UNIVERSITY *of* NORTH TEXAS
HEALTH SCIENCE CENTER *at Fort Worth*

FOURTEENTH ANNUAL

RESEARCH Appreciation Day

APRIL 7, 2006

Center for BioHealth

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AGENDA

7:30 - 8:00 AM	Assemble Posters	Center for BioHealth, 2nd Floor
8:00 - 9:00 AM	Faculty/Non-Student Poster Session	Center for BioHealth, 2nd Floor
9:00 - 11:30 AM	Poster Presentation Competition A	Center for BioHealth, 2nd Floor
	SPH Oral Presentation Competition	Center for BioHealth, 202
12:00 - 2:00 PM	**LUNCH AND KEYNOTE ADDRESS**	Center for BioHealth, 200

Welcome and Overview of RAD 2006 Activities
Thomas Yorio, Ph.D.
Vice President for Research and
Dean of the Graduate School of Biomedical Sciences

Introduction of Keynote Speaker
Peter Raven, Ph.D.
Professor
Department of Integrative Physiology

"High blood pressure: is it caused by vascular inflammation in the brainstem?"
Julian F. R. Paton, Ph.D.
Professorial Research Fellow
Department of Physiology
University of Bristol

2:00 - 5:00 PM	Poster Presentation Competition B	Center for BioHealth, 2nd Floor
	GSBS Oral Presentation Competition A	Center for BioHealth, 201
	GSBS Oral Presentation Competition B	Center for BioHealth, 202
ALL DAY	**VENDOR FAIR**	Center for BioHealth, 2nd Floor
5:00 - 5:30 PM	Remove Posters	Center for BioHealth, 2nd Floor
5:30 PM	**AWARD CEREMONY**	Center for BioHealth, 200

KEYNOTE SPEAKER

Julian F. R. Paton, Ph.D.
Professor of Integrative Physiology
Bristol Heart Institute, School of Medical Sciences
University of Bristol
Bristol, England

"High blood pressure: is it caused by vascular inflammation in the brainstem?"

Julian Paton, Ph.D., this year's keynote speaker, holds a personal Chair in Integrative Physiology at the University of Bristol, England. He runs a research group interested in the central neural regulation of arterial blood pressure and respiration and is funded mainly by the British Heart Foundation and National Institute of Health. Prior to his present position, Julian obtained his PhD at the University of London (UK; 1987), then worked as a visiting scientist at E.I. du Pont de Nemours, Wilmington, Delaware and as an Alexander von Humboldt Fellow at the University of Göttingen, Germany.

Julian's research interests include essential hypertension. He is assessing changes in gene expression profiles within brainstem samples from hypertensive animal models and human subjects with essential hypertension. He employs viral vectors and *in vivo* somatic gene transfer to assess the functional implications of differential gene expression on cardiovascular homeostasis as well as neurophysiological and dynamic confocal imaging techniques to probe central neuronal circuitry controlling blood pressure.

Julian was awarded with the Sharpey-Schafer Lecture and Prize in 1999 at University College London, England, and the Carl Ludwig Distinguished Lecture & Prize in 2005 at the joint IUPS-FASEB meeting in San Diego.

ALCON RESEARCH, LTD. AWARDS

THE ALCON GROUP

Alcon is the global leader in the research, development, manufacture and marketing of ophthalmic products, including surgical instruments and accessory products, intraocular lenses, prescription drugs and contact lens care solutions.

Founded in Fort Worth, Texas in 1947, the Alcon group now employs 12,700 individuals around the world. Total sales for 2005 exceeded $4.3 billion, with 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 690,000 square-foot William C. Conner Research Center, the largest and most sophisticated eye research center in the world. Over the next four years, Alcon plans to spend nearly $2.4 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 oral presentations. In addition, Alcon Research, Ltd. sponsors the Postdoctoral Fellow Poster Competition Award. All RAD 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. This year, GSA has provided funding for a session of the basic science oral presentation competition as well as the basic science poster presentation competition.

The GSA Poster Presentation Awards are given to the top three student poster presentations in each session in the basic sciences category. Awardees are determined by a panel of judges.

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 two oral presentations and the top two poster presentations by a panel of public health judges.

TEXAS COLLEGE OF OSTEOPATHIC MEDICINE AWARDS

The Texas College of Osteopathic Medicine (TCOM) is committed to clinical research excellence by its students and faculty. TCOM educates osteopathic physicians and other health professionals 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 two student/resident poster presentations as determined by a panel of judges.

TECH FORT WORTH INNOVATION AWARD

The Tech Fort Worth Innovation Award is sponsored by Tech Fort Worth, a privately funded non-profit business incubator designed to provide specialized and industry-specific business assistance to technology start-up companies. This economic development effort provides a mechanism that facilitates the growth and development of emerging technology companies in Fort Worth.

Its mission is to encourage business development in the Greater Fort Worth area by attracting, growing, and graduating successful technology companies that become financially viable and freestanding.

The Incubator invests time and expertise in emerging companies and entrepreneurs that demonstrate the potential for economic and commercial success. Technology companies such as these also diversify the Fort Worth economy and make it less reliant on a single industry, while creating high-wage and high-quality jobs.

To increase the probability of success by the portfolio companies, ensure a high graduation rate, and sound decision making by the entrepreneurs, Tech Fort Worth provides a wide range of specialized business services that, in a pro-active approach, are critical for the participating companies.

In addition, Tech Fort Worth offers introductions and connections to a network of corporate investors, such as venture capitalists, investment and merchant bankers, angel networks and matchmaking services. Also, Tech Fort Worth manages a new, 20, 000 sq. feet facility that offers executive suites, internet access, conference rooms, ample parking, and 24 hour security to client companies. Also, it manages several laboratories at UNTHSC's new Center for Biohealth. The labs will be made available to start-up, life science ventures.

See Tech Fort Worth online at www.techfortworth.org

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1150 S. Freeway, Suite 129
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TRAVEL SERVICE EVERYWHERE

Travel Service Everywhere and its affiliates are long-standing supporters of the Graduate School of Biomedical Sciences and UNT Health Science Center. Their support of Research Appreciation Day 2006 includes the donation of one round-trip airline ticket for the first place winner of the basic sciences oral presentation competition 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.

JUDGES

Graduate School of Biomedical Sciences judges are:

Bruce Benz, Ph.D.
Texas Wesleyan University

Dennis Cheek, Ph.D., R.N., F.A.H.A.
Texas Christian University

Oswald D'Auvergne, Ph.D.
Southern University

Debra Fleenor, Ph.D. ('00)
Alcon Research, Ltd.

Peggy Hellberg, M.S.
Alcon Research, Ltd.

Jami Kern, Ph.D. ('02)
Alcon Research, Ltd.

Kerry Markwardt, Ph.D. ('96)
Alcon Research, Ltd.

Leslie Napier, Ph.D. ('97)
Alcon Research, Ltd.

Melody Phillips, Ph.D.
Texas Christian University

Victoria Rudick, Ph.D.
UNT Health Science Center (Retired)

Roberta Troy, Ph.D.
Tuskegee University

David Bernard, Ph.D.
University of Texas at Arlington

Abe Clark, Ph.D.
Alcon Research, Ltd.

Edward Elko, Ph.D.
UNT Health Science Center, Professor Emeritus

Jannon Fuchs, Ph.D.
University of North Texas

Nasreen Jacobson, Ph.D. ('03)
Alcon Research, Ltd.

Michael Lawrence, Ph.D. ('01)
UT Southwestern Medical Center

Mitchell McCartney, Ph.D.
Alcon Research, Ltd.

Iok-Hou Pang, Ph.D.
Alcon Research, Ltd.

Michael Rudick, Ph.D.
Texas Woman's University (Retired)

Nancy Street, Ph.D.
UT Southwestern Medical Center

School of Public Health judges are:

Roberto Cardarelli, D.O., M.P.H., F.A.A.F.P.
UNT Health Science Center

Witold Migala, Ph.D.
Fort Worth Health Department

Sonja Johnson, R.S., M.P.H.
City of Grand Prairie

JUDGES

Texas College of Osteopathic Medicine judges are:

Robert S. Capper, M.D.
Private Practice

Jay Haynes, M.D.
JPS Health System

Gregory G. Friess, D.O.
Private Practice

David Rittenhouse, D.O.
Private Practice

Fort Worth judges are:

Fulton Murray
Hunt Ventures, LP

Alan Weiner, Ph.D.
Alcon Research, Ltd.

Lawton Seal, Ph.D.
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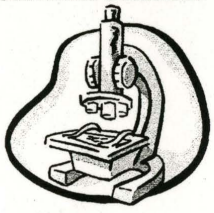

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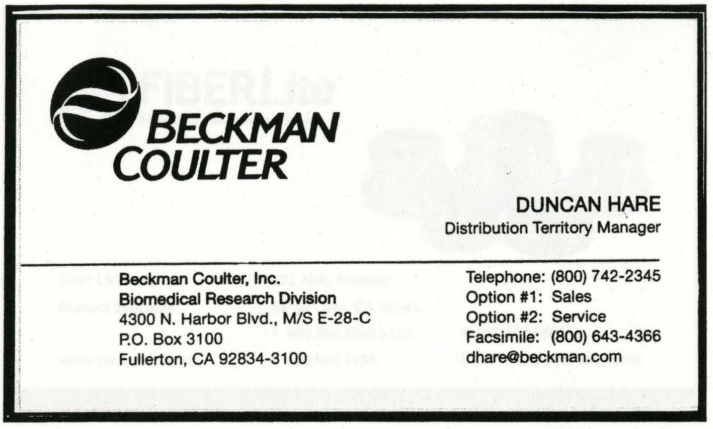
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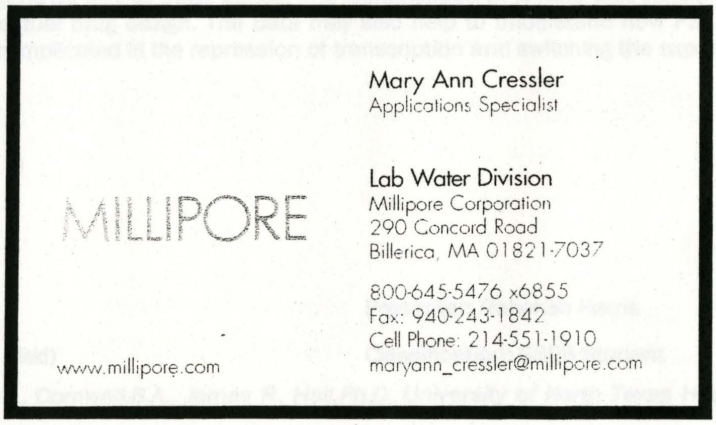
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100 *(Poster)*

Author: Martine Pastorcic

Presenter: Martine Pastorcic

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

Martine Pastorcic 1 and Hriday K. Das 1,2 1 Department of Pharmacology & Neuroscience, 2 Department of Molecular Biology & Immunology, and Institute of Cancer Research University of North Texas Health Science Center at Fort Worth 3500 Camp Bowie Boulevard Fort Worth, Texas 76107

CHD3 INTERCTS WITH ETS TRANSCRIPTION FACTOR ERM AND REPRESSES THE TRANSCRIPTION OF THE HUMAN PRESENILIN I GENE

Purpose: ERM acts as a specific activator of PS1 transcription. In order to analyze its mechanism of action we have searched for ERM interacting proteins by yeast two-hybrid selection in a human brain cDNA library using the C-terminal 984 amino acid of ERM as a bait.

Methods: Yeast 2 hybrid screening and analysis of protein-protein interactions - Transfections assays in SH-SY5Y neuroblastoma cells: the PS1CAT hybrid construct between the PS1 promoter and the CAT reporter gene was cotransfected with CHD3 expression plasmids. The activity of the PS1 gene was monitored by CAT activity. Chromatin immunoprecipation (ChIP). The complexes of proteins cross-linked to chromatin were precipitated with specific antibodies. DNA fragments included in the complexes are in turn detected by PCR analysis.

Results: One of the proteins interacting with ERM was CHD3, a known chromatin remodeling factor. The two CHD3 clones identified by yeast 2-hybrid selection include a C-terminal fragment of CHD3 extending from amino acid 1675 to 2000. We show that the same 325 amino acid C-terminal fragment drastically (90%) represses the transcription of PS1 in SH-SY5Y cells whereas a N-terminal fragment of CHD3 inhibits PS1 transcription by 50%.N-terminal deletions of the 325 amino acid fragment indicated that crucial sequences are located between amino acid 1862 and 1944 which includes a proline rich region. Data from chromatin immunoprecipitation (ChIP) indicate that CHD3 indeed interacts with the PS1 promoter in vivo.

Conclusions: The identification of CHD3 as a factor interacting specifically with the Ets factor ERM may reveal new mechanisms by which ERM activates the PS1 gene as well as other genes. The identification of factors that control the expression of PS1 in vivo provides molecular targets for eventual drug design. The data may also help to understand how PS1 is controlled during development since CHD3 proteins have been implicated in the repression of transcription and switching the expression of genes during the development of embryos.

Sponsor: *N/A*

101 *(Poster)*

Author: Rebekah Harris

Presenter: Rebekah Harris

Department: Psychology (in Int Med)

Classification: GSBS Student

Rebekah L. Harris,B.A., Sonya L. Cornwell,B.A., James R. Hall,Ph.D, University of North Texas Health Science Center, Ft. Worth, TX, 76107.

DIAGNOSTIC UTILITY OF CURRENT METHODS IN IDENTIFYING MILD COGNITIVE IMPAIRMENT

Purpose: Recent research examining the effects of medication to delay the transition from MCI to Alzheimers disease warrants a proactive approach in identifying and treating MCI. This study seeks to determine and utilize the most reliable diagnostic tools for early detection of MCI.

Methods: 240 geriatric patient charts were reviewed. The geriatric patients were referred to the University of North Texas Health Science Center for neuropsychological evaluation. Of the initial 240 charts, 83 (25 males, 58 females; mean age 77.7, SD 7.6 years, range 57-93 years) met inclusion criteria of initial primary care diagnosis, Magnetic Resonance Imaging (MRI) and comprehensive neuropsychological assessment. Initial primary care diagnosis (PC), MRI and comprehensive neuropsychological assessment diagnosis (NP) were categorized as follows: MCI, Neurodegenerative Dementia (i.e., Alzheimers disease, fronto-temporal dementia, Picks Disease), Vascular Dementia and Mixed (e.g., meeting criteria for both Neurodegenerative and Vascular Dementias).

Results: 86% of initial PC diagnoses of MCI were not supported by MRI findings. Additionally, 80% of PC diagnoses were not supported by NP findings. Sensitivity, specificity and positive predictive value are higher for NP than PC.

Conclusions: Doctors initial screen for memory impairment may account for MCI to a higher degree than MRI findings. However within this sample, other variance is accounted for by an increased detection in neurodegenerative and vascular dementia with NP testing. The use of neuropsychological assessments is crucial in detecting MCI. Although the initial primary care diagnosis accounts for MCI, oftentimes patients do not receive additional evaluative methods until further declines in memory are noted.

Sponsor: *N/A*

102 *(Poster)*

Author: Ran Liu

Presenter: Ran Liu

Department: Pharmacology & Neuroscience

Classification: Staff

R. Liu1; S. Yang1; E. J. Perez1; S. Wang1; Z. Y. Cai2; D. F. Covey2; J. W. Simpkins1 1Department of Pharmacology & Neuroscience, UNTHSC Fort Worth, TX, USA, 2 Department of Molecular Biology and Pharmacology, Washington University of Medicine, St. Louis, MO, USA

NEUROPROTECTIVE POTENCY OF ZYC-26, A NON-FEMINIZING ESTROGEN IN A RODENT PERMANENT CEREBRAL ISCHEMIA MODEL: DOSE-RESPONSE RELATIONSHIP

Purpose: It has been well demonstrated that estrogens are potent neuroprotectants and are very effective against ischemia-induced brain damage. But the side effects of feminizing estrogens which are mediated by estrogen receptor a in estrogen responsive tissues may limit their use for the protection of stroke. Our previous in vitro study show a non-feminizing estrogen, ZYC-26, is more potent than 17ß-estradiol (E2) but does not bind to estrogen receptors thus presenting a safe alternative to the current use of feminizing estrogen. Here we determined the optimal doses of 2 lead compounds: E2 and ZYC-26.

Methods: Ovariectomized female Sprague-Dawley rats were subjected to permanent MCAO. E2, ZYC-26 or vehicle was administered through IV injection immediately after MCAO. We examined the efficacy of E2 and ZYC-26 at 4 doses: 1?g/kg, 10?g/kg, 100?g/kg, and 1000?g/kg. Ischemic lesion volume was determined by 2, 3, 5-triphenyltetrazolium chloride staining and the uteri were collected and weighed.

Results: Treatment of E2 and ZYC-26 caused a dose-dependent decrease of ischemic infarct volume. At 10?g/kg and 100?g/kg dosage, ZYC-26 significantly reduced the infarct volume by 48% and 53% respectively whereas 100?g/kg and 1000?g/kg of E2 were needed to reach the same protection. The optimal dose of E2 and ZYC-26 were 1000?g/kg and 100?g/kg, respectively. E2 treatment dose- dependently induced uterine weight increase from 112.8±5.3mg to 195.4±8.7mg. ZYC-26 showed no feminizing effects and produced uterine weights that ranged from 101.0±6.8mg to 117.9±4.2mg over the dose range tested. Collectively our data suggest that ZYC-26 is 10-times more potent than E2 in vivo and its neuroprotective effects are not estrogen receptor dependent.

Conclusions: Non-feminizing estrogens may be useful alternatives for estrogen induced neuroprotection.

Sponsor: *NIH grants AG10485 and AG 22550 and Texas Higher Education Coordination Board*

103 *(Poster)*

Author: Amit Vashist

Presenter: Amit Vashist

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Amit Vashist, Michael J. Forster Pharmacology and Neuroscience, Univ. of North Texas Health Science Ctr., Fort Worth, TX, USA

SHORT-TERM PHYTOESTROGEN SUPPLEMENTATION EXERTS OPPOSITE EFFECTS ON COGNITIVE AND PSYCHOMOTOR PERFORMANCE OF MALE AND FEMALE MICE

Purpose: The goal of this ongoing study is to determine the effects of short-term phytoestrogen intake on cognitive and motor performance of young and old mice. At a broader level, this study will indicate if age related deficits in cognitive and motor abilities, resulting in part from hormonal losses, could be overcome by intake of phytoestrogens.

Methods: Separate groups of young (3 months) and old (18 months) male and female C57BL6 mice were placed on either a control diet or a phytoestrogen-rich diet containing 600 µg/g phytoestrogens for a period of 14 weeks. After 8-weeks on the diets, the mice were subjected to a battery of behavioral tests for cognitive and motor performance. The tests included locomotor activity, motor skills test (wire suspension and bridge walking), rotorod test (measuring fine motor coordination, balance and fatigue), swim maze test (measuring spatial memory of mice), and startle response (measuring reaction time to auditory and shock stimuli).

Results: Based on the data collected so far, female mice (young and old) supplemented with phytoestrogens exhibited improved coordinated running ability and motor skills performance when compared with age-matched controls. Phytoestrogen-treated female mice also displayed faster learning of the swim maze task. Phytoestrogen intake led to deterioration of the coordinated running ability as well as the motor skills performance of male mice (young and old) compared with age-matched controls. Phytoestrogen intake failed to improve the swim maze performance of male mice.

Conclusions: The data suggest that phytoestrogen intake may improve cognitive and motor performance in female mice, but may exert a deleterious effect on the psychomotor functions of male mice.

