and other lab results were closely monitored in the Intensive Care Unit after little improvement during the first two days. Blood work returned positive for both Toluene and cocaine. Serum Protein Electrophoresis and Urine Protein Electrophoresis with immunofixation studies were completed to evaluate the possible presence of multiple myeloma. Chest X-rays showed no acute process present.

Results: Preliminary results from the SPEP/UPEP studies showed a monoclonal component. However, the final results confirmed there was no presence of multiple myeloma in this patient. The patient, upon presentation to the hospital, did suffer other effects from toluene abuse including high creatinine and abnormal electrolytes. After repletion of fluids the patient s creatinine and electrolyte abnormalities resolved. The patient s initial nausea and vomiting also resolved after treatment.

Conclusions: This patient presented with multiple medical conditions including high toluene exposure, paraplegia at levels T12-L1, cocaine use, history of three myocardial infarctions, and thyroid cancer two years prior to this admission. Toluene can be very damaging to the body. Although multiple myeloma was not present in this patient, it is important to be aware of the possible effects of chronic toluene exposure and begin treatment as soon as possible. This patient is chronically exposed to toluene and is thus at increased risk for developing toluene related problems in the future and requires regular follow-up with a doctor.

Sponsor: N/A

## ORAL PRESENTATION COMPETITION FOR GSBS (CBH-230)

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2:45 PM	Devin Flaherty PYRUVATE-ENRICHED RINGER'S RESUSCITATION BOLSTERS CYTOPROTECTIVE DEFENSES IN REPERFUSED HINDLIMB IN THE SETTING OF HEMORRHAGIC SHOCK	#313
3:00 PM	Jerel Fields MOLECULAR REGULATION OF ASTROCYTE-TIMP-1 EXPRESSION IN NEUROINFLAMMATION	#405
3:15 PM	Karen Meeks IL-23 AND THE IL-17 RECEPTOR ARE REQUIRED FOR PROTECTION AGAINST LISTERIA MONOCYTOGENES	#901
3:30 PM	Adam Odeh REGULATORY T CELLS DAMPEN MYCOPLASMA RESPIRATORY DISEASE SEVERITY WITHOUT IMPACTING CLEARANCE OF INFECTION	#903
3:45 PM	Lauren Currie EFFECT OF OBESITY ON COGNITIVE FUNCTION IN YOUNG MALE AND FEMALE OB/OB MICE	#1702

## ORAL PRESENTATION COMPETITION FOR SPH (CBH-240)

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2:30 PM	Felichia Fields LIKELIHOOD OF INSTITUTIONALIZATION AMONG NON-HISPANIC WHITE, AFRICAN-AMERICAN AND HISPANIC CAREGIVERS OF INDIVIDUALS WITH DEMENTIA	#101
2:45 PM	Damilola Funmilayo DESCRIPTIVE ANALYSIS OF TUBERCULOSIS INFECTED PEOPLE IN DISTRICT OF COLUMBIA, 1992-2007	#1510
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