Sponsor: *Grant P01 AG022550 from NIH National Institute on Aging*

104 *(Poster)*

Author: Nathalie Sumien

Presenter: Nathalie Sumien

Department: Pharmacology & Neuroscience

Classification: Faculty

Nathalie Sumien, Micaela N. Sims, Hilary J. Taylor, Michael J. Forster UNTHSC, Dpt of Pharmacology & Neuroscience, Fort Worth, TX 76107

MULTIVARIATE PROFILING OF PSYCHOMOTOR AND COGNITIVE FUNCTIONS OF A NEW FOUR WAY CROSS MOUSE MODEL DURING AGING

Purpose: Gerontological studies often use inbred strains due to their genetic uniformity, stable characteristics and ample literature available for reference.However, these strains are not representative of a whole population and display strain-specific pathologies hindering potential observable age effects.An alternative to using these mice has been proposed recently in the form of a four way cross model, introducing reproducible genetic variations.However, to date no studies have reported whether this new model could be utilized in brain function studies of aging.Therefore, the purpose of our study was to address this issue by behaviorally characterizing these mice at different ages.

Methods: Young (3-4 mo) and old (22-25 mo) CB6F1 x C3D2F1 mice were obtained from the National Institute on Aging and were acclimated to the UNTHSC vivarium for 2 weeks prior to the start of behavioral testing.Body weights and survival were followed throughout the duration of the study, and food intake and water intake were also measured as part of a general assessment of the mice.The behavioral tests were then administered in the following order: spatial swim maze, locomotor activity, reflexes and motor function, coordinated running, auditory and shock startle, simple discrimination and visual tests.

Results: No effect of age was found on food and water intake.Arousal, ambulation, and turning were impaired by age, however stereotypy remained unaffected.Strength, balance and coordination were diminished with age, yet motor learning was not different between young and old mice.No age effect was found in reaction time to a shock stimulus, however old mice reacted with less force to low intensities of an auditory or shock stimulus.Older mice had a decreased spatial learning efficiency, whereas young mice exhibited a better retention of the information acquired after a 60-hr delay and had a stronger bias towards the platform location.Furthermore, young mice swam at a much faster speed than the old ones. Results from the visible platform test eliminated a visual dysfunction as a potential factor for the decreased spatial learning efficiency. No age effects were observed on the simple discrimination task.

Conclusions: The four-way cross mice exhibited age-related impairments on most measures from the tests administered in this study, which seems to make them reliable tools for studies of brain function during aging, and additionally they may be more applicable models of genetic variance.

Sponsor: *N/A*

105 *(Poster)*

Author: Nopporn Thangthaeng

Presenter: Nopporn Thangthaeng

Department: Psychology

Classification: GSBS Student

Nopporn Thangthaeng and Michael J. Forster University of North Texas Health Science Center, Fort Worth, TX 76107

SHORT-TERM GALACTOSE SUPPLEMENTATION EXACERBATES AGE-DEPENDENT MOTOR DEFICITS

Purpose: The purpose of the current study was to determine if dietary galactose supplementation affects the cognitive or motor performance of young or old mice.

Methods: Separate groups of young (6 months) or old (18 months) mice were assigned to receive either a control diet or a diet containing 40% galactose for a period of 14 weeks. After 8-weeks on the diets, the mice were subjected to a series of behavioral tests to assess cognitive and motor performance. These tests included measurement of spontaneous locomotor activity, motor skills (wire suspension, elevated path test, rotorod test), swim maze learning and the startle reflex.

Results: Galactose-supplemented groups had an approximately 4-fold increase in water intake and significant reduction in weight when compared to the age-matched control groups. Age-related motor impairment between the control groups was observed for performance in wire suspension, elevated path and rotorod tests. Additionally, old controls had decreased auditory and shock startle reactivity and increased reaction time. Swim maze performance of the young and old control groups did not show a significant difference. Galactose supplementation in old mice exacerbated age-related deficits in rotorod, auditory startle amplitude and reaction time. Furthermore, galactose supplementation in old mice reduced locomotor activity. There was no significant difference in swim maze performance between the galactose-supplemented groups. Interestingly, galactose-fed young mice showed increased auditory startle reactivity.

Conclusions: Galactose supplementation targets neural systems involved in age associated motor dysfunctions. The pattern of impairment across behavioral tests implies that galactose supplementation may effect structural components of auditory and vestibular components, that would require further investigation.

Sponsor: *N/A*

106 *(Poster)*

Author: Daisha Cipher

Presenter: Daisha Cipher

Department: Psychiatry

Classification: Faculty

Daisha J. Cipher, Ph.D. Associate Director of Research Department of Psychiatry UNT Health Science Center Fort Worth, TX 76107 P. Andrew Clifford, Ph.D. Clinical Research Director Mind-Body Wellness of Dallas Dallas, TX 75230

BEHAVIORAL MANIFESTATIONS OF PAIN IN ELDERS WITH DEMENTIA

Purpose: The prevalence of pain in United States nursing homes has been estimated to be as much as three times higher than among the younger adult populations. The prevalence of behavioral disturbances ranges between 64% and 83%. When long-term care residents begin to suffer from dementia, pain is difficult to communicate to caregivers. Thus, pain is likely to be expressed in the form of behavioral disturbances, and may include agitation and other observable behaviors associated with discomfort. However, until the recent work of our research team, the behavioral disturbances exhibited by long-term care residents who are suffering from dementia have not been empirically linked to acute or chronic pain conditions.

Methods: A secondary data analysis of 278 persons aged 60 and older was conducted to 1) determine the influence of pain on the number, intensity, frequency, and duration of dysfunctional behaviors; 2) investigate the differences between residents with varying levels of dementia who were suffering from acute pain in the intensity, frequency, and duration of 19 behavioral categories; and 3) investigate the differences between residents with varying levels of dementia who were suffering from chronic pain in the intensity, frequency, and duration of 19 behavioral categories.

Results: Results revealed that pain has a significantly stronger influence on behavioral disturbances among those with severe dementia than those with moderate or mild dementia, and residents with chronic pain who have severe dementia exhibit significantly more dysfunctional behaviors than those with earlier-stage dementia.

Conclusions: These findings support the utility of assessing the intensity, frequency, and duration of dysfunctional behaviors in long-term care. Moreover, our results imply that pain must be adequately treated in order to reduce behavioral disturbances and improve quality of life.

Sponsor: *N/A*

107 *(Poster)*

Author: Ritu Shetty

Presenter: Ritu Shetty

Department: Pharmacology & Neuroscience

Classification: GSBS Student

R.A.Shetty; M.J.Forster; K.R.Heinrich; M.Rutledge; N.Sumien; N.Thangthaeng; S.Yang; J.W.Simpkins Dept of Pharmacol & Neurosci, Univ. of North Texas Health Sci. Ctr., Ft. Worth, Fort Worth, TX, USA*

TRANSIENT CEREBRAL ISCHEMIA CAUSES A PROGRESSIVE DECLINE IN BRAIN FUNCTION

Purpose: Recent studies have identified common elements in brain pathology produced by transient hypoperfusion of the brain and progressive age-associated neurodegenerative diseases (Brain Research, 1022: 30-38, 2004). The goal of this study was to determine whether or not a progressive decline in cognitive or psychomotor function was associated with brain damage produced by transient middle cerebral artery occlusion (tMCAO).

Methods: Female Sprague-Dawley rats were ovariectmized at 3 months of age and received tMCAO, a sham procedure, or no treatment at 4 months of age. Separate groups of these rats were then subjected to a battery of behavioral tests for cognitive and psychomotor performance either 7- or 30-days following tMCAO. These tests included spontaneous locomotor activity, coordinated running performance, swim maze and acoustic startle response.

Results: The tMCAO groups showed poorer learning of the swim maze task when compared to the age-matched sham or control groups. However, the 30-day post tMCAO group tended to perform worse than the 7-day post tMCAO group in learning to locate the platform in swim maze task. In the test for spontaneous locomotor activity there was an increase in activity following tMCAO, with the 30-day post tMCAO group showing higher activity when compared to the 7-day post tMCAO group. In the test for acoustic startle response, both tMCAO groups habituated to an acoustic stimulus more slowly than did controls, with the 30-day post tMCAO group tending to sustain a high level of response for longer than the 7-day post tMCAO group. In a test for coordinated motor ability, there was no difference in performance in both tMCAO and control groups.

Conclusions: The results indicate that, over a period of 30 days following tMCAO, there is a decline in brain function involving both cognitive and psychomotor performance. The results also indicate that the battery of behavioral test can be used to assess transient middle cerebral artery occlusion associated cognitive and motor decline in function.

Sponsor: *N/A*

108 *(Poster)*

Author: James Hall

Presenter: Janice Dunn

Department: Psychology (in Int Med)

Classification: Dual Degree Student

Janice Dunn, MA University of North Texas Denton, TX 76201 James R. Hall, Ph.D., FABMP Clinical Health Psychologist Associate Professor Department of Internal Medicine Division of Geriatrics Chair Department of Health Psychology University of North Texas Health Science Center 855 Montgomery Street Fort Worth, Texas 76107

FACTOR STRUCTURE OF THE GERIATRIC DEPRESSION SCALE SHORT FORM IN COGNITIVELY IMPAIRED ADULTS

Purpose: The Geriatric Depression Scale (GDS) was developed as a depression screening instrument for the elderly. A previous study explored the factor structure of the GDS-Long Form (GDS-LF) in an elderly population that was diagnosed with some level of cognitive impairment. This study reports the factor structure of the GDS-Short Form (GDS-SF) in the same population.

Methods: The study sample consisted of 236 community-dwelling patients with a mean age of 79.14 (SD = 7.17) who participated in neuropsychological evaluations for dementia at a metropolitan outpatient clinic. Principle components analysis was conducted to achieve a five factor model.

Results: The resulting five factors were labeled Dysphoria, Hopelessness, Social Comparison, Apathy, and Life Satisfaction. In contrast, the previous study revealed only four factors. Although similar items loaded on the Dysphoria scale in both studies, the other factors had differing item content.

Conclusions: Studies have shown that the GDS-SF is highly correlated with the GDS-LF and both have similar sensitivity and specificity rates in identifying depression, but the differing factor structures of the two forms indicate that they may be assessing different dimensions of depression.

Sponsor: *N/A*

109 *(Poster)*

Author: Sonya Cornwell

Presenter: Sonya Cornwell

Department: Psychology (in Int Med)

Classification: GSBS Student

Sonya L Cornwell, BA, Rebekah L Harris, BS, James R Hall, PhD and Amir Ramezani, BA. Clinical Health Psychology/Behavioral Medicine, University of North Texas (Consortium)UNT Health Science Center,Ft. Worth, TX, 76107

NECESSITY OF NEUROPSYCHOLOGY AND NEUROIMAGING TO THE DIFFERENTIAL DIAGNOSIS OF DEMENTIA

Purpose: Dementia affects about 5% of the population older than age 65 and is most frequent in those older than age 75. The prevalence of dementia and our ever aging population presents a strong need for standard and reliable diagnostic methods.It was hypothesized that both NP and MRI would vary significantly from the initial clinical examination. Moreover, it was hypothesized that MRI and NP would be high in agreement with the final collaborative diagnosis. If both prove high in agreement, perhaps one or the other would be sufficient for differential diagnosis.

Methods: Retrospective analysis was completed on 83 patients evaluated by physicians in the Geriatric Assessment Program at the UNT Health Science Center. Patients diagnosed with dementia or memory impairment were referred for NP and MRI screens. Patients had a mean age of 77.7, ranging from 57 to 93 years of age. Neuropsychological investigation was performed using the Consortium to Establish a Registry for Alzheimers disease (CERAD) test battery and the Wechsler Memory Scale III. MRI and NP findings were grouped into four categories including neurodegenerative dementia (ND), findings compatible with vascular dementia (VD), mixed findings of both atrophy and ischemic change (MD) or no findings (XD). Significant differences from chance level regarding the transitions between the diagnostic categories (initial vs final diagnosis) were calculated by 95% confidence interval. A measurement of agreement between the NP and MRI was also performed in order to infer the necessity of both in the final differential diagnosis.

Results: NP and MRI led to a significant change of the final comprehensive diagnosis (p

Conclusions: Neuropsychological testing plus MRI as part of the diagnostic work-up of patients with cognitive disturbances improves the differential diagnosis of dementia. MRI and NP provide very different, although valuable information to the final differential diagnosis of dementia.

Sponsor: *N/A*

110 *(Oral)*

Author: Vaibhav Pawar

Presenter: Vaibhav Pawar

Department: Cell Biology and Genetics

Classification: GSBS Student

Vaibhav Pawar(1),Nila Patel(1),Liu Jingjing(1),Paul Doetsch(2),Gerald Shadel(3)and Wolfram Siede(1). (1)Dept. Cell Biology and Genetics, University of North Texas Health Science Center, Fort Worth,Tx. (2)Depts. Biochemistry/Radiation Oncology, Emory University School of Medicine, Atlanta, GA. (3) Dept. Pathology, Yale University School of Medicine, New Haven, CT.

CHRONOLOGICAL LIFESPAN OF SACCHAROMYCES CEREVISIAE: A SIGNIFICANT MODEL TO STUDY AGING OF POSTMITOTIC CELLS IN HIGHER ORGANISMS?

Purpose: The main goal of this research is to investigate the mechanisms that are involved in the repair of endogenous DNA damage during chronological lifespan of Saccharomyces cerevisiae, which will set an indispensable model to study post-mitotic aging in higher organisms.

Methods: Principal methods used in this research are PCR assisted gene replacement to delete one or more pathways of DNA repair, phosphorylation of check point kinase Rad53p has been detected by immunoblotting, cell survival measured by the colony forming ability of individual cells, mitochondrial DNA detected by mitochondrial staining to confirm rho mutants.

Results: We have observed Rad9p dependent Rad53p checkpoint kinase phosphorylation in stationary phase S. cerevisiae if two major pathways of DNA damage repair, base excision repair and nucleotide excision repair are compromised. This Rad53p response is absent in rho0 (lacking detectable mitochondrial DNA) strains, also in cor1 and coq3 deletion mutants. We have extended this analysis to other repair deficient mutants and mutant combinations. Certain mutants such as rad52 (homologous recombination) show Rad53p modification in logarithmic phase also in stationary phase. Interestingly, a combination of a yku70 deletion (the budding yeast Ku 70 homolog) and rad52 or rad4 (NER) elicits the Rad53p phosphorylation response in stationary phase. The survival of yeast mutants shows that double mutants have low survial than that of their single mutants. And the survival of berner mutant improves after antioxidant treatment.

Conclusions: Our results conclude that two major pathways of oxidative damage repair, base excision repair and nucleotide excision repair must be inactivated to get check point activation in stationary phase. And this effect is strictly dependent on mitochondrial function. Also our findings indicate an unsuspected role of non-homologous end joining (NHEJ) and nucleotide excision repair in oxidative damage repair. Alternatively, the known telomere alteration in yku70 mutants may synergize with an independent repair defect of oxidative damage in rad52 or NER mutants to trigger Rad53p phosphorylation, which supports the premature aging phenotype of mice deleted for Ku. The stationary phase S. cerevisiae mimics the state of post mitotic cells, the checkpoint response and survival of repair deficient strains in the stationary phase may relate to the aging phenotype of post mitotic cells.

Sponsor: *NIH grants ES11163 and CA87381 to Dr.Siede.*

111 *(Poster)*

Author: Anna Rodriguez

Presenter: Anna Rodriguez

Department: Pharmacology & Neuroscience

Classification: GSBS Student

AV Rodriguez, KD Yi, JW Simpkins. University of North Texas Health Science Center, Department of Pharmacology and Neuroscience, Fort Worth, TX 76107

17 BETA-ESTRADIOL ATTENUATES GLUTAMATE INDUCED INCREASES IN INTERGRIN BETA-1

Purpose: It has been previously shown that 17 beta-estradiol is neuroprotective against various cellular insults. The mechanism by which 17 beta-estradiol is neuroprotective is yet unclear. However, there is evidence that the actions of 17 beta-estradiol is via a receptor independent mechanism that may involve variously cellular signaling pathways. Integrins are transmembrane proteins that have been shown to be increased in cell death. The purpose of this study was to investigate the role of integrins in the protective effect of estrogens against glutamate-induced oxidative stress in HT-22 cells.

Methods: HT-22 cells were exposed to varying concentrations of glutamate in the absence or presence of 17 beta-estradiol. Cell viability was measured by Calcein AM, a nonfluorescent, 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. Protein expression was measured by western blot analysis.

Results: Glutamate caused a dose-dependent decrease in cell viability. 17 beta-estradiol treatment simultaneously with glutamate showed significant preservation in cell viability. In addition, ß1 subunit of the integrin protein was increased with glutamate treatment as compared to non-treated and vehicle controls. The presence 17beta-estradiol attenuated this increase in ß1 subunit; however, estrogen by itself did not affect the expression of ß1 subunit.

Conclusions: The present study demonstrates that 17 beta-estradiol can attenuate cell death caused by oxidative stress induced by glutamate. It also demonstrates that 17 beta-estradiol attenuates the increase in the protein expression of ß1 induced by glutamate treatment; however, further studies need to be conducted to determine role of integrins in estrogen mediated neuroprotection. (Supported by NIH grants AG10485 and AG22550.)

Sponsor: *N/A*

112 *(Oral)*

Author: Kun Yi

Presenter: Kun Yi

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Kun Don Yi, MS, and James W. Simpkins, PhD. University of North Texas Health Science Center. Fort Worth, TX 76107.

PP2A IS INVOLVED IN NEUROPROTECTIVE EFFECTS OF 17?-ESTRADIOL

Purpose: Estrogens are a potent neuroprotectant against various cellular effects such as oxidative stress, excitotoxicity, inflammatory responses, mitochondrial dysfunction, and apoptosis. There is considerable evidence that estrogens act on neurons through a variety of signal transduction pathways to induce rapid, but acute phosphorylation and dephosphorylation of signaling proteins. However, the exact mechanisms by which estrogens are neuroprotective remain unclear. Therefore, this study investigated the role of protein phosphatases in the neuroprotective effects of estrogens against oxidative stress in vitro and in vivo.

Methods: Primary cortical neurons were exposed to glutamate insult in the absence or presence of estrogen and/or protein phosphatase inhibitors. Cell viability was measured by Calcein AM, a nonfluorescent, electrically neutral nonpolar analog of fluorescein diacetate, which passively crosses cell membranes and is cleaved to a fluorescent derivative by nonspecific intracellular esterases. Middle cerebral arteries of female rats were occluded transiently for one hour and the area allowed to reperfuse for 24 hr. The area of infarction was measured. Proteins were analysized by western blots.

Results: Okadaic acid (OA) and calyculin A (CA), non-specific serine/threonine PP inhibitors, caused a dose-dependent decrease in cell viability. Neither simultaneous nor pretreatment of 17ß-estradiol prevented the cell death caused by OA or CA. Moreover, the presence of these serine/threonine PP inhibitors completely abolished the neuroprotective effects of 17ß-estradiol against glutamate toxicity. Western blot analysis showed that treatment with estrogens in the presence of glutamate caused an increase in protein level of PP2A. Phosphorylated ERK was increased on the ischemic damaged brain. In conjunction, the ischemic side of the brain also showed increased PP2A.

Conclusions: The present study demonstrates that inhibition of protein phosphatases antagonized the neuroprotective effects of estrogens in both in vitro and in vivo. One of the mechanism by which estrogens is protecting cells may be via activation of PP2A to dephosphorylated ERK in an estrogen receptor independent pathway.

Sponsor: *AG 10465 and AG 22550*

200 *(Poster)*

Author: Rusha Thomas

Presenter: Rusha Thomas

Department: Molecular Biology and Immunology

Classification: GSBS Student

Rusha Thomas and Myoung H. Kim Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, Texas 76107.

TARGETING THE HYPOXIA INDUCIBLE FACTOR PATHWAY WITH MITOCHONDRIAL UNCOUPLERS

Purpose: Hypoxia inducible factor-1 (HIF-1) is central to most adaptation responses of tumors to hypoxia, and consists of a hypoxia inducible HIF-1 alpha or HIF-2 alpha subunit, and a constitutively expressed HIF-1 beta subunit. Previously, mitochondrial uncoupler, FCCP, was shown to increase the rate of cellular O2 consumption and to inhibit hypoxia-induced HIF-1 alpha expression. In this study, we determined the effect of mitochondrial uncouplers, rottlerin and FCCP, on normoxic and hypoxic HIF-1 alpha and HIF-2 alpha protein levels, transcriptional activity and nuclear localization in PC-3 prostate cancer cells.

Methods: Luciferase assays were used to study HIF transcriptional activity, cellular localization of HIF was analyzed by immunocytochemistry and western blots, and effect of mitochondrial uncouplers on HIF target gene expression was studied by RT-PCR and luciferase assays.

Results: In this study, we determined that mitochondrial uncouplers, rottlerin and FCCP, significantly decreased hypoxic as well as normoxic HIF-1 transcriptional activity which was in part mediated by down-regulation of HIF-1 alpha and HIF-2 alpha protein levels in PC-3 prostate cancer cells. Our results also revealed that mitochondrial uncouplers decreased the expression of HIF target genes, VEGF and VEGF receptor-2.

Conclusions: Taken together, our results indicate that functional mitochondria are important in HIF-1 alpha and HIF-2 alpha protein stability and transcriptional activity during normoxia as well as in hypoxia, and that mitochondrial uncouplers may be useful in the inhibition of HIF pathway in tumors.(NIH grant # 1R21CA102382 to M. H. Kim)

Sponsor: *NIH grant # 1R21CA102382 to M. H. Kim*

201 *(Poster)*

Author: Sushoban Das

Presenter: Cherice Anderson

Department: Molecular Biology and Immunology

Classification: GSBS Student

Cherice Anderson UNTHSC Sushoban Das UNTHSC J.K Vishwanatha UNTHSC

ANNEXIN 2 AND STAT6 INTERACTION IN PROSTATE CANCER

Purpose: To investigate the regulation of prostate cell proliferation by annexin II (ANX2)via a novel interaction with STAT6.

Methods: We have performed the chromatin immunoprecipitations (ChIPs)and identified STAT6 as an annexin II-interacting protein. The DNA fractions of ANX2 chIPs show that the promoter region of IgE can be identified via Polymerase chain reactions (PCR). STAT6 is the transcriptional promoter of IgE. Immunocytochemistry experiments in prostate cancer cell lines also show colocalization.

Results: Expression of annexin II from a regulatable vector in LNCaP stable clones enhanced STAT6 transcriptional acitvity in luciferase reporter assays. We have found that STAT6 DNA binding activity is also increased when annexin II is expressed.

Conclusions: Neither the role of the STAT6 pathway in prostate cancer progression or the gravity of the ANX2-STAT6 interaction is known at this time and warrants further investigation.

Sponsor: *N/A*

202 *(Poster)*

Author: Maya Nair

Presenter: Maya Nair

Department: Molecular Biology and Immunology

Classification: Faculty

NAIR, M.P., MOOBERRY L, S. PARANJPAE, Mc CONATHY WJ, LACKO AG. Department of Molecular Biology and Immunology University of North Texas Health Science Center, Fort Worth, TX 76107

FOLIC ACID CONJUGATED RECONSTITUTED HIGH DENSITY LIPOPROTEIN FOR TARGETED CHEMOTHERAPY OF OVARIAN CANCER

Purpose: Major barriers to effective cancer chemotherapy include the limited penetration of the anti-cancer drugs into tumor tissue, toxic side effects and multi-drug resistance developed by tumors during treatment. To overcome these obstacles, we have developed a novel drug delivery system employing folic acid as a targeting ligand, attached to reconstituted high density lipoprotein (FA-rHDL), against ovarian cancer cells.

Methods: We have used paclitaxel (Ptx) as the chemotherapeutic agent enclosed in the rHDL nanoparticles. The FA-rHDL/Ptx nanoparticle is designed to minimize the uptake of the drug by normal cells and enhances its uptake and retention by cancer cells. The rationale for the targeting strategy is based on the findings that folate receptors are over expressed by 90% of the malignant ovarian tumors while they are not detectable in normal tissues.

Results: Preliminary data showed that the use of folic acid conjugated rHDL substantially enhanced the uptake of Ptx by ovarian cancer cells over that of the free drug and even the rHDL encapsulated Ptx,

Conclusions: Future studies: In vitro studies will be conducted to evaluate the effect of loading paclitaxel into FA-rHDL on the properties of rHDL and Ptx cytotoxicity to human carcinoma cells. Ovarian cancer cell lines that over expresses folate receptor OVCAR3 will be used to study the mode of uptake and cytotoxic effect as compared to Taxol®. Similar studies will be carried out with normal human ovarian surface epithelial cells (OSE). In vivo studies will be conducted to find out how effective is FA-rHDL/Ptx in improving the animal survival by reducing the tumor burden and minimizing the potential side effects due to enhanced targeting.

Sponsor: *N/A*

203 *(Poster)*

Author: Jiyoung Lee

Presenter: Jiyoung Lee

Department: Molecular Biology and Immunology

Classification: GSBS Student

J. Lee and A. Basu, University of North Texas Health Science Center, Fort Worth, TX, 76107.

ROLE OF TYROSINE PHOSPHORYLATION OF PKC DELTA IN CISPLATIN-INDUCED APOPTOSIS

Purpose: Cisplatin is one of the most important anticancer agents used to treat solid tumors including human cervical cancer and ovarian cancer. Cisplatin can cause apoptosis by damaging DNA. Protein kinase C (PKC) is a family of serine/threonine kinase involved in signaling pathways of growth regulation and programmed cell death. PKC delta, a novel member of the PKC family, plays an important role in DNA damage-induced apoptosis. PKC delta can be regulated by phosphorylation at the tyrosine residues. Src family of tyrosine kinases have been shown to phosphorylate PKC delta at several tyrosine sites. The objective of this project is to investigate the role of tyrosine phosphorylation of PKC delta in cisplatin-induced apoptosis. In addition, we have examined if tyrosine phosphorylation influences resistance to cisplatin.

Methods: Human cervical cancer (HeLa) and ovarian cancer (2008) as well as their cisplatin-resistant counterparts were used in this study. Cells were treated with several tyrosine kinase inhibitors, including PP2 (an inhibitor of Src family tyrosine kinases), herbimycin (a general inhibitor of tyrosine kinases) and AG1478 (an inhibitor of EGFR tyrosine kinase) in the presence or absence of cisplatin. Tyrosine phosphorylation was detected by Western blot. Cell death was measured using a colorimetric cell survival assay, activation of caspases, and flow cytometric DNA analysis using propidium iodide. Src kinase was depleted by transfecting siRNA corresponding to Src kinase.

Results: Phosphorylation at Y311 site of PKC? by cisplatin preceded cleavage of PKC?. PP2 decreased phosphorylation of PKC? at Y311 site and enhanced cisplatin-induced cell death, whereas AG1478 did not increase cisplatin-induced cell death. Depletion of Src by siRNA decreased phosphorylation of PKC? at Y311 site and sensitized both HeLa and HeLa/CP cells to cisplatin.

Conclusions: Inhibition of PKC delta tyrosine phosphorylation at Y311 by Src kinase enhanced cisplatin-induced apoptosis. (NCI/NIH grant CA85682)

Sponsor: *N/A*

204 *(Poster)*

Author: Subhamoy Dasgupta

Presenter: Subhamoy Dasgupta

Department: Molecular Biology and Immunology

Classification: GSBS Student

Subhamoy Dasgupta(1), Susobhan Das(1), and Jamboor K Vishwanatha(1,2),(1)Department of Molecular Biology and Immunology, (2)Institute for Cancer Research,University of North Texas Health Science Center, Fort Worth, TX 76107

EXPRESSION AND CELLULAR LOCALIZATION OF C17ORF37/MGC14832 IN CANCER CELLS

Purpose: MGC14832/ORB3/XTP4 is located in the hot spot locus of chromosome 17q12 in cancer. Expression levels of these transcripts in primary breast tumors showed a highly significant association between amplification and expression levels for six of these genes including ERBB2 and two uncharacterized hypothetical proteins MGC9753 and MGC14832. By yeast two-hybrid analysis our laboratory established that MGC14832 interacts with Annexin II which belongs to the family of Ca+2 dependent membrane binding protein called annexins. Annexin II has been reported to be over- expressed in many cancers and is an important molecule in finbrinolysis and neoangiogenesis. The objective of this study is to characterize the expression, sub-cellular localization and functional role of the hypothetical protein MGC14832 in cancer progression.

Methods: GFP fused MGC14832 construct was transfected in DU-145 and LNCaP prostate cancer cells and OSC-2 oral cancer cells followed by immunofluorescence microscopy to study the sub-cellular localization. We also made a GST fused MGC14832 construct and checked for GST fused protein expression using western blot. Western blot analyses of different prostate cancer cell lysates were performed to detect the endogenous MGC14832 protein expression. Total RNA was isolated from prostate cancer cells and RTPCR was performed to check the differential expression of MGC14832 mRNA.

Results: Immunofluorescence microscopy showed GFP-fused MGC14832 expression in the cells, predominantly in the cytoplasm. Some nuclear staining was observed. Fusion of MGC14832 with GST (26 kDa) results in a protein of ~40 kDa in Western blots. MGC14832 cDNA (348 bp) encodes a predicted protein of ~13.7 kDa. Western blot analysis of cell lysates shows endogenous MGC14832 expression in DU145 and LNCaP prostate cancer cells at ~48kDa. mRNA expression of MGC14832 was found to be more in prostate cancer cells compared to normal prostate cells.

Conclusions: Our results show that MGC14832 predominantly expresses in the cytosol of the prostate cancer cells. Further studies are directed towards the functional role of the protein in cancer progression and characterization of Annexin II □MGC14832 interaction.

Sponsor: *N/A*

205 *(Poster)*

Author: Eswar Shankar

Presenter: Eswar Shankar

Department: Molecular Biology and Immunology

Classification: Postdoctoral Fellow/Resident

Eswar Shankar, Usha Sivaprasad and Alakananda Basu. Department of Molecular Biology and Immunology University of North Texas Health Science Center and Institute for Cancer Research, Fort Worth, TX, 76107.

PROTEIN KINASE C EPSILON CONFERS RESISTANCE TO TUMOR NECROSIS FACTOR RELATED APOPTOSIS INDUCING LIGAND-INDUCED APOPTOSIS BY ALTERING LEVELS OF PRO- AND ANTI-APOPTOTIC BCL-2 FAMILY PROTEINS

Purpose: Tumor necrosis factor-Related Apoptosis-Inducing Ligand (TRAIL) is a member of the tumor necrosis factor (TNF) family that promotes apoptosis primarily in cancer cells, without any detectable toxicity to normal cells. TRAIL induces apoptosis via receptor mediated pathway and mitochondrial pathway. Protein kinase Cs (PKC) are a family of phospholipid-dependent serine/threonine kinases that play an important role in cell survival and apoptosis. Our lab has previously shown that PKC epsilon is an anti-apoptotic protein that inhibits TNF-alpha-induced apoptosis in MCF-7 cells. In the present study we investigated the mechanism by which PKCepsilon influences TRAIL mediated cell death.

Methods: MCF-7 cells were stably transfected with either with vector alone or with a PKC epsilon construct, were treated with different concentrations of TRAIL and protein expression of Bcl-2, Bid, PARP and caspases analyzed by immunoblotting. mRNA expression was studied using RT-PCR and Knockdown of Bcl-2, Bid and PKCepsilon was achieved by siRNA against these proteins.

Results: MCF-7 cells overexpressing PKCepsilon (MCF-7/PKCepsilon) were refractory to TRAIL-induced apoptosis compared to vector-transfected MCF-7 cells (MCF-7/Neo), as evident from the activation of caspases and the cleavage of poly (ADP-ribose) polymerase (PARP) in TRAIL-treated cells. In addition, depletion of PKCepsilon by siRNA or inhibition of PKCepsilon activity by overexpression of a dominant-negative mutant enhanced cellular sensitivity to TRAIL. Overexpression of PKCepsilon attenuated the release of mitochondrial cytochrome c induced by TRAIL. Since Bcl-2 family proteins regulate the intrinsic cell death pathway, we compared the pattern of expression of Bcl-2 family members in MCF-7/Neo and MCF-7/PKCepsilon cells. Overexpression of PKC epsilon in MCF-7 cells resulted in an increase in anti-apoptotic Bcl-2 and a decrease in pro-apoptotic Bid compared to MCF-7/Neo cells. Depletion of Bid using siRNA conferred resistance to MCF-7/Neo cells from TRAIL-induced death. Furthermore, depletion of Bcl-2 from MCF-7/PKCepsilon cells by siRNA dramatically increased their susceptibility to TRAIL-induced apoptosis.

Conclusions: These results demonstrate that a decrease in the ratio of pro- to anti-apoptotic Bcl-2 family members was associated with the anti-apoptotic function of PKCepsilon during TRAIL-induced apoptosis. (This work was supported by the grant CA71727 from the NCI.)

Sponsor: *NCI*

206 *(Poster)*

Author: Linda Mooberry
Presenter: Linda Mooberry
Department: Molecular Biology and Immunology
Classification: GSBS Student
Linda Mooberry, Maya Nair, Sulabha Paranjape, Walter McConathy, Andras Lacko Department of Molecular Biology and Immunology, Department of Internal Medicine, Institute of Cancer Research, Unviersity of North Texas Health Science Center, Fort Worth TX 76107

SELECTIVE RECEPTOR-MEDIATED UPTAKE OF ANTICANCER DRUGS FROM RECONSTITUTED HIGH DENSITY LIPOPROTEIN NANOPARTICLES

Purpose: The purpose of these studies is to develop a novel drug delivery strategy for overcoming current barriers to cancer chemotherapy, including i) the limited accessibility of the drugs to tumor tissue, ii) toxic side effects and iii) multi-drug resistance developed by malignant tumors during treatment. The rHDL vehicle used in these studies has substantial advantages over conventional drug delivery strategies, including its small size and its resemblance to natural plasma components. A further advantage of the rHDL drug delivery model is the selective lipid uptake mechanism by which cholesteryl esters are delivered to target cells via the scavenger receptor, class B, Type I (SR-BI) or C36 and LIMP-II analogous protein-1 (CLA-1). The purpose of these experiments was to measure the anticancer activity of the paclitaxel formulation (rHDL/Ptx) and to examine the mechanism of paclitaxel uptake by cancer cells from rHDL nanoparticles.

Methods: PTX uptake mechanism: The rHDL/Ptx was double-labeled with 125-Iodine in the protein component, Apo A-I and with 14C-paclitaxel in the core. The prostate cancer cell line, PC3, was incubated with media containing double-labeled rHDL/Ptx alone or rHDL/Ptx with a 10-fold excess of Apo A-I, Apo A-I/Phosphatidyl Choline Discs or HDL3. The cells were processed to determine the internalization of rHDL/Ptx and selective paclitaxel uptake Anticancer Activity: PC3 cells were incubated with rHDL containing no Ptx, with rHDL/Ptx at 0.1, 0.2,or 0.5 microM for 24, 48, 72, and 96 hours. Cell viability was measured with the MTT assay.

Results: Eighteen percent of the paclitaxel was taken into the cell through endocytosis; 333.8 ± 36.8 ng of paclitaxel were selectively taken up. Incubation of the cells with the natural ligand of SR-BI, HDL3, decreased paclitaxel uptake to 30.6% as compared to rHDL/Ptx alone (p

Conclusions: The majority of the paclitaxel was taken up by selective uptake, presumably mediated by the CLA-1/SRB-I mechanism. The inhibition of paclitaxel uptake by HDL3 supports the hypothesis that paclitaxel delivery from rHDL is a receptor-mediated mechanism. The anticancer activity of rHDL/PTX was effective at low concentration; rHDL could be an advantageous anticancer drug delivery vehicle.

Sponsor: *N/A*

207 *(Poster)*

Author: Rohini Dhar
Presenter: Rohini Dhar
Department: Molecular Biology and Immunology
Classification: GSBS Student
R. Dhar, A. Basu University of North Texas Health Science Center, Fort Worth, TX, 76107.

REGULATION OF P70S6K BY CISPLATIN IN LUNG CANCER CELLS.

Purpose: cis-Diamminedichloroplatinum(II) or cisplatin is one of the most effective anticancer drugs used in the treatment of solid tumors, including lung cancers. One of the fundamental problems with cancer chemotherapy for lung cancer is the resistance by tumor cells to the anti-cancer drug. p70S6k, a serine/threonine kinase regulates the progression of cells from the G0 to G1 phase of cell cycle by translational upregulation of a family of mRNA transcripts. It has also been shown that p70S6k is constitutively phosphorylated and activated in lung cancer cells. Resistance to chemotherapy may occur due to enhanced cell survival signaling pathways or due to an aberration in apoptotic pathways. Caspases are central to the apoptotic machinery and they are known to be activated by cisplatin. The purpose of this study is to determine the role of p70S6k in cisplatin-induced apoptosis in human small cell lung cancer cells.

Methods: Human small cell lung cancer H69 and cisplatin-resistant H69/CP cells were treated with cisplatin for the indicated time period. p70S6k protein and phosphorylation levels were detected by immunoblotting using total and phospho specific antibodies. Cell death was determined by monitoring cleavage of Poly-ADP-ribo-polymerase (PARP) and by the appearance of sub-diploid DNA peak in flow cytometer.

Results: Cisplatin treatment caused a decrease in phosphorylation of p70S6k in the H69 cells, but not in the H69/CP cells. The levels of phospho-p70S6k in the unstimulated H69/CP cells was higher compared to the H69 cells although total p70S6k levels were lower in the H69/CP cells. Rapamycin, an inhibitor of p70S6k, completely blocked the activation of p70S6k in both H69 and H69/CP cells. Rapamycin alone did not cause PARP cleavage, but it enhanced cisplatin-induced PARP cleavage. Treatment of H69 cells, with broad specificity caspase inhibitor ZVAD prior to cisplatin treatment, caused an increase in phospho-p70S6k levels and reversed cisplatin induced PARP cleavage. Furthermore, caspase inhibition completely reversed the downregulation of p70S6k induced by cisplatin.

Conclusions: These results suggest that inhibition of p70S6K may enhance sensitivity of small cell lung cancer cells to cisplatin. Furthermore, enhanced phosphorylation of p70S6k may be associated with cisplatin resistance.

Sponsor: *NIH grant CA85682*

208 *(Poster)*

Author: Rajeev Nagarad

Presenter: Rajeev Nagarad

Department: Molecular Biology and Immunology

Classification: GSBS Student

Rajeev Nagarad and Alakananda Basu University of North Texas Health Science Center

PROTEIN EXPRESSION IN CISPLATIN SENSITIVE AND CISPLATIN RESISTANT HELA CELLS USING TWO-DIMENSIONAL GEL ELECTROPHORESIS

Purpose: Proteomics has emerged as an important means to understand cellular function. Even though most of the earlier research was on understanding the genome there has been increasing emphasis on the study of proteins themselves. This is especially important in the light of the observation that the model of 1 gene=1 protein is incorrect and in eukaryotic cell there could actually be 6-8 proteins/gene. In addition the proteins are subject to high amount of independent processing and interaction with other proteins which determine cellular function. Cis-Diamminedichloroplatinum (II) or Cisplatin is one of the most important anticancer drugs to treat solid tumors including cervical cancer. However the development of resistance by tumor cells to cisplatin limits its therapeutic use. The aim of my project is to look for any differences in proteins in cisplatin- sensitive and cisplatin-resistant Hela cells using proteomics tools.

Methods: Our lab has developed human cervical cancer cells resistant to cisplatin (Hela/CP) by in vitro selection. We have isolated proteins from Hela (cisplatin sensitive) and Hela/CP cells and subjected to two-dimensional gel electrophoresis. This method involves separation of proteins based on their PI in one dimension and by their molecular weight in the other dimension. Separation in the first dimension was achieved by using immobilized strips of different pH range and lengths. Separation in the second dimension was done by SDS-PAGE. The proteins are then compared by gel staining or by western blotting.

Results: We could separate the proteins by two-dimensional gel electrophoresis and there are some differences in protein patterns in cisplatin-sensitive and cisplatin-resistant Hela cells.

Conclusions: We are currently trying to standardize the protocol and because of the numerous proteins that could be different in cisplatin sensitive and cisplatin resistant cells we are trying to perform two dimensional gel electrophoresis following immunoprecipitation to focus on the protein of our interest.

Sponsor: *NCI/NIH Ca85682*

209 *(Poster)*

Author: Usha Sivaprasad

Presenter: Usha Sivaprasad

Department: Molecular Biology and Immunology

Classification: Postdoctoral Fellow/Resident

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

RIBOSOMAL S6 KINASE (S6K) AND MITOGEN-ACTIVATED PROTEIN KINASE (MAPK) DIFFERENTIALLY REGULATE TUMOR NECROSIS FACTOR-A (TNF)-INDUCED AUTOPHAGY AND APOPTOSIS IN BREAST CANCER CELLS

Purpose: Tumor necrosis factor-a (TNF) is a cytokine that induces apoptosis in cancer cells. Recent data suggest that TNF can also induce autophagy, a process of degradation of cytoplasmic components in lysosomal compartments called autophagosomes. Autophagy can prolong cell survival in stressful conditions and is therefore implicated in cancer progression and resistance to chemotherapy. Intracellular signaling mechanisms that regulate TNF-induced autophagy are unclear. The ribosomal S6 kinase (S6K) pathway has been linked to autophagy induced by starvation. S6K is a serine/threonine kinase that regulates cell cycle progression. MCF-7 cells carry an amplification of the S6KI gene and S6K is constitutively activated in some cancer cells. The mitogen-activated protein kinase (MAPK) pathway regulates cell survival and has also been implicated in autophagy. Furthermore, there may be a cross-talk between S6K and MAPK. Therefore, the objective of the present study was to delineate the role of S6K and MAPK in TNF-induced autophagy in human breast cancer MCF-7 cells.

Methods: Western blotting was used to determine PARP cleavage (a measure of apoptosis) and conversion of the autophagy marker protein LC3-I to LC3-II). To examine the association of LC3-II to autophagosomes, MCF-7 cells were stably transfected with vectors expressing EGFP alone or EGFP-tagged human LC3. S6K was depleted by transfecting MCF-7 cells with siRNA.

Results: TNF stimulated a time-dependent phosphorylation of S6K and MAPK and induced autophagy in MCF-7 cells. Inhibition of MAPK by U0126 or PD98059 abolished TNF-induced autophagy as evidenced by a decrease in both LC3-I conversion and in the number of cells displaying LC3-GFP associated with autophagosomes. In contrast, the MAPK inhibitors enhanced TNF-induced apoptosis. Inhibition of S6K activity using rapamycin or depleting S6K using siRNA decreased TNF-induced autophagy but did not affect TNF-stimulated apoptosis. Interestingly, inhibition of MAPK also attenuated TNF-stimulated S6K phosphorylation. This suggests that S6K may be a downstream target of MAPK in the regulation of TNF-induced autophagy in MCF-7 cells.

Conclusions: These preliminary data suggest that both p70S6K and MAPK regulate TNF-induced autophagy in MCF-7 cells. Suppressing autophagy by inhibiting MAPK, but not S6K, was accompanied by an increase in apoptosis. Thus, delineating relative contribution of signaling pathways to autophagy or apoptosis is important to design effective anti-cancer therapies.

Sponsor: *NCI/NIH grant CA71727*

210 *(Poster)*

Author: Ritu Pabla

Presenter: Ritu Pabla

Department: Cell Biology and Genetics

Classification: GSBS Student

Ritu Pabla and Wolfram Siede Department of Cell biology and Genetics University of North Texas Health Science Center Fort worth,TX, 76107

UBIQUITINATION OF DNA POLYMERASE ETA: ESSENTIAL FOR SURVIVAL IN S.CEREVISIAE

Purpose: To investigate regulation of RAD30 encoded DNA Polymerase eta(Pol?) after UV induced DNA damage in S.cerevisiae.

Methods: mRNA levels of RAD30 were determined by Northern blot analysis. Myc-tagged Rad30p levels were determined by Western blot analysis. Cycloheximide was used to inhibit de novo protein synthesis.Alpha factor was used to synchronize cells.Immuneprecipitation was accompalished with anti-Myc mouse monoclonal antibody bound to sepharose beads. Ub-agarose was used to pull down (possibly modified)form of Pol?.

Results: : mRNA levels of RAD30 encoded Pol? are upregulated after UV induced DNA damage. This increase in message is not reflected at protein level. There is a constitutively high expression of Pol? /Rad30p which does not change after DNA damage. There appears to be no change in the stability of Rad30p after DNA damage.Interestingly,we detect a S-phase specific modification of Rad30p irrespective of DNA damage. A dominant mutant harbouring a point mutation in UBZ (Ubiquitin binding Zinc-finger) domain of Pol? shows significantly reduced survival after UV induced DNA damage.

Conclusions: It is tempting to speculate that posttranslational modification of Pol? in □S phase may regulate its compartmentalization in or out of replication factories. In UBZ* mutant strain, there are two possibilities for reduced survival after DNA damage: its inability to undergo modification during □S phase of the cell-cycle or reduced/no interaction with ubiquitinated PCNA after DNA damage.

Sponsor: *N/A*

211 *(Poster)*

Author: Krithi Rao

Presenter: Krithi Rao

Department: Molecular Biology and Immunology

Classification: GSBS Student

Krithi Rao, Stephen Mathew and Porunelloor Mathew Dept. of Molecular Biology & Immunology, University of North Texas Health Science Center, Fort Worth, TX 76107

FUNCTIONAL ROLE OF HUMAN 2B4 ISOFORMS 2B4-A AND 2B4-B

Purpose: Natural Killer cells (NK cells) are a type of cytolytic lymphocyte that recognize and kill virally infected cells, parasites and certain tumor cells. The mechanisms that control NK cell activation and cytotoxicity are believed to be determined by a delicate balance between stimulatory and inhibitory signals received from surface receptors. 2B4 (CD244), a member of the CD2 subset of the Ig superfamily receptors, is one such receptor expressed on all human NK cells, a subpopulation of T cells, basophils and monocytes. Two isoforms of the 2B4 receptor have been found to exist, 2B4-A and 2B4-B, and are both expressed on NK cells. The purpose of this study was to clone the extracellular domain of h2B4-A and h2B4-B in pCD5Ineg1 vector for the production of recombinant fusion proteins for determining their functional role in NK cells.

Methods: Human 2B4-A was PCR amplified using sequence specific primers. The PCR product was ligated into a pGEM-T easy vector followed by transformation into DH5a Escherichia coli cells. Plasmid DNA was isolated and digested with NheI and Bam HI. The insert was gel purified and then ligated into a pCD5Ineg1 mammalian expression vector which has the human IgG-Fc region. The ligated product was transformed into MC1061 cells followed by mini prep plasmid isolation. The plasmid was digested with NheI and Bam HI to confirm the insert and the clone was sequenced.

Results: The extracellular domain of human 2B4-A was cloned and sequenced in pCD5Lneg mammalian expression vector which would be transfected into B16F10 mouse melanoma cells to produce a recombinant 2B4-IgG fusion protein.

Conclusions: The 2B4 recombinant fusion protein obtained from this study will help us to investigate the functional role of these two isoforms in NK cell activation.

Sponsor: *N/A*

212 *(Poster)*

Author: Shalini Persaud

Presenter: Shalini Persaud

Department: Molecular Biology and Immunology

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

REGULATION OF CELL DEATH SIGNALING BY NOVEL PKC-ETA

Purpose: PKCeta is a member of the novel group of protein kinase C (PKCs), which plays a major role in cell proliferation and differentiation, especially in epithelial cells. In many cancers, such as breast tumors, PKCeta levels are upregulated Our laboratory has shown that PKCeta functions as an anti-apoptotic protein because overexpression of PKCeta prevents cell death by apoptosis when induced by tumor necrosis factor ? (TNF). Therefore, targeting PKCeta downregulation in breast cancer is an important strategy in cancer therapy. Phorbol esters are compounds which activate and subsequently downregulate many PKC isozymes. However, prolonged cellular exposure to phorbol esters which activate PKCs was shown to upregulate PKCeta expression, and PKC inhibitors led to the downregulation of PKCeta, suggesting that PKCeta is uniquely regulated. The tumor promoting ability of phorbol esters may be associated with the induction/activation of PKCeta. Since PKCs are activated by phosphorylation at conserved residues, we hypothesize that the stability of PKCeta is regulated by phosphorylation. The overall objective of this study is to investigate the regulation of PKCeta and the involvement in cell death.

Methods: A molecular approach was utilized using site-directed mutagenesis to mutate three conserved PKCeta phosphorylation sites to a nonphosphorylatable form by substituting the Ser/Thr residues with alanine or negatively-charged glutamate to mimic the phosphorylated state. PKCeta constructs were tagged with EGFP and will used in the future for localization studies. The effect of PKC activators and inhibitors on PKCeta content will be determined by Western blot analysis using phospho-specific PKCeta antibodies and antibodies against EGFP. We overexpressed PKCeta in two breast cancer cell lines and tested the effect of the overexpression on cell death induced by Tumor Necrosis Factor Apoptosis-Inducing Ligand (TRAIL).

Results: Preliminary results indicate that the triple mutations did not affect PKCeta stability in response to PKC activators and inhibitors. Breast cancer cells (1806) overexpressing PKCeta were resistant to cell death induced by TRAIL as indicated with decreased PARP and caspase 7 cleavage. MCF7 breast cancer cells depleted of PKCeta by siRNA showed an apoptotic morphology suggesting PKCeta is important for cell survival.

Conclusions: Overall, PKCeta plays an antiapoptotic role in breast cancer cells.

Sponsor: *NIH/NCI CA71727 and NSF Project SCORE*

213 *(Poster)*

Author: Prauttus Samuel

Presenter: Prauttus Samuel

Department: School of Public Health

Classification: SPH Student

Prauttus Samuel SPH Student Forth Worth, TX 76107

SOCIAL AND DEMOGRAPHIC DESCRIPTORS OF MEN WHO PARTICIPATE IN COMMUNITY BASED PROSTATE SCREENING

Purpose: While there has been development in research, and health promotion targeting African American men, disparities still exist. Previous research has proposed factors ranging from genetics, lack of knowledge, psychosocial, under use of early detection technology and inadequate health care access. This report will address the research questions; what are the social, demographic and clinical characteristics associated with men who participate in a Dallas County hospital sponsored community-based prostate screening problem. Secondly, what social, behavioral and clinical characteristics are associated with reported risk factors.

Methods: Existing data from a prostate screening and awareness program in Dallas County, Dallas, Texas from August 1, 2000 to July 31, 2004 was analyzed to determine what social and demographic descriptors are associated with men who participate in community-based prostate screening. The data set was stratified by African American, Caucasian, Asian and Hispanic men who reside in Dallas-Forth Worth Metroplex area. Descriptive statistics was utilized to examine the demographic and risk factors and familial history reported by each stratified group. Frequencies, chi square, binary analysis , and odds ratio analysis were used to determine associations of demographic variables, risk factors variables and screening participation for each subgroup with African American males being the group of interest

Results: Data shows race, education and employment to be statistically significant (p=

Conclusions: Results of study are similar to other research findings. African American men are more likely to consume a high fat diet, not exercise, than Caucasians. Yet, African American men are less likely to smoke as compared to Hispanics. However, men in moderate income level (>$35K) are more likely to have elevated PSA and glucose levels. Such findings may provide regional and local benefit to continuing health promotional efforts.

Sponsor: *N/A*

300 *(Poster)*

Author: Janneth Guarin

Presenter: Janneth Guarin

Department: Family Medicine

Classification: Faculty

Janneth Guarin, UNTHSC Dept of Family Medicine, Fort Worth, TX 76107 Roberto Cardarelli, DO, MPH, UNTHSC Dept of Family Medicine, Fort Worth, TX 76107 Kathryn Cardarelli, PhD, UNTHSC, School of Public Health, Dept of Epidemiology, Fort Worth, TX 76107

THE RELATIONSHIP BETWEEN SOCIAL SUPPORT, SENSE OF CONTROL, AND CORONARY CALCIUM SCORES

Purpose: The purpose of this study is to determine if low social support and poor sense of control are associated with an objective measure of atherosclerotic disease using an Electron-Beam computed tomography (EBCT) to calculate a calcium score.

Methods: This was a cross-sectional study that used subjects enrolled in the Traditional and Emerging Risk Factors for Individuals Developing Diabetes, Metabolic Syndrome, and Coronary Heart Disease. Eighty two potential participants were approached and 80 agreed to participate in our study. A validated questionnaire was used to assess social support.6 A personal control scale created by Mirowsky & Ross was used to measure sense of control. The sense of control scale was calculated as a mean score of the responses to eight questions. The score directly correlated with the level of sense of control.7 Information on age, gender, and race/ethnicity was also collected. Socioeconomic status was measured using income and education levels. Clinical and lifestyle factors were collected to control for potential confounders. EBCT reports were subsequently obtained and all data was managed using Microsoft Access. Chi Square and t-tests were used to assess differences among groups. Multivariate logistic regression was performed to control for confounding variables and to assess for associations between the dependent and independent variables. All analyses were tested at a level significance of 0.05 using SPSS software.

Results: Multivariate analysis controlling for age, race, stress level general health and medical history did not reveal a significant association between Social Support or Sense of Control and abnormal calcium score.

Conclusions: Poor social support and a lack of sense of control was not associated with an abnormal calcium score. This finding may be due to an inadequate number of participants in our sample which resulted in low statistical Power.

Sponsor: *N/A*

301 *(Poster)*

Author: Roberto Cardarelli

Presenter: Roberto Cardarelli

Department: Family Medicine

Classification: Faculty

Roberto Cardarelli, DO, MPH, UNTHSC, TCOM, Dept of Family Medicine, Fort Worth, TX 76107 Kathryn Cardarelli, PhD, UNTHSC, SPH, Dept of Epidemiology, Fort Worth, TX 76107 Joan Carroll, PhD, UNTHSC, GSBS, Dept of Intergrative Physiology, Fort Worth, TX 76107 Ana Chiapa, MS, UNTHSC, TCOM, Dept of Family Medicine, Fort Worth, TX 76107

THE NORTH TEXAS HEALTHY HEART STUDY

Purpose: Aim: To assess whether experiences of perceived discrimination, unfair treatment, social support, or a sense of personal control are associated with cardiovascular serum markers and calcium scores. Hypotheses: 1. Experiences of perceived discrimination or unfair treatment are associated with elevated levels of cardiovascular serum markers and an elevated calcium score. 2. High social support is associated with low levels of cardiovascular serum markers and a low calcium score. 3. Strong sense of control is associated with low levels of cardiovascular serum markers and a low calcium score.

Methods: A cross-sectional study that will utilize validated instruments to assess various life stressors and their relationship to the development of heart disease. All participants will under waist/ hip circumferences, multi-slice computed tomography to assess calcium scores and visceral fat, and standard and emerging serum cardiovascular profiles. Participants will be followed for three years.

Results: Bivariate analyses will be performed to assess for differences between the dependent and independent variables at a level of significance of <0.05.(43)

Conclusions: Findings from this study will allow a better understanding of how stressors contribute to the development and/or exacerbation of heart disease.

Sponsor: *NIH, EXPORT Center*

302 *(Poster)*

Author: Sushmita Purkayastha

Presenter: Sushmita Purkayastha

Department: Integrative Physiology

Classification: Staff

Sushmita Purkayastha, Shigehiko Ogoh, David M. Keller, and Peter B. Raven, FACSM UNTHSC, Fort Woth, Tx, 76107

MODULATION OF VASCULAR IMPEDANCE IN THE FEMORAL ARTERY OF HUMANS WITH NECK PRESSURE AND NECK SUCTION WITH KATP CHANNEL BLOCKADE

Purpose: This study was designed to evaluate blood flow impedance properties of healthy human subjects at rest via augmentation and withdrawal of sympathetic nerve activity using neck pressure (NP) and neck suction (NS), respectively, during resting conditions with and without oral glyburide blockade of KATP channels.

Methods: Four healthy subjects (age, 27 ± 1.6 years; height, 176.7 ± 2.1 cm; weight, 76.32 ± 5.13 kg; mean ± SEM) participated in the present study. Acute changes in carotid sinus transmural pressure were evoked using 5 s pulses of NP at +40 Torr and NS at -40 Torr with and without oral ingestion of 5 mg glyburide (KATP channel inhibitor). Arterial blood pressure was obtained from a teflon catheter placed in the femoral artery and femoral artery blood flow was determined using pulsed Doppler ultrasound velocimetry. All measurements were recorded throughout the study. Vascular impedance was then determined from the Fourier analysis of the appropriate blood pressure and flow waves within the femoral artery.

Results: : A significant increase in impedance at zero frequency (0 Hz) was observed with the application of NP in both the control (+0.45 ± 0.2 mmHg/ml/min, P=0.034) and glyburide (+0.54 ± 0.2 mmHg/ml/min, P=0.038) conditions. However there were no significant differences across the impedance frequency spectrum identified between KATP channel blockade and NS conditions.

Conclusions: Carotid baroreflex mediated sympathetic activation increased vascular impedance at 0 Hz intensity with and without KATP channel blockade. The changes in impedance were consistent with conductance changes calculated from the mean arterial pressure and mean femoral blood flow.

Sponsor: *N/A*

303 *(Poster)*

Author: Myoung-gwi Ryou

Presenter: Myoung-gwi Ryou

Department: Integrative Physiology

Classification: GSBS Student

Myoung-gwi Ryou1, Pu Zong1, Jie Sun1, Eugenia B. Manuhkina2, H. Fred Downey1, Robert T. Mallet1 1Integrative Physiology, University of North Texas Health Science Center at Fort Worth, 3500 Camp Bowie Blvd, Fort Worth, TX, 76107, USA: 2 Regulatory Mechanisms of Adaptation, Institute of General Pathology and Pathophysiology, 8 Baltijskaya Street, Moscow, 125315, Russian Federation

INTERMITTENT HYPOXIC CONDITIONING SUPPRESS CYTOTOXIC NITRIC OXIDE PRODUCTION UPON MYOCARDIAL REPERFUSION

Purpose: Background: Physiological concentrations of nitric oxide (NO) are generally beneficial, but excessive NO formation can injure ischemic myocardium by producing cytotoxic peroxynitrite upon reperfusion. Recently we reported that intermittent hypoxia conditioning (IHC) produced remarkable cardioprotection against infarction and lethal arrhythmias in a canine model of coronary occlusion-reperfusion. Hypothesis: IHC suppresses myocardial formation of NO by the endothelial NO synthase isoform (eNOS) upon coronary artery reperfusion.

Methods: Methods: Mongrel dogs were conditioned by a 20 d program of intermittent normobaric hypoxia (FIO2 9.5-10%; 5-10 min/cycle, 5-8 cycles/d with intervening 4 min normoxia), and compared with non-hypoxic control dogs. One day later, myocardium was sampled for measurement of left ventricular NOS activity (colorimetric assay) and eNOS content (Western blot). In other anesthetized dogs, myocardial nitrite release, an index of NO formation, was measured at baseline and during reperfusion following 1 h occlusion of the left anterior descending coronary artery (LAD).

Results: Results: IHC lowered left ventricular NOS activity 53%, from 92 ± 8 to 43 ± 6 mU/g protein (P

Conclusions: Conclusion: IHC suppressed myocardial NOS activity and eNOS content. Reperfusion NO release was decreased in IHC myocardium without compromising reactive hyperemia.

Sponsor: *NIH support: HL-64785 and HL-71684*

304 *(Poster)*

Author: Robert Mallet

Presenter: Robert Mallet

Department: Integrative Physiology

Classification: Faculty

Robert T. Mallet, Ph.D.; Myoung-Gwi Ryou, Ph.D.; Arthur G. Williams, Jr.; Linda L. Howard; H. Fred Downey, Ph.D. Department of Integrative Physiology University of North Texas Health Science Center

BETA-ADRENERGIC SIGNALING AND HYPOXIA-INDUCED CARDIOPROTECTION

Purpose: Background: Intermittent, normobaric hypoxia conditioning (IHC) prevents myocardial ischemic injury, but the mechanisms of this robust cardioprotection are unknown. Sympathetic activation of the heart during hypoxia may evoke mechanisms which are cardioprotective during subsequent ischemia-reperfusion. Objective: To determine whether ß1-adrenergic activity during hypoxia mobilizes mechanisms which protect myocardium during subsequent ischemia and reperfusion.

Methods: Methods: Dogs were conditioned by a 20 day program of 5-8 daily, 5-10 min cycles of hypoxia (FIO2 9.5-10%), or sham conditioned with normoxic air. To interrogate the role of ß1-adrenoceptor activation in IHC-induced cardioprotection, the ß1-adrenoceptor antagonist metoprolol was administered throughout the IHC program. 24 h after the last IHC session, the left anterior descending coronary artery was occluded for 60 min, then reperfused for 5 h, while lead II electrocardiogram was monitored. Area at risk (AAR) was demarcated by Evans blue dye, and infarct size (IS) was determined by 2,3,5-triphenyl tetrazolium staining.

Results: Results: IHC lowered IS/AAR from 38 +/- 6% in sham-conditioned dogs to 1.1 +/- 0.3% ($P < 0.001$), and eliminated ventricular tachycardia (VT) and fibrillation (VF) that occurred in every sham-conditioned dog. Metoprolol blunted IHC-evoked cardioprotection: IS/AAR was 27 +/- 3%, and VT and/or VF occurred in 5 of 6 dogs. Metoprolol did not exacerbate ischemic injury in sham-conditioned dogs (IS/AAR 38 +/- 2%). Neither IHC nor metoprolol affected hematocrit or collateral blood flow to the ischemic region. A single IHC session failed to protect ischemic myocardium (IS/AAR 36 +/- 8%), and protection was incomplete after 10 days of IHC (IS/AAR 13 +/- 5%), suggesting that the protection required de novo protein synthesis.

Conclusions: Conclusion: Episodic ß1-adrenergic activation of intermittently hypoxic myocardium evokes progressive development of powerful resistance to myocardial ischemia.

Sponsor: *NHLBI*

305 *(Poster)*

Author: R Brothers

Presenter: R Brothers

Department: Integrative Physiology

Classification: GSBS Student

R. Matthew Brothers1, Mads L. Haslund2,3, D. Walter Wray1, Michael L. Smith1, Peter B. Raven1, Mikael Sander2,3. 1Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, Texas 76107, U.S.A., 2Copenhagen Muscle Research Centre, National Hospital, Copenhagen, DK., 3The Flight Medicine Unit, Department of Cardiology, National Hospital, Copenhagen, DK.

EXERCISE INDUCED INHIBITION OF AT1 AND ALPHA-1 MEDIATED VASOCONSTRICTION

Purpose: Metabolic inhibition of adrenergic vasoconstriction in exercising muscles is evident in both animals and humans. However, the underlying mechanisms are still incompletely understood. We aimed to test whether metabolic inhibition is specific to adrenoreceptor-mediated vasoconstriction.

Methods: We compared the thigh vasoconstrictor responses to wide dose-ranges of intra-femoral-artery phenylephrine (PE) and angiotensin-II (AngII) in healthy humans (n=11) during rest and dynamic knee-extensor exercise at 7 and 27W. Ultrasound Doppler and thermodilution provided direct measurements of femoral blood flow (FBF) and intraarterial pressures were used to calculate vascular conductance (FVC).

Results: PE (0.2 µg / kg) and Ang?? (4 µg / kg) produced comparable reductions in FBF and FVC at rest (-50 ± 5 and -54 ± 7 %, respectively for both variables). Despite increased dosing, PE (1.6 µg / kg) and Ang?? (32.0 µg / kg) elicited significantly smaller changes in FBF (-30 ± 3 and -28 ± 5 %) and FVC (-36 ± 6 and -40 ± 5 %) during 7W exercise. PE (1.6 µg / kg) and Ang?? (32.0 µg / kg) resulted in even smaller reductions in FBF (-16 ± 2 and -13 ± 5 %) and FVC (-25 ± 6 and -27 ± 6 %) during 27W exercise.

Conclusions: Collectively, these data demonstrate that vasoconstriction following administration of Ang?? and PE is inhibited to a similar degree in the human thigh during mild-moderate exercise. These results suggest that exercise either produces a non-specific blunting of vasoconstrictor effects, or perhaps interferes with a signal-transduction pathway common to both alpha1-adrenergic- (PE-activated) and Ang??-receptors.

Sponsor: *N/A*

306 *(Poster)*

Author: Megan Hawkins

Presenter: Megan Hawkins

Department: Integrative Physiology

Classification: GSBS Student

Megan N. Hawkins1, Peter B. Raven1, Benjamin D. Levine2 1Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, Texas 76107, U.S.A; and 2Institute of Exercise and Environmental Medicine, Presbyterian Hospital of Dallas and University of Texas Southwestern Medical Center, Dallas, Texas 75235, U.S.A.

MAXIMAL OXYGEN UPTAKE AS A PARAMETRIC MEASURE OF CARDIOPULMONARY CAPACITY

Purpose: The purpose of this investigation is to retrospectively reanalyze 156 VO2max tests and their subsequent supramaximal exercise tests to verify that VO2 does indeed attain a maximal value which subsequently plateaus or decreases with further increases in exercise intensity.

Methods: 52 subjects performed three separate incremental VO2max tests, while measuring VO2max using the Douglas bag method. On the day immediately following each VO2max test the subjects returned for a supramaximal test during which they performed a run at 8% grade with the speed chosen individually to exhaust the subject between 2 and 4 min, while VO2 at supramaximal exercise intensities was measured.

Results: Mean incremental VO2max and supramaximal VO2max for all 156 tests were compared, and there was no significant difference ($p = 0.77$).

Conclusions: These data substantiate the evidence provided from previous experiments that there is indeed a peak and subsequent plateau in VO2 during maximal exercise intensity. Therefore, VO2max is a valid index outlining the limits of the cardiopulmonary systems ability to transport oxygen from the air to the tissues.

Sponsor: *N/A*

307 *(Oral)*

Author: Arti Sharma

Presenter: Arti Sharma

Department: Integrative Physiology

Classification: GSBS Student

Shaohua Yang, Mathew A Barlow, Arthur G. Williams, Linda Howard, Jie Sun, Robert T. Mallet University of North Texas, Health Science Center, Fort Worth, Texas-76107

PYRUVATE THERAPY DURING CARDIOPULMONARY RESUSCITATION PROTECTS POST-ARREST NEUROLOGICAL FUNCTION

Purpose: Cardiac arrest inflicts ischemic injury to the brain that contributes to pos-arrest morbidity and mortality. Intravenous administration of pyruvate, a natural antioxidant and energy substrate in the myocardium and brain, improves left ventricular mechanical recovery and electrocardiographic function following cardiac arrest-resuscitation in dogs. Pyruvate prevents energy depletion in porcine brain during hemorrhagic shock, but its ability to protect brain following cardiac arrest-resuscitation has not been determined.

Methods: Intravenous pyruvate therapy during cardiopulmonary resuscitation prevents neurological impairment after cardiac arrest. Methods: Mongrel dogs were subjected to 5 min fibrillation cardiac arrest, then 5 min open-chest cardiac massage (58 +/- 2 compressions/min; arterial pressure 38 +/- 5 mm Hg; ventilations 12/min) before defibrillation with epicardial countershocks. Pyruvate (n=8) or NaCl (n=7) vehicle were infused i.v. (0.125 mmol/kg/min) during cardiac massage and 55 min post-defibrillation. Sham controls (n=6) underwent identical surgery without arrest. Neurological deficit scoring (NDS) and cardiac ultrasonography were performed pre-arrest and at 60 h and 72 h recovery respectively.

Results: Data are mean +/- S.E.M., presented as pre/post arrest; *P

Conclusions: Intravenous pyruvate therapy during resuscitation enhanced neurological recovery from cardiac arrest.

Sponsor: *N/A*

308 *(Poster)*

Author: Christina Pacchia

Presenter: Christina Pacchia

Department: Integrative Physiology

Classification: GSBS Student

Christina Pacchia, M.S., UNTHSC, Fort Worth, TX, 76107 MIchael Smith, Ph.D., UNTHSC, Fort Worth, TX, 76107 M. Hamdan, M.D., UT Southwestern Medical Center, Dallas, TX, 75390 S. Wasmund, Ph.D., UT Southwestern Medical Center, Dallas, TX, 75390

SYMPATHOEXCITATION DURING ATRIAL FIBRILLATION: ROLE OF RHYTHM IRREGULARITY

Purpose: The purpose of this study was to test the hypotheses that 1) atrial fibrillation is associated with increased sympathetic nerve activity and 2) the increase in sympathetic nerve activity is in part due to the irregular ventricular response during AF.

Methods: Fourteen patients (age 62 ± 8 yrs) from the VA Medical Center in Dallas, TX were recruited to the cardiac electrophysiology lab. All patients were being treated for supraventricular or atrial tachycardia and had no history of atrial fibrillation. Atrial fibrillation was induced using bursts of rapid atrial pacing with or without atrial premature beats. A pacing electrode was placed in the right atrium to control heart rate and rhythm. Arterial pressure, central venous pressure, muscle sympathetic nerve activity (microneurography), and heart rate and rhythm (electrocardiogram) were measured directly and recorded under 4 conditions. Each condition lasted 3 minutes and included normal sinus rhythm (NSR), induced atrial fibrillation (AF), atrial pacing at the AF heart rate and fixed rhythm (RAR), and atrial pacing at the AF heart rate and AF rhythm (RAI). Paired t-tests were applied to determine significant differences in SNA between the conditions. Relationships between variables were also examined using Pearson's correlation coefficient to quantify associations.

Results: There was a significant increase ($p < .001$) in SNA response during the AF condition (2924 ± 284 units/min) compared to the NSR condition (1700 ± 110 units/min). In addition, there was a significant increase ($p = .014$) in SNA during the RAI condition (3175 ± 448 units/min) compared to the RAR condition (1881 ± 156 units/min). There were no significant differences in SNA response between the AF and RAI conditions and the NSR and RAR conditions ($p > .35$ and $p > .73$, respectively). The percent change in SNA was significantly correlated with the standard deviation in R-R interval (SDRRI) during the AF condition ($r = .81$, $P < .001$). In addition, there was a significant correlation between ejection fraction and the NSR-AF difference in SNA response ($p < .001$, $r = .85$).

Conclusions: We conclude that atrial fibrillation is associated with an increase in SNA. This increase is mediated by the hemodynamic response caused by rhythm irregularity and is affected in part by the ventricular rate. This may explain, in part, the poor prognosis of heart failure patients with AF.

Sponsor: *N/A*

309 *(Poster)*

Author: Ellen Dawson

Presenter: Ellen Dawson

Department: Integrative Physiology

Classification: Postdoctoral Fellow/Resident

Ellen A. Dawson (1,2), Stefan P. Mortensen (1), Rasmus Damsgaard (1), Niels Secher (1), José González-Alonso (1). (1) Copenhagen Muscle Research Center, Rigshospitalet, University of Copenhagen, (2) Dept. of Integrative Physiology, University of North Texas Health Science Center, TX 76107, USA

CENTRAL HEMODYNAMICS WITH ADENOSINE TRIPHOSPHATE AND KICKING EXERCISE MEDIATED INCREASES IN LEG BLOOD FLOW

Purpose: Graded intrafemoral artery infusion of ATP produces increases in leg blood flow (LBF) that are similar to those induced by incremental leg-kicking and cycling exercise. Whether ATP infusion mimics the exercise central hemodynamics, despite the absence of the muscle pump not increasing venous return has not been investigated. The aim of the study was to determine whether the central hemodynamic changes induced by intrafemoral artery ATP infusion were similar to those produced by dynamic one-legged kicking exercise.

Methods: 7 healthy volunteer men performed three-minute bouts of one-legged kicking exercise at 25%, 50% and 75% of their peak power. ATP was infused into their femoral artery at 1, 4 and 16 µmol/min, in doses chosen to match the LBF response to the progressive increase in exercise intensity while seated upright. Mean arterial pressure (MAP), central venous pressure (CVP), heart rate (HR), stroke volume (SV) and cardiac output (CO) were obtained at rest and during each stage of exercise and ATP infusion.

Results: There was no difference in the LBF response to leg kicking and its matched ATP infusion increases. There was no significant difference in CVP and CO between ATP infusion and leg kicking exercise (CO increases from rest (P0.05, and was increased 38% by KE, $P<0.05$.

Conclusions: These results indicate that intrafemoral artery ATP infusion can match the CO response to one-legged kicking exercise, by mainly elevating SV. This suggests that the activation of the muscle pump is not essential to increase venous return and CO during small muscle mass exercise in humans.

Sponsor: *Supported by the Novo Nordisk foundation*

310 *(Poster)*

Author: Tushar Thakre
Presenter: Tushar Thakre
Department: Integrative Physiology
Classification: GSBS Student

1. Tushar P. Thakre, Integrative Physiology, UNTHSC, Fort Worth, TX-76107 2. Jeffrey C. Siu, Integrative Physiology, UNTHSC, Fort Worth, TX-76107 3. Joseph Raven, Integrative Physiology, UNTHSC, Fort Worth, TX-76107 Suzanne Shaffer, Cell Biology and Genetics, UNTHSC, Fort Worth, TX-76107 4. Margaret Garner, Cell Biology and Genetics, UNTHSC, Fort Worth, TX-76107 5. Michael L. Smith, Integrative Physiology, UNTHSC, Fort Worth, TX-76107

EVIDENCE OF ABNORMAL VASOPRESSOR RESPONSES IN INDIVIDUALS WITH POLYMORPHISMS OF THE ATP1A2 GENE

Purpose: Hypertension is a major public health problem in the US affecting more than 65 million people. Racial differences in prevalence of hypertension have been described, with the disease being more common among African Americans than among Caucasians. A polymorphism at the 3-end of the ATP1A2 gene has been found to be more common in hypertensives as well as in African Americans. This study addressed the hypothesis that the individuals carrying the polymorphism would have exaggerated cardiovascular responses to pressor stimuli as compared to those not carrying the mutation.

Methods: 33 normotensive human volunteers (20 Caucasians, 13 African Americans; 21 females, 12 males) aged 18-51 years were recruited for genotyping. Blood samples were collected from the volunteers and DNA was isolated from white cells. The DNA was subjected to Bgl II restriction enzyme digestion and the fragments were identified using specific radiolabeled probes. After genotyping, changes in blood pressure and muscle sympathetic nerve activity in response to pressor stimuli were studied in 17 individuals (10 normal variants and 7 with the polymorphism). The pressor stimuli used were cold water (at 2, 10, and 18 degrees C) and hypoxic apnea (at 12, 16, and 21% oxygen concentrations in the inhaled air).

Results: Of the 13 African Americans, 4 had the normal variant, 8 were heterozygous for the polymorphism and 1 was homozygous for the polymorphism. Of the 20 Caucasians, 14 had the normal variant, 5 were heterozygous and 1 was homozygous for the polymorphism. Muscle sympathetic nerve activity responses to both hypoxic apnea and cold water were not different among people with and without the polymorphism. Blood pressure responses were similar in the two groups in response to hypoxic apnea and cold water at 2 degree C. However, changes in both diastolic and systolic blood pressure were significantly greater in individuals carrying the polymorphism than in individuals without the polymorphism with the 10 degree C cold water stimulus ($p < 0.037$).

Conclusions: The polymorphism is more common in African Americans as compared to Caucasian Americans. Blood pressure changes in response to a 10 degree C cold water challenge are greater in individuals with the polymorphism as compared to individuals without the polymorphism. This suggests that the polymorphism is associated with exaggerated cardiovascular responses to pressor stimuli and could be responsible for conferring a greater susceptibility to hypertension upon its carrier.

Sponsor: *N/A*

311 *(Poster)*

Author: Joseph Raven
Presenter: Joseph Raven
Department: Integrative Physiology
Classification: GSBS Student

Raven JS, Jeffrey Siu, Ronak Patel, Michael L. Smith UNTHSC Fort Worth, Tx. 76107

SHORT-TERM BARORECEPTOR MODULATION OF PAIN-INDUCED SYMPATHETIC ACTIVATION

Purpose: Cold elicits a pain stimulus which results in a sympathoexcitation-mediated (SE) increase in blood pressure (BP) known as a Cold Pressor Stimulus (CP). This laboratory uses CP and other stimuli to assess BP control as a means to discern anomalies of neural and end-organ control mechanisms among subjects. Yet, the manner in which arterial baroreceptors modulate the SE during a pain stimulus remains ill-defined. This study attempts to elucidate the regulation of SNA during opposing and buttressing stimuli through the duration of maximal CP stimulation; and to investigate the degree of modulation occurring within the stimulus and rest periods. We hypothesized that intermittent baroreceptor unloding using Neck Pressure (NP) would enhance firing rate but not affect the total number of bursts over time. Also, we hypothesized that intermittent baroreceptor loading using Neck Suction (NS) stimuli would reduce firing rate but not affect the total number of bursts over time.

Methods: We recorded Sympathetic Nervous Activity (SNA) in 18 volunteers exposed to two minutes of CP; during which intermittent (5-sec intervals) suction (-40mmHg) or pressure (40mmHg) stimulation to the neck at the level of the carotid sinus was administered. SNA, arterial pressure, and heart rate were measured continuously at baseline CP, for two minutes of intermittent neck pressure stimuli, and for five minutes of recovery from CP. Statistical analysis of the main effect differences was achieved through use of one-way ANOVA, with post hoc analyses to distinguish specific differences.

Results: Consistent with our first hypothesis, the total of SNA bursts were not significantly changed in either the suction or pressure groups compared to baseline ($p > 0.8$). Neck pressure stimuli (baroreceptor unloading) produced a transient increase in SNA ($p < 0.02$) which was compensated for during the off-stimulus period. As noted above, the net increase in SNA during CP with or without the NP was not different. In contrast, NS stimuli did produce a subtle, but insignificant change in SNA ($p > 0.1$).

Conclusions: These data support the hypothesis that short-term exposure to intermittent baroreceptor stimuli modulates the SNA response to pain (CP). This modulation is dependent on the direction of the baroreceptor pressure stimulus (increased versus decreased) suggesting that the resetting of the baroreceptors may be shifted to the curvilinear portion of the hypertension region of the stimulus-response function curve.

Sponsor: *N/A*

312 *(Poster)*

Author: Nichole Miller

Presenter: Nichole Miller

Department: Integrative Physiology

Classification: GSBS Student

Nichole Miller, Patrick Chanthavong, Dhanashri Kohok, Frederic Schaller, Nancy Tierney, and Xiangrong Shi. Departments of Integrative Physiology and Internal Medicine, UNT Health Science Center, Fort Worth, TX 76107

IS CEREBRAL HEMODYNAMIC FUNCTION IMPAIRED WITH AGING IN HUMANS?

Purpose: The question remained elusive as to whether cerebral hemodynamic regulation was impaired in elderly adults. The aim of this study was to assess the effect of age on maintaining cerebral blood flow during hypotensive challenge.

Methods: Thirteen healthy young (25.6±1.0 yr and 22.9±1.0) and 13 elderly (age and body mass index: 67.5±1.1 yr and 26.1±1.1) healthy subjects participated in the study during which the responses of heart rate (HR), mean arterial pressure (MAP, Tonometry), and middle cerebral arterial blood flow velocity (V, Transcranial Doppler Sonography) were compared after the thigh cuff deflation following 3-min supra-systolic bilateral inflation.

Results: The elderly group had lower baseline HR and V compared to the young group (elderly vs. young HR: 58±3 vs. 68±3 bpm, P

Conclusions: We concluded that dynamic response regulation of cerebral blood flow during hypotensive challenge was less efficient in the elderly, probably resulting from an age-related diminution of autonomic function. (Supported in part by NIH grant HL65613)

Sponsor: *NIH Grant HL65613*

313 *(Poster)*

Author: Walter McConathy

Presenter: Sulabha Paranjape

Department: Internal Medicine

Classification: Staff

Walter McConathy, Sulabha Paranjape, Michael Clearfield, Ben Willis, Sabitha Buttreddy, Karan Singh, and Craig Spellman. Texas College of Osteopathic Medicine and School of Public Health, University of North Texas Health Science Center, Fort Worth, Texas 76107

LOW DENSITY LIPOPROTEIN PHENOTYPE AND CORONARY CALCIUM SCORES. DREAMS 2

Purpose: An increase in plasma triglycerides and a decrease in high-density lipoprotein (HDL) are associated with the prevalence of small, dense low-density lipoprotein (LDL) particles. The present study investigated the clinical significance of LDL size as related to the accumulation of calcium in the coronary arteries as part of the DREAMS study program.

Methods: To explore the role of emerging risk factors (ERF) in CHD, we studied groups of subjects (n= 208) free of evidence of CHD who were at the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) goals (study groups: Hispanic diabetic/MS [HD], nonHispanic diabetic/MS [nonHD], and candidates for bariatric surgery [Ba] controls [C]). A fifth group with CHD was also included, acute coronary syndrome patients (ACS). ERF assessed include: apolipoproteins A-I and B; Lp(a); hsCRP; homocysteine; PAI-1; myeloperoxidase; resistin, IL-6, and leptin. LDL size was assessed by gradient gel electrophoresis with LDL characterized by relative mobility (Rf) or phenotyped as large LDL particles (LLDL), pattern A phenotype) or small, dense LDL (sLDL) particles (pattern B phenotype). Electron beam computed tomography (EBCT) for coronary calcium (Ca) quantification was used as the assessment of CHD risk and Ca scores were log transformed or grouped as categories.

Results: When comparing the subjects grouped by LDL phenotype (sLDL vs LLDL), both waist/hip circumference and BMI were significantly higher in subjects with the sLDL phenotype (p100 ($p<0.009$).

Conclusions: These findings support the relationship of small, dense LDL (sLDL) with metabolic diseases like diabetes and metabolic syndrome.The relationship of Ca scores and sLDL demonstrated an association of the LDL phenotype with CHD. These studies are consistent with a reduced LDL particle diameter being a significant predictor of CHD.

Sponsor: *CDC*

314 *(Poster)*

Author: Michael Clearfield

Presenter: Walter McConathy

Department: Internal Medicine

Classification: Staff

Michael Clearfield,Craig Spellman,Adam Smith, Ben Willis,Enisa Arslanagic,Michael Clearfield,Rubina Muzina,Mabyn Hager,Joice Carter, Sabitha Buttreddy,Sulabha Parajape,Karan Singh,and Walter McConathy Texas College of Osteopathic Medicine and School of Public Health, University of North Texas Health Science Center, Fort Worth, Texas 76107

OBESITY AND CARDIOVASCULAR RISK. DREAMS 2

Purpose: Centrally distributed visceral fat represents a major health issue. It is frequently associated with Type 2 diabetes (DM) and cardiovascular disease (CVD) and has become a major public health challenge around the world. Our objective was to assess the impact of varying degrees of obesity on parameters related to CVD.

Methods: Based on the DREAMS protocol, we compared three obese groups: subjects with metabolic syndrome (MS, n=51), Type 2 diabetics (DM, n=61) and bariatric surgery candidates without DM (BA, n=26). The three groups of subjects were free of evidence of CHD and both MS and DM were at National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) goals. In these three groups we determined the prevalence of traditional and emerging risk factors (ERF) for obese individuals. ERF assessed included: apolipoproteins B and A-I; Lp(a); hsCRP; homocysteine; PAI-1; myeloperoxidase; resistin, IL-6, and leptin. Electron beam computed tomography (EBCT) was used for coronary calcium (Ca) quantification as an assessment of CHD risk.

Results: With respect to anthropomorphic parameters, the BA group was younger than the DM and MS groups ($p < 0.02$) while Lp(a) was higher in BA (p

Conclusions: These studies demonstrate that DM with the highest Ca score had the most normal lipoprotein pattern of the 3 groups while carbohydrate metabolism was the most deranged. The variation in cytokines between these groups is consistent with the degree of variation in obesity of these 3 groups. These studies point to the need to identify new markers for CHD risk in obese subjects since individuals at risk without currently recognized risk factors still experience CHD events. Identification of these factors will serve as a basis for the application of more stringent primary prevention strategies in populations previously not considered at risk relative to their LDL-C.

Sponsor: *CDC*

315 *(Poster)*

Author: Benjamin Willis

Presenter: Benjamin Willis

Department: Internal Medicine

Classification: SPH Student

Ben Willis,Walter McConathy,Sulabha Paranjape,Michael Clearfield,Sabitha Buttreddy,Enisa Arslanagic,Fidelita Weis,Rubina Muzina,Mabyn Hager,Joice Carter, Karan Singh,and Craig Spellman, Texas College of Osteopathic Medicine and School of Public Health, University of North Texas Health Science Center, Fort Worth, Texas 76107

EMERGING RISK FACTOR (ERF) PATTERNS IN PATIENTS WITH METABOLIC SYNDROME, TYPE II DIABETES, AND CONTROLS. DREAMS 2

Purpose: Three subsets of patients identified with Diabetes Type II(DM), Metabolic Syndrome without diabetes (MS) and Control (C) were evaluated regarding emerging risk factors (ERF)in coronary heart disease(CHD). These groups were evaluated to better understand ERF pattern istinctions between diabetic patients and metabolic syndrome patients at risk.

Methods: ERF assessed include:apolipoproteins B and A-I;lipoprotein (a);hsCRP; homocysteine;PAI-1;myeloperoxidase;resistin,IL-6,TNF-alpha,and leptin. Low-density lipoprotein size was assessed by gradient gel electrophoresis with LDL characterized by relative mobility (Rf) or phenotyped as large low-density lipoprotein (LDL) particles (LLDL, pattern A phenotype) or small, dense low-density lipoprotein (sLDL) particles (pattern B phenotype).Electron beam computed tomography (EBCT) for coronary calcium (Ca)quantification was used as the assessment of CHD risk.

Results: Both the DM group and MS group differed from C in regard to standard anthropomorphic and biochemical metrics for the metabolic syndrome and a number of traditional CHD risk factors. Systolic blood pressure (SBP), BMI, waist circumference, hip circumference, insulin levels, and triglycerides were greater in both MS and DM groups compared to control ($p < 0.001$) but did not differ significantly between MS and DM. The MS group did show significantly higher diastolic blood pressure than DM ($p=0.01$). Glucose and hemoglobin A1c (HbA1c) were significantly higher in DM than MS and Control ($p < 0.001$). TNF-a was significantly lower in MS than in C ($p=0.024$), but no other group differences were significant.LDL phenotype comparisons showed significantly higher proportion of DM and MS exhibiting sLDL compared to C ($p = 0.002$) but no significant differences between MS and DM. Ca quantification showed significantly greater Ca score in DM than in C ($p=0.006$), or MS ($p=0.003$) while MS and C did not differ significantly.

Conclusions: These findings suggest that while metabolic syndrome and Type II diabetes share a number of increased traditional and ERF for CHD, the development of diabetes predicts a higher risk of CHD.Subtle differences in apolipoprotein patterns and the interaction of TNF-a in insulin resistance syndrome may help explain this risk profile.

Sponsor: *CDC*

316 *(Poster)*

Author: Leticia Gonzalez

Presenter: Letecia Gonzalez

Department: Integrative Physiology

Classification: GSBS Student

Leticia Gonzalez, Matthew Barlow, Shekhar Deo, Darice Yoshishige, Harlan Jones and James L. Caffrey. Integrative Physiology and Immunology.

PROENKEPHALIN DERIVED PEPTIDES IN CANINE NEUTROPHILS

Purpose: The current study is being conducted to evaluate the role of neutrophil-derived enkephalins in cardioprotection and reperfusion injury. Neutrophils were isolated from whole canine blood to test the hypothesis that they contain abundant supplies of enkephalin which is released during exposure to inflammatory mediators

Methods: Canine neutrophils were isolated by centrifugation on a discontinuous Ficol-Histopaque 1077/1119 gradient and quantified manually in a hemocytometer. They were incubated at 37 degrees in Hanks balanced salt solution and then separated from the media by centrifugation. They were diluted with HTAB and endogenous enzyme activity was terminated in a boiling water bath. The peptides were extracted in three sonication/freeze/thaw cycles followed by high speed centrifugation. The resulting supernatant was applied to a Biogel P10 column and eluted with an acid solution. Fractions were combined to comprise large, intermediate and small molecular weight peptides and then each was dried under vacuum. The samples were reconstituted in assay buffer and the enkephalin content of each was determined by radioimmunoassay.

Results: All three sizes were well represented in both the cellular content and in the surrounding incubation medium. Large amounts of precursor were identified and smaller somewhat amounts of fully processed enkephalin. Met-enkephalin was the predominant small peptide. MEAP was largely undetectable. Provoking the cells with an inflammatory mediator resulted in an apparent decrease in the enkephalin in the culture medium.

Conclusions: Canine neutrophils are replete with large amounts of enkephalin. We have established a working method for isolating canine neutrophils and quantifying their constituent opioids. These methods appear suitable for evaluating the interactions among neutrophils, opioids and reperfusion injury in heart.

Sponsor: *N/A*

317 *(Poster)*

Author: Dhanashri Kohok

Presenter: Dhanashri Kohok

Department: Integrative Physiology

Classification: GSBS Student

Dhanashri Kohok, Patrick Chanthavong, Nichole Miller, Frederic Schaller, Nancy Tierney, and Xiangrong Shi. Departments of Integrative Physiology and Internal Medicine, UNT Health Science Center, Fort Worth, TX 76107

HEMODYNAMIC RESPONSE TO ORTHOSTASIS IN OLDER ADULTS : GENDER DIFFERENCE

Purpose: Data are scanty with regards to the gender-related difference in arterial blood pressure (ABP) regulation of the elderly people. This study sought to compare the effect of gender on hemodynamic response to orthostatic challenge.

Methods: Eleven women (66.9±1.8 yr) and 9 men (68.3±1.7 yr) were tested by orthostatic stress simulated by graded lower-body negative pressure (LBNP, -10, -15, -20, -30, -40 and -50 Torr) during which heart rate (HR), ABP (Tonometry), stroke volume (SV) and CO (CO, Impedance Sonograph) were continuously monitored.

Results: There was no gender-related difference in baseline HR (men vs. women 60±3 vs. 68±3 bpm), SV (47.4±3.1 vs. 41.4±4.1 ml), CO (2.80±0.17 VS. 2.77±0.28 L/min), or mean ABP (93±1.8 vs. 89±3.2 mmHg). During LBNP, ABP was similarly maintained in both groups despite a significant decrease in CO, suggesting a vasoconstrictive compensation. However, decrease in CO during LBNP appeared less in men than women ($P<0.01$).

Conclusions: Decrease in CO during LBNP appeared less in men than women (P

Sponsor: *NIH Grant HL65613*

318 *(Poster)*

Author: Shigehiko Ogoh

Presenter: Quinton Barnes

Department: Integrative Physiology

Classification: GSBS Student

Shigehiko Ogoh, Quinton Barnes, Peter Raven University of North Texas Health Science Center

THE EFFECTS OF PARASYMPATHETIC DYSFUNCTION ON THE CAROTID-CARDIAC BAROREFLEX DURING HEAD-UP TILT

Purpose: We sought to determine whether parasympathetic dysfunction was an underlying etiology of postural syncope.

Methods: We evaluated the influence of the carotid-cardiac baroreflex on beat-to-beat blood pressure regulation during supine rest and 40° head-up tilt (HUT) in 9 healthy subjects with and without complete cardiac vagal blockade. The CBR responsiveness or maximal gain (Gmax) was assessed from the beat-to-beat changes in heart rate (HR) and mean arterial pressure (MAP) by neck pressure (NP) and neck suction (NS) ranging from +40 to -80 Torr, with and without glycopyrrolate(12.0±1.0 μg/kg body weight; mean±SE)

Results: In the supine position glycopyrrolate increased the HR from 54±3 to 91±3 beats/min; MAP from 76±2 to 89±2 mmHg; and cardiac output from 4.9±0.3 to 6.8±0.3 l/min (P

Conclusions: These data suggest that both at rest and during the reduced central blood volume induced HUT, carotid baroreflex control of HR occurred by the modulation of vagal activity, while the glycopyrrolate reduction of the carotid-cardiac baroreflex responsiveness had no significant effect on the control of MAP at rest or during HUT. We conclude that parasympathetic dysfunction is minimally involved in postural syncope.

Sponsor: *NIH*

319 *(Poster)*

Author: Patricia Gwirtz

Presenter: Patricia Gwirtz

Department: Internal Audits

Classification: Faculty

Patricia A. Gwirtz, Ph.D., FACC and Linda Howard University of North Texas Health Science Center Department of Integrative Physiology Fort Worth, Texas 76107

EFFECT OF CHRONIC NICOTINE EXPOSURE ON CORONARY MICROVASCULAR RESPONSIVITY

Purpose: Cigarette smoking is a major risk factor for development of coronary artery disease and hypertension. Nicotine is implicated as the chief culprit in smoking-induced cardiovascular comorbidities. The mechanisms by which nicotine impairs coronary dilation are largely unknown. Studies tested the hypotheses that chronic nicotine exposure alters coronary vasomotion via decreased elasticity, increased myogenic responsivity, and/or impaired vascular endothelial function.

Methods: Intermediate sized resistance epicardial coronary arteries (312±36 μm diameter) were harvested from control rabbits and rabbits subjected to 4 weeks of chronic nicotine exposure. Experiments were conducted using an in vitro isolated, pressurized vessel method.

Results: Coronary arteries from nicotine exposed rabbits demonstrated a significant increase in wall thickness, cross sectional area, and wall/lumen ratio. There was no change in the coronary vascular myogenic response to changes in pressure in nicotine exposed vessels. To test the whether chronic exposure to nicotine impairs vascular endothelial-mediated dilation via NO, a concentration-response to acetylcholine (ACh), 10-9 to 10-3 M, was performed. In control rabbits. The arterial dilator response to ACh was 81±4% of Dmax; ED50= 0.087 ±0.005 uM. In contrast, the arterial response to ACh was a dilation at lower doses and a constriction at higher doses in vessels from rabbits chronically exposed to nicotine, suggesting endothelial damage occurred. Exposing the vessels to the NO substrate, L-arginine did not restore the normal response to ACh, indicating that the impairment was probably not due to substrate deficiency. To test whether nicotine impairs smooth muscle relaxation to adenosine, a concentration-response to adenosine, 10-9 to 10-3 M, was performed. In control rabbits, the arterial dilator response to adenosine was 96±1% of Dmax; ED50=0.095±0.005 uM. In nicotine vessels , the arterial dilator response to adenosine was reduced. It is not know at this time if the impaired response to adenosine is due to impaired NO-mediated dilation or to impaired endothelium-independent dilation since adenosine acts via both mechanisms.

Conclusions: These data support the hypothesis that chronic nicotine exposure induces significant structural changes in coronary vasculature and impairs endothelial and perhaps smooth muscle-induced coronary dilator capacity.

Sponsor: *N/A*

320 *(Poster)*

Author: Disha Dumka

Presenter: Disha Dumka

Department: Molecular Biology and Immunology

Classification: GSBS Student

Disha Dumka, UNTHSC Julian Borejdo, UNTHSC

THE CROSS-BRIDGE KINETICS OF THE E22K MUTATION OF THE MYOSIN RLC THAT CAUSES FAMILIAL HYPERTROPHIC CARDIOMYOPATHY IN HETEROZYGOUS MOUSE MYOCARDIUM

Purpose: As a subunit of myosin, the RLC is known to stabilize the neck region of myosin head, also called the lever arm. Recent studies have revealed that the ventricular RLC is one of the sarcomeric proteins associated with familial hypertrophic cardiomyopathy (FHC). The E22K-RLC mutation has been associated with a rare variant of cardiac hypertrophy defined by mid-left ventricular obstruction due to papillary muscle hypertrophy. The three-dimensional structure of the RLC demonstrates the close proximity of E22K mutation to the phosphorylation site of the RLC (Ser-15) and the Ca2+ binding site (amino acids 37-48). Studies with transgenic mice demonstrated that the E22K-RLC mutation when over-expressed in mouse cardiac muscle, significantly increased Ca2+ sensitivity of myofibrillar ATPase activity and steady state force. In order to shed more light on the E22K-mediated abnormalities of muscle contraction we will study kinetics of the cross-bridge cycle during force generation in cardiac muscle of transgenic mice carrying the E22K mutation. The following parameters will be studied: (i) dissociation time, t1, of myosin heads from thin filaments, (ii) re-binding time, t2, of the cross-bridges to actin, and (iii) the dissociation time, t3, of ADP from the active site of myosin.

Methods: Rotations of a small number of actin and myosin molecules during transient contraction in a cardiac myofibril will be measured. The rotations will be measured by following the time course of anisotropy of emission dipoles of fluorescent dyes.

Results: t1 was statistically greater in transgenic-mutated (Tg-m) than in controls. The time of rebinding of the lever arm to thin filaments t2 was shorter in Tg-m than in non-transgenic (non-Tg) but the same as in transgenic wild type (Tg-wt). The time of ADP dissociation,t3, was the same in Tg-m and in controls. In an effort to see if bserved differences in was due to intrinsic differences in myosin, binding of Tg-m and Tg-wt myosin to fluorescently labeled actin was measured. No differences in binding were observed.

Conclusions: These results suggest that E22K mutation have no effect on mechanical properties of cross-bridges. The slight increase in t1 was probably caused by myofibrillar disarray. The decrease in t2 of Tg hearts was probably caused by replacement of the mouse RLC for the human isoform in the transgenic mice.

Sponsor: *N/A*

321 *(Poster)*

Author: Sujung Jun

Presenter: Sujung Jun

Department: Molecular Biology and Immunology

Classification: GSBS Student

Sujung Jun, Andrej Mirossay and Ladislav Dory, UNT HSC at Fort Worth, Department of Mol. Biol. & Immunol., Fort Worth TX 76107

GENERATION OF CONGENIC MICE WITH SHORT (129) OR LONG (C57) EXTRACELLULAR SUPEROXIDE DISMUTASE ALLELE ON C57 BACKGROUND.

Purpose: In a previous study, we reported a novel allele for ecSOD expressed in the 129P3/J (129) strain only. All other strains examined thus far have the normal, □long allele. The short allele is associated with a specific phenotype of increased circulating and heparin-releasable ecSOD activity and mass. We also noted that some genetically modified mice on the C57 background (e.g. the LDLR KO mice) continue to carry the 129 allele for ecSOD. This may result in serious data misinterpretation when studying diseases where reactive oxygen species and ecSOD may be involved. This observation underlines the need for extensive backcrossing of genetically modified mice. In order to examine the different properties of the two forms of ecSOD in an identical environment, we are generating, by extensive backcrossing of ecSOD heterozygous progeny to C57 females, a congenic C57 strain with the 129 (or C57) ecSOD allele (C57.129-sod3).

Methods: In order to monitor the progress of congenic generation, we genotyped heterozygous progenies (wrt ecSOD) from generation 2 to 6 by PCR, using six microsatellite polymorphism markers for the 129 and C57 strains. Each marker is amplified from genomic DNA obtained from the tail of heterozygous progeny, and separated by 12-15% PAGE. This analysis is used to estimate the extent of genomic homogeneity with C57 and the extent of remaining 129 sequences for the best choice of males for subsequent mating with C57 females.

Results: Theoretically, generation 6 of the congenic strain has a 98.44% homology with the recipient strain; the elimination of heterozygosity is retarded significantly in regions of the genome that are linked to the donor allele. In this study, we confirmed that by generation 6 mice achieved complete homozygosity with C57 for the six chosen markers including one very near (14 cM) the ecSOD locus.

Conclusions: The congenic mice, providing two very different phenotypes, should be very useful for studies investigating the role of ecSOD in disease

Sponsor: *N/A*

322 *(Poster)*

Author: Tahir Tak

Presenter: Tahir Tak

Department: Internal Medicine

Classification: Faculty

Tahir Tak MD, PhD, University of North Teexas, Fort Worth, TX Martha Lin PA, Marshfield Clinic, Marshfield, WI Zahir Rashid MD, Marshfield Clinic, Marshfield, WI

OVERALL CLINICAL OUTCOME IN ELDERLY PATIENTS UNDERGOING OFF-PUMP CORONARY ARTERY BYPASS SURGERY

Purpose: Advancement in technology and surgical techniques have resulted in increased interest in off-pump coronary artery bypass (OPCAB) procedures. We compared the preoperative risk profile and overall outcome in all patients (pts), including pts. = 70 years, undergoing OPCAB and compared it to those undergoing conventional coronary artery bypass surgery (CCAB).

Methods: Data from our prospective computerized database were analyzed retrospectively between 2001 to 2005. Chi square test was used for categorical variables to evaluate the significance of results. For continuous variables Wilcoxon Rank-sums test was performed. We looked at in-hospital mortality, postoperative stroke, myocardial infarction, acute renal failure, atrial fibrillation and postoperative bleeding requiring re-exploration

Results: 364 patients underwent OPCAB as opposed to 866 CCAB. The overall morbidity and mortality were lower in the OPCAB group. The length of hospital stay in OPCAB was 7 days versus 9 days in CCAB pts. ($p = 0.009$). The blood transfusion rate was higher in CCAB pts. compared to OPCAB ($p = 0.06$). The OPCAB pts. had a lower incidence of postoperative respiratory failure ($p = 0.002$). There were 181 elderly pts. (=70 years) in the OPCAB group compared to 383 pts. in the CCAB group. In this elderly group of pts., the hospital mortality, blood transfusion rate, postoperative respiratory failure, postoperative renal failure requiring dialysis and hospital stay, were significantly less in OPCAB group. ($p = 0.05$)

Conclusions: OPCAB is a safe technique with comparable morbility and mortality to CCAB. In our experience OPCAB shows lower postoperative complications. This improved outcome is also seen in elderly patients. Prospective randomized studies in a larger series of pts. are needed to corroborate our findings.

Sponsor: *N/A*

323 *(Poster)*

Author: Matthew Barlow

Presenter: Matthew Barlow

Department: Integrative Physiology

Classification: GSBS Student

Matthew A. Barlow, Shekhar Deo, and James L. Caffrey. Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, TX 76107

ENKEPHALIN MODULATION OF HIND LIMB BLOOD CONDUCTION

Purpose: Arteriosclerosis obstructs blood flow especially in the lower extremities. The resulting intermittent claudication and ischemia causes local leg pain especially during exertion. The process is common in aging, diabetic, and smoking populations. Interventions though not particularly effective are directed toward dilating the vessels and increasing blood flow. Opioid peptides are widely used analgesics and may have utility as vasodilators. Enkephalins specifically bind to ?-opioid receptors (?-OR) which selectively modulate the release of acetyl choline at autonomic junctions in the heart. The goal of the present study was to determine the function of enkephalin in the control of femoral blood flow. This study was designed to test the hypothesis that systemically administered enkephalins modulate autonomic control of blood flow in the hind limb via ?-ORs.

Methods: Mongrel dogs were anaesthetized and the femoral arteries were instrumented to measure heart rate, arterial pressure and central venous pressure. The carotid arteries were isolated and fitted with plastic snares to reversibly occlude them bilaterally (BCO). Enkephalin was administered into the descending aorta and the femoral flow responses were recorded. Cumulative antagonist dose responses (0.3 ug/kg to 10 ug/kg) were then constructed with either the ?1-OR antagonist BNTX or the ?-2 antagonist naltribein (NTB).

Results: Enkephalin increased the femoral blood flow sharply and NTB quickly blocked the effect at rest and during sympathetic activation during BCO. The effect of enkephalin was duplicated with the selective ?2-agonist, deltorphin II which was also blocked by NTB. The ?1-agonist, TAN-67 and the ?1-antagonist, BNTX were much less effective.

Conclusions: Enkephalins can modulate sympathetic control of vasculature smooth muscle in the hind limb through the activation of the ?2-opioid receptors perhaps by moderating ganglionic transmission.

Sponsor: *AHA TX Affiliate*

324 *(Poster)*

Author: Jonathan Matthews

Presenter: Jonathan Matthews

Department: Internal Medicine

Classification: Postdoctoral Fellow/Resident

Jonathan Matthews, D.O., Kyle Hendrix MSIV, Michael Clearfield, D.O., Craig Spellman, Ph.D., Walter McConathy, Ph.D., D.O., Ben Willis, M.D.; Enisa Arslanagic, M.D.; Fidelita Weis, R.N; Rubina Muzina, M.D.; Mabyn Hager, RN,; Joice Carter, DE;.Sabitha Buttreddy, MS.; Karan Singh, Ph.D

TRADITIONAL AND EMERGING RISK FACTORS IN INDIVIDUALS WITH ACUTE CORONARY SYNDROME

Purpose: Current LDL-C goals as stated by the Nat.l Cholesterol Ed Program Adult Treatment PanelIII (NCEP-ATP III) recommend an LDL-C

Methods: To explore the role of traditional and emerging risk factors, ACS subjects were evaluated at one month after stabilization from their acute events and at baseline in controls who were non-overweight, non-diabetic, non-CVD subjects at NCEP-ATP III goals. ACS is defined as individuals with ischemic EKG changes including ST segment elevation or depression, elevated troponin levels, or unstable angina with a coronary lesion of > 70% stenosis. Exclusion criteria included patients with prior percutaneous intervention procedure within the last year or cardiogenic shock. Traditional risk factors included a history of hypertension, diabetes, smoking, family history of premature CHD, or and HDL-C< 40 mg/dl. Emerging risk factors assessed included: LDL particle size; apolipoproteins B and A-I; lipoprotein (a); hsCRP; homocysteine; PAI-1; myeloperoxidase; resistin, IL-6, and leptin.

Results: Mean LDL-C levels in ACS subjects was 83.2 mg/dl compared to 106 mg/dl in the control group(p=0.112). Those subjects with ACS had significantly higher levels of TG and lower levels of TC and HDL-C. ACS subjects also were noted to have significantly increased BMI, waist circumference, waist/hip ratio, history of smoking and family history of premature CHD. In the ACS group 40% had DM and 52% had metabolic syndrome (METS). Of the non-traditional risk factors, only elevated levels of hs-CRP, homocysteine, interleukin 6 and myeloperoxidase reached significance. 89.5% ACS patients had either a CRP > 3 mg/L, DM or METS.

Conclusions: The prevalence of ACS in individuals at their stated LDL-C goal is not a rare occurrence. In DREAMS-ACS 19 subjects with a LDL-C 3 was 89.5%. The addition of the emerging risk factor homocysteine did not add to the ability to predict ACS risk. Therefore, in individuals presenting with LDL-C at goal, the presence of METS, DM or an elevated CRP > 3 mg/L predicted 90% of those who went on ACS.

Sponsor: *N/A*

325 *(Poster)*

Author: Shekhar Deo

Presenter: Shekhar Deo

Department: Integrative Physiology

Classification: GSBS Student

SH. Deo, MA. Barlow, D. Yoshishige, JL. Caffrey. University of North Texas Health Science Center, Fort Worth, TX, USA

ROLE OF 4-TYROSYL-ENKEPHALINS IN MEDIATING INFLAMMATORY EFFECTS IN CANINE HEART

Purpose: Enkephalins are the class of cardiac opioids that are shown to be anti-arrhythmic and cardioprotective. They exert vagotonic and vagolytic effects respectively by acting on d1-and d2- opioid receptors (OR) on the pre-junctional post-ganglionic parasympathetic nerve endings in the canine heart. It is previously proved that preconditioning of the SA node is mediated by d1-OR. The beneficial effects of these opioid peptides are determined by their local concentration and the relative proportions of the d-OR. Activated leukocytes also produce enkephalins along with oxyradicals following an ischemic insult. These oxyradicals in turn hydroxylate the anti-inflammatory enkephalins in to their pro-inflammatory 4-tyrosyl forms. The study was designed to test the hypothesis that hydroxylated pro-oxidant enkephalins produced during reperfusion reverse preconditioning and/or aggravate reperfusion injury by stimulating leukocyte oxyradicals and damaging d1-mediated responses. The resultant elevated ratio of d2/d1 responses would then oppose vagal transmission. However, very little is known about the biological activity of these novel hydroxylated enkephalins.

Methods: Mongrel dogs were anesthetized and intubated. Supplemental anesthetic was administered as required. Room air and supplemental oxygen were delivered by a mechanical respirator. Right femoral artery and vein were catheterized. Right sided thoracotamies were performed and a microdialysis probe was inserted into sinoatrial node of heart for introduction of opioids. Opioids are delivered into the SA node by microdialysis during vagal stimulation.

Results: Dose-response curves (ranging from 50 fmole/min to 3 nmole/min) were performed for the enkephalins; met-enkephalin (ME) and leu-enkephalin (LE) and their corresponding 4-tyrosyl derivatives; 4-tyrosyl-met-enk (4TME) and 4-tyrosyl-leu-enk (4TLE). ME and LE showed significant vagolytic effects from 50 pmole/min. However, 4TME and 4TLE did not show these effects.

Conclusions: High doses of enkephalins are vagolytic however hydroxyalation of these enkephalins may have altered their role to impair the vagal function. Further role of hydroxylated enkephalin remains to be determined.

Sponsor: *AHA TX Affiliate*

326 *(Poster)*

Author: Nyaz Didehbani

Presenter: Nyaz Didehbani

Department: Integrative Physiology

Classification: GSBS Student

Nyaz Didehbani, B.S., Kathryn A. Kaiser, B.S., David R. Phelps, M.D., Susan F. Franks, Ph.D., and Joan F. Carroll, Ph.D. University of North Texas HSC, Fort Worth, Texas, United States, 76107.

BODY COMPOSITION AND CARDIOVASCULAR RISK FACTORS IN BARIATRIC PATIENTS (DREAMS: DIABETES, RESEARCH, EDUCATION, AND METABOLIC STUDIES)

Purpose: Increased waist circumference (WC) and waist/hip ratio (WHR) have both been positively related to cardiovascular risk factors because of their presumed relation with underlying visceral adipose tissue (VAT). However, obtaining accurate circumference measurements in morbidly obese individuals is difficult. Whether any simple anthropometric measurement can reflect the risk associated with increasing adiposity in this population is unclear. Therefore, the purpose of this study was to determine the correlation between body composition (determined by both abdominal CT and anthropometry) and cardiovascular risk factors in morbidly obese subjects.

Methods: Thirty five candidates for bariatric surgery volunteered for the study. Prior to surgery, L4-L5 VAT and total VAT were quantified from an abdominal CT scan. Body weight was measured and percent body fat estimated using a bio-impedance analyzer (Tanita, model TBF-310). WC and WHR were measured using a non-stretchable tape. Blood pressure was measured, and fasting blood samples were taken to determine plasma concentrations of inflammatory and metabolic risk factors.

Results: Mean (±SE) and ranges for body composition measures were: L4-L5 VAT: 244±18 cm2, 62-512 cm2; total VAT: 5.9±0.4 kg, 1.5-12.5 kg; body weight: 266±7 lbs, 189-345 lbs; percent body fat: 50±1%, 37-58%; WC: 51.8±1.2 in, 40-63 in; WHR: 0.94±0.01, 0.80-1.06; BMI: 42.7±0.8, 32.4-54.0. Systolic blood pressure was positively associated with total VAT. Total cholesterol was positively related to percent fat as measured by impedance, while HDL cholesterol was negatively related with both total and L4-L5 VAT. Insulin resistance, indicated by increased fasting insulin, HOMA, and HbA1c, was positively correlated with both total and L4-L5 VAT. Homocysteine was positively related with total and L4-L5 VAT, but other emerging risk factors, such as ApoB and C-reactive protein, were not significantly related to any measure of body composition used in this study. Further, none of the risk factors correlated significantly with BMI.

Conclusions: These data indicate that simple anthropometric measures of body composition are not useful to define additional cardiovascular risk within a morbidly obese population, and may underestimate the risk associated with increasing body fat. When visceral body fat was accurately determined using CT scan techniques, these data demonstrated that increasing VAT, even within a morbidly obese population, is associated with worsening of traditional risk factors.

Sponsor: *Support by CDC grant H75/CCH224064*

400 *(Oral)*

Author: Dongmei Lu

Presenter: Dongmei Lu

Department: Molecular Biology and Immunology

Classification: GSBS Student

Dongmei Lu, Jie Huang and Alakanada Basu Department of Molecular Biology & Immunology, University of North Texas Health Science Center, Fort Worth, Texas, 76107

ANTI-APOPTOTIC SIGNAL OF PROTEIN KINASE C-EPSILON

Purpose: The survival of cancer cells in response to tumor necrosis factor-alpha (TNF) depends on the presence of antiapoptotic signals. TNF not only stimulates apoptosis through a caspase cascade, but also amplifies the cell death signal through mitochondria-mediated intrinsic pathway that is critically regulated by Bcl-2 family members. We have previously shown that protein kinase C-epsilon (PKC-epsilon) protects breast cancer cells from TNF-induced cell death. The objective of this study is to delineate the mechanism by which PKC-epsilon exerts its anti-apoptotic signal in breast cancer cells.

Methods: PKC-epsilon or protein kinase B(PKB)/Akt was overexpressed by introduction of vectors containing PKC-epsilon or Akt constructs. These proteins were depleted by transfection of small interfering RNA (siRNA) against PKC-epsilon or Akt. Western blot analysis was employed to determine the protein level. Akt in vitro kinase assay was performed to determine the kinase activity. Cell death was examined using a flow cytometer. JC-1 staining was used to detect the mitochondria depolarization. Immunostaining was used to detect Bax translocation.

Results: Overexpression of PKC-epsilon in breast cancer MCF-7 cells increased Akt phosphorylation and activation. Knockdown of PKC-epsilon by siRNA decreased TNF-induced Akt phosphorylation/activation and increased cell death. Introduction of constitutively-active Akt (CA-Akt) partially restored cell survival in PKC-epsilon-depleted cells. Depletion of Akt in MCF-7 cells abolished the anti-apoptotic effect of PKC-epsilon. Furthermore, overexpression of wild-type PKC-epsilon (WT-PKC-epsilon) but not dominant-negative PKC-epsilon (DN- PKC-epsilon) attenuated TNF-mediated mitochondria depolarization. PKC-epsilon overexpression decreased the Bax translocation and dimerization. The association of PKC-epsilon with Bax was detected in PKC-epsilon overexpressing cells.

Conclusions: These results suggest that PKC-epsilon plays antiapoptotic role through activating Akt and interacting with Bax.

Sponsor: *CA71727*

401 *(Poster)*

Author: Sherry Sours

Presenter: Sherry Hannon

Department: Integrative Physiology

Classification: Staff

Sherry Sours, Joseph Oberdorfer, Min Ding, Juan Du, Rong Ma Dept. of Integ. Physiol., Univ. of North Texas Health Science Center, Fort Worth, TX 76107

FUNCTION OF TRPC1/TRPC4 COMPLEX IN MESANGIAL CELLS

Purpose: Mesangial cells (MCs) are located within glomerular capillary loops and contribute to the physiological regulation of glomerular hemodynamics. Store-operated Ca2+ channel (SOC) in glomerular MCs mediates Ca2+ entry in response to circulating or locally produced vasoactive peptides. Recent evidence suggests that members of the canonical transient receptor potential (TRPC) protein family may constitute SOC. However, expression of TRPC subtypes and formation of TRPC heteromultimeric complex appear to be cell-type specific. Our laboratory has recently characterized TRPC expression in human mesangial cells (HMCs), which includes TRPC1, 3, 4, and 6 at detectable protein levels. This study examines the interaction between two of these subtypes, TRPC1 and TRPC4, and whether they form a functional complex to mediate store-operated Ca2+ entry in HMCs.

Methods: In this study, HMCs were cultured using standard tissue culture techniques. Western blot analysis using co-immunoprecipitation as well as fluorescent immunocytochemistry was used to demonstrate association and co-localization of TRPC1 and TRPC4. Patch clamp technique in the cell-attached configuration was used to measure single-channel Ca2+ currents in response to thapsigargin (TG)-induced store-depletion. Ca2+ transients upon stimulation with TG were examined using fluorescent ratiometry. These measurements were made with control cells as well as cells transiently transfected with over-expression or RNA interference plasmids for TRC1 and/or TRPC4.

Results: In the present study, we show that TRPC1 associates with TRPC4 by co-immunoprecipitation and by fluorescent immunocytochemistry. The RNA interference (RNAi) of TRPC1 expression, or inclusion of a TRPC1-specific antibody in the patch pipette significantly depressed thapsigargin (TG) -induced Ca2+ currents as measured by patch clamp. Accordingly, fluorescent ratiometry showed that over-expression of TRPC1 enhanced TG-induced capacitative Ca2+ entry, while RNAi blockade of TRPC1 expression reduced this response. Knocking out TRPC4 with RNAi had a similar effect on TG-induced Ca2+ entry as TRPC1. In addition, concurrent RNAi of TRPC1 and TRPC4 had comparable effect to individual TRPC1 or TRPC4 knocked out. Furthermore, TRPC1 over-expression had a positive effect, but TRPC1 knock-out had a negative effect on HMC proliferation and contraction.

Conclusions: These data suggest that TRPC1 and TRPC4 form a functional complex in tandem to mediate store-operated Ca2+ entry in HMCs.

Sponsor: *American Heart Association, National Kidney Foundation*

402 *(Poster)*

Author: Juan Du

Presenter: Juan Du

Department: Integrative Physiology

Classification: Postdoctoral Fellow/Resident

Juan Du, Sherry Sours, Min Ding and Rong Ma Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, TX 76107

REGULATION OF CONTRACTILE FUNCTION OF MESANGIAL CELLS BY PKD2

Purpose: The present study was performed to test the hypothesis that PKD2 and its binding partner constitute nonselective cation channel in human mesangial cells (HMCs) and contribute to contractile function of the cells.

Methods: Western blotting, Immunocytochemistry, Immunohistochemsitry , Co-immunoprecipitation, Cell-attached patch clamp experiments.

Results: Western blotting and immunocytochemistry showed PKD2 expression in cultured HMCs. The existence of PKD2 in HMCs was further confirmed by immunohistochemsitry in rat and human kidney sections. Co-immunoprecipitation showed a selective interaction of PKD2 with TRPC1 and TRPC4. Cell-attached patch clamp experiments revealed nonselective cationic currents stimulated by Ang II. The Agonist-induced currents were enhanced by over-expressing PKD2, but attenuated by knocking down PKD2. Corresponding to the increase in channel currents, Ang II stimulation increased expression of PKD2 in the cell surface as well as interaction with TRPC4. Furthermore, Ang II-induced MC contraction was reduced in PKD2 knocked out MCs.

Conclusions: These data suggest that PKD2 might selectively assemble with specific isoforms of TRPC proteins to form a nonselective cation channel in HMCs and this channel complex contributes to contractile function of HMCs(This study was supported by AHA National Scientist Development Grant)

Sponsor: *AHA National Scientist Development Grant*

403 *(Oral)*

Author: T.J. Bartosh

Presenter: T.J. Bartosh

Department: Cell Biology and Genetics

Classification: GSBS Student

T.J. Bartosh, Zhaohui Wang, Armando A. Rosales, Rouel S. Roque. Department of Cell Biology and Genetics, University of North Texas Health Science Center, 3500 Camp Bowie Blvd., Fort Worth, Texas 76107.

CARDIAC STEM CELL COMPARTMENT-SPECIFIC DIFFERENCES IN GROWTH AND DIFFERENTIATION

Purpose: Stem-cell replacement of ischemic or failing hearts can be achieved by transplantation of a stem cell source of cardiomyocytes and establishment of viable vasculature to nourish the stem cell graft. We have previously shown that cardiac stem cells (CSC) from adult canine hearts differentiate in vitro into 3D cell aggregates, called □cardiospheres, that display characteristics of adult myocardium. More recent findings in our laboratory suggest a compartment-specific distribution of CSC exhibiting either cardiomyocyte precursor (CP) or vascular cell precursor (VCP) phenotypes. The following study was designed to characterize the growth potential of VCP from the epicardium-containing thickness of the left ventricle (LVEP) of adult dog hearts.

Methods: CSC isolated from the LVEP were expanded in vitro, induced to form cardiospheres, and characterized using ICC, Western blot, and RT-PCR. Ultrastructural analyses of cardiospheres were performed using TEM. Growth factor-mediated cell proliferation and migration were determined using MTS and sprouting assays, respectively. To test for cell viability and tumor formation in vivo, fluorescent-tagged cardiospheres were visualized under the confocal microscope following subcutaneous or intramuscular injections in mice.

Results: CSC isolated from the myocardial fraction of the left ventricle expressed the stem cell marker c-kit initially, but with prolonged culture, formed cardiospheres composed predominantly of cardiomyocytes and CP. CSC obtained from the LVEP also expressed c-kit and formed cardiospheres, however, they expressed markers of VCP such as von Willebrand factor (endothelial cells) or smooth muscle actin (smooth muscle cells). In addition to bFGF and IGF, VEGF and HGF stimulated proliferation of VCP and/or sprouting from cardiospheres. The cells maintained viability without becoming tumorigenic, when evaluated three weeks post-transplantation.

Conclusions: This study describes compartment-specific differences in CSC growth and differentiation, such as in the LVEP of dog hearts which serves as a source of VCP for revascularization of ischemic myocardium or stem cell grafts. The viability of transplanted cardiospheres and their lack of tumorigenic potential bodes well for their utility in stem-cell replacement therapy. Understanding compartment-specific variations in CSC-specification will provide relevant and practical knowledge of individual-based stem cell-assisted therapeutic strategies for cardiac repair or intervention.

Sponsor: *N/A*

404 *(Poster)*

Author: S Sarkar

Presenter: Lonell Smith

Department: Pharmacology & Neuroscience

Classification: GSBS Student

S. Sarkar, Lonell Smith, James W Simpkins Fort Worth, Texas 76107

SIRNA DELIVERY TO RAT PRIMARY HIPPOCAMPAL AND CORTICAL NEURONS

Purpose: To Study the function of estrogen receptor beta in primary neuronal cells.

Methods: Adeno-associated virus mediated er-beta siRNA delivery and Penetratin conjugated siRNA oligoribonucleotides mediated siRNA delivery.

Results: NA

Conclusions: NA

Sponsor: *N/A*

405 *(Poster)*

Author: Shanmuga Priya Muthu Thanu

Presenter: Shanmuga Priya Muthu Thanu

Department: Molecular Biology and Immunology

Classification: GSBS Student

S.P.Muthu-UNTHSC, I.Akapova-UNTHSC, T.P.Burghardt -Mayo Clinic, Rochester, MN,J.Borejdo-UNTHSC

ROTATIONS OF MUSCLE CROSS-BRIDGES MEASURED BY CONFOCAL TOTAL INTERNAL REFLECTION MICROSCOPY

Purpose: During muscle contraction, myosin heads cyclically interact with actin filaments. It is believed that the ATPase activity (fATP) of whole muscle is equal to this frequency (fc). It has been suggested so far that in isolated cross-bridges the two are equal. Until now there has been no direct evidence obtained in working muscle. To do this we need to measure the kinetics of individual cross-bridges in working muscle. This is difficult because a single muscle fiber contains billions of cross-bridges. Moreover, it is possible that cross-bridges in functioning muscle behave differently than in solution. Here, we used a new method to measure fc of just a few cross-bridges in muscle.

Methods: Myosin of skeletal myofibrils was fluorescently labeled at Cys707. To prevent shortening during contraction, they were cross-linked. The anisotropy was measured in the prismless confocal total internal reflection microscope. Myofibrils were illuminated by 532 nm light from an expanded DPSS laser beam. The beam was focused at the back focal plane of the objective and directed to its periphery. The fluorescent light was collected through the objective and focused by the tube lens at the conjugate image plane. A confocal aperture was inserted at this plane. Polarized fluorescence was subsequently measured.

Results: Fluorescence polarization from a myofibril preparation in rigor and in contraction was measured. Polarization is low in rigor, intermediate in relaxation and high in ADP. The control experiments revealed that myofibrils did not shorten at all during contraction. Also, two fluorescent images were taken of the same myofibril, one in rigor and the other in contraction. The paired t-test showed that the difference was not statistically significant. The ATPase of uncrosslinked and crosslinked myofibrils was measured. It was seen that in solution, crosslinking S1 to F-actin accelerates ATPase 200-300 fold for rabbit skeletal proteins.

Conclusions: The present work shows that cross-bridge cycling frequency is approximately equal to the bulk ATPase rate of the whole muscle. Also, it can be said that the weakly bound cross-bridges do not contribute at all TO the observed fluctuations. Likewise, the unbound heads rotate freely, because the hinge connecting them to the C-terminal part of the molecule is flexible. But even if weakly attached heads are oriented and attachment-detachment results in orientation fluctuation, such fluctuations are too rapid to be detected.

Sponsor: *N/A*

500 *(Poster)*

Author: John Fling

Presenter: Chris Larson

Department: Pediatrics

Classification: Dual Degree Student DO/MS

John Fling, M.D., UNTHSC, Fort Worth, TX 76107 Chris Larson, B.B.A., UNTHSC, Fort Worth, TX 76107 Richard Virgilio, D.O., UNTHSC, Fort Worth, TX 76107

ASSESSMENT OF DIABETES MELLITUS TYPE 2 SCREEENING COMPLIANCE WITH THE ADA GUIDELINES IN A UNIVERSITY BASED PEDIATRIC CLINIC

Purpose: Diabetes mellitus type 2 (type 2 DM) has historically been considered a disease of the adult population. However, in the last decade there has been an increase in the prevalence of type 2 DM among the younger population. In March 2000, an expert committee convened by the American Diabetes Association (ADA) recommended testing criteria for type 2 DM in children and adolescents. The objective of this study is to determine the percentage of ADA defined at-risk cases that are screened for diabetes.

Methods: Pediatric chart review at the University of North Texas Health Science Centers pediatric clinic. A total of 99 charts representing 10-19 year old patients who met the ADA criteria for a type 2 DM screening were reviewed. Data gathered included if the patient was screened and if so, what type of test was recommended.

Results: About 10% of the patients that met the ADAs testing criteria guidelines were recommended for testing. Patients with acanthosis nigricans and hypertension had odds ratios of 70 (95% CI = 3 - 1,440) and 36 (95% CI = 2 - 721) times more likely, respectively, than patients without these risk factors to be screened. When screening was recommended, 80% of these tests where fasting plasma glucose, with the remainder being random plasma glucose tests. None of those tested had overt diabetes or insulin resistance.

Conclusions: BMI calculation results and BMI plotting were rarely completed. A formal education protocol for the healthcare providers has been provided and a pre-post analysis is under consideration.

Sponsor: *N/A*

501 *(Poster)*

Author: Craig Spellman

Presenter: Craig Spellman

Department: Internal Medicine

Classification: Staff

Craig Spellman,Ximena Urrutia-Rojas,John Menchaca, and Walter McConathy. Texas College of Osteopathic Medicine and School of Public Health, University of North Texas Health Science Center, Fort Worth, Texas 76107

DETECTION OF CHILDREN AT RISK FOR TYPE 2 DIABETES

Purpose: Screening programs are based on the premise that there is a marker with high sensitivity for a particular disease and that early detection of at-risk persons will decrease the impact of the disease. Public school programs are currently operating in Texas to find children at risk to develop type 2 diabetes. These screening programs focus on finding children with acanthosis nigricans (AN) or high body mass index (BMI) and referring for further diagnostics.

Methods: We evaluated approximately 1100 fifth grade children in the Fort Worth ISD. We obtained history and physical information, various anthropometric measurements and laboratory studies of glucose, lipids, CRP and insulin levels

Results: We analyzed the data to determine if BMI or AN would detect children at risk for type 2 diabetes. We defined at-risk children to be those with impaired fasting glucose (IFG), the direct precursor of type 2 diabetes. We found that neither phenotypic marker had sufficient sensitivity to justify its use as a screening tool.

Conclusions: Specifically, about 40% of children with IFG would not be found using AN as the screening tool. About 35% of children with IFG would not be found using BMI as the screening tool. The results from our Forth Worth study have triggered reevaluation of the Texas screening programs to find at-risk children and start early intervention.

Sponsor: *Bristol/Myers UNTHSC*

502 *(Poster)*

Author: Mary Jane Rorick
Presenter: Mary Jane Rorick
Department: Physician Assistant Studies
Classification: TCOM MPAS Student
Mary Jane Rorick, PA-S; Laurie Hill, MHS, PA-C; Olive Chen, PhD University of North Texas Health Science Center at Fort Worth Physician Assistant Studies 3500 Camp Bowie Boulevard Fort Worth, TX 76107-2699

PUBLIC AWARENESS OF TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS

Purpose: The purpose of this study was to investigate the general publics awareness and knowledge of type 2 diabetes in children and adolescents. The research questions were: 1)What is the publics awareness of type 2 diabetes in children and adolescents? 2)Is there a difference in the level of awareness between different ethnic population groups, specifically between Caucasians, African-Americans, and Hispanics? 3)Do people want healthy eating, lifestyle choices and physical education taught in the schools?

Methods: A 19 question survey was developed in English and Spanish, to collect the data. Convenience sample was used to collect data at two major locations: Stonebriar Center in Frisco, TX and Marcus Recreation Center, Dallas, TX. Frequency, T-test, ANOVA and Chi square analyses were used on subsets of the data to test whether or not there were significant differences in overall knowledge between groups.

Results: A total of 186 surveys were collected. Most of the respondents were Caucasian (50.5%) and Hispanic (24.7%). The mean score for overall knowledge for all participants was 8.5 out of 11. Gender was the only factor producing significant differences: women scored higher in overall knowledge than men, with a mean score of 8.9 versus 8.1 ($t=-3.145$, $p=0.002$). There were no significant differences between age groups, education levels or different ethnic groups in overall knowledge. The majority of respondents expressed their support for the inclusion of healthy lifestyle education in the schools ($x2= 144.602$, $p< 0.001$).

Conclusions: Individuals sampled in this study appear to have a fair knowledge of type 2 diabetes. The results showed that respondents recognize that schools play a role in shaping the health habits of children. The results also showed that women appear to have better knowledge of type 2 diabetes than men. This indicates that diabetes educators may need to target men in their teaching in order to increase their male patients knowledge and awareness of the disease. Limitations of this study were: an unvalidated survey, lack of randomization because of the sampling method, and small sample sizes for several of the respondent groups. Further studies might investigate the long-term impact of the institution of healthy lifestyle and physical education in the schools and the possible benefits resulting from these changes.

Sponsor: *N/A*

503 *(Poster)*

Author: Mary Luna Hollen
Presenter: Mary Luna Hollen
Department: School of Public Health
Classification: Faculty
Mary Luna Hollen, PhD, RD, LD, Dept Social & Behavioral Sciences, UNTHSC School of Public Health, Fort Worth, Tx 76107; Ximena Urrutia-Rojas, DrPH, RN, Dept Social & Behavioral Sciences, UNTHSC School of Public Health, Fort Worth, Tx 76107; Sejong Bae, PhD, Dept Biostatistics, UNTHSC School of Public Health, Fort Worth, Tx 76107; Isabel Vecino, MD, Dept Internal Medicine, UNTHSC, Fort Worth, Tx 76107; Mateo Stahl, BS, Dept Social & Behavioral Sciences, UNTHSC School of Public Health, Fort Worth, Tx 76107; Enisa Arslanagic, MD, Dept Internal Medicine, UNTHSC, Fort Worth, Tx 76107.

HISPANIC FAMILY DIABETES PROJECT PRELIMINARY BASELINE DATA

Purpose: DREAMS Project1 provided bilingual culturally competent healthy lifestyle behavior education through the utilization of lay health educators (promotores de salud) and culturally sensitive bilingual print materials to Hispanic families with overweight or obese children previously identified as "at risk" for Type 2 Diabetes Mellitus (T2DM) to decrease the risk factors of T2DM and Cardiovascular (CVD) related to lifestyle (e.g. lack of physical activity and poor eating patterns). The purpose of this study was to determine if social and demographic factors are associated with disease risk factors and/or lifestyle behaviors at baseline. The research question asks Is there concordance between and among independent variables (preferred language, number of years in the US, foreign or US-born, number of family members living in the houseold, and number of family members pledging to participate in the educational program) and dependent variables (number of disease risk factors and healthy lifestyles) in intervention and/or control families.

Methods: Previously identified overweight Hispanic children at risk of diabetes and cardiovascular disease, and their family members were enrolled in DREAMS Project1 in 2005; Two hundred and forty families were randomly assigned to an intervention group (n=120) utilizing promotores de salud in family sessions and blingual culturally competent print material, and to a control group (n=120) receiving blingual culturally competent print material only. Baseline data was collected and analyzed from the demographics, disease history and behavioral risk factors, and self-reported pre-test lifestyle behavior questionnaire datasets.

Results: Multi-variate analyses measured concordance between and among independent variables (preferred language, number of years in the US, foreign or US-born, number of family members living in the houseold, and number of family members pledging to participate in the educational program) and dependent variables (number of disease risk factors and healthy lifestyles in intervention and control families.

Conclusions: Results provided a baseline evaluation and associations among variables of significance. Additionally, this study strengthened the role of promotores de salud in identifying social and behavioral determinants of health.

Sponsor: *US DHHS*

600 *(Poster)*

Author: Pam McFadden

Presenter: Andrew Crim

Department: PROFESSIONAL AND CONTINUING EDUCATION (PACE) **Classification:** Staff

Pam McFadden Associate Vice President of Professional & Continuing Education University of North Texas Health Science Center at Fort Worth Fort Worth, Texas 76107 Andrew Crim Executive Director of Professional & Continuing Education University of North Texas Health Science Center at Fort Worth Fort Worth, Texas 76107

CHANGING COURSE: DIAGNOSING AND TREATING TYPE 2 DIABETES

Purpose: The purpose of this activity is to equip individual healthcare providers and healthcare teams with information to enhance their understanding of type 2 diabetes. The goal of this activity is to improve the outcomes of patients with type 2 diabetes through earlier diagnosis and more effective treatment and management.

Methods: Following a thorough needs assessment, which included literature reviews, surveys, interviews and a technology assessment of the target audience, nationally-recognized experts in Type 2 diabetes were filmed (at 30 frames per second) responding to a series of questions related to diagnosing and managing the disease. Responses were edited together to form a unique educational activity offering up to six hours of continuing education credit.

Results: PACE proposed Changing Course with a built-in evaluation and outcomes component. The initial proposal included a pilot study and follow-up surveys and interviews with participants to measure the effectiveness of the activity. In addition, sanofi-aventis committed to contracting with an independent organization, Outcomes, Inc., to measure initial and long term effectiveness of this type of education with a selected group of activity participants. PACE is also measuring the success of this activity using non-traditional outcomes, including awards received, partnerships established and adaptation of the medium for other activities.

Conclusions: Selected responses from activity evaluation summary (n=431) Respondents who agree the activitys learning objectives were satisfied = 95% Respondents who agree the DVD is effective as an instructional method = 91% Respondents who agree the activity was presented WITHOUT commercial bias = 96% Conclusion of independent outcomes assessment: ☐Changing Course&has proved to be a well-developed, effective and credible source of information for [physicians]. This DVD series has been effective in facilitating a more aggressive approach to the management of type 2 diabetes in order to prevent complications. The [University of North Texas Health Science Center at Fort Worth] has developed an excellent educational product...

Sponsor: *sanofi-aventis*

601 *(Poster)*

Author: Robert Kaman

Presenter: Robert Kaman

Department: Office of Outreach

Classification: Staff

Robert L. Kaman, JD, PhD, GSBS Outreach, UNTHSC

OUTREACH PROGRAMS

Purpose: The Office of Outreach administers programs whose principal goal is to increase the numbers of under-represented, disadvantaged or first generation college students entering the health professions and the biomedical sciences. The programs currently in place are the Adopt-A-School Program, SMART, McNAIR, More Knowledge In The Sciences (MKITS), The Go Center Project and Bridges to the Doctoral Degree.

Methods: Each Program is distinct, but offers summer research internships for college (SMART, McNAIR), experience in teaching science in K-12 (MKITS and SCORE), K-12 mentoring, tutoring and advising (Adopt-A-School, MKITS ,SCORE, Go Center), support for graduate training (Bridges), and involvement of student organization in a variety of activities (Adopt-A-School, MKITS, Go Center). Several partnerships with minority serving institutions have been developed, and a student pipeline established between them and the various programs at the health science center.

Results: As a result of these efforts, the Office of Outreach has been recognized by Clinton and Bush White House Administrations for its success. The National Association of Outreach Admissions Professional named it the 1999 winner of its Excellence in Minority Admissions award and Minority Access, INC., has named the University of North Texas Health Science Center for the role model institution.

Conclusions: Efforts by the Office of Outreach have enabled the health science center to achieving great success in creating a diverse student population that leads the state in that area.

Sponsor: *N/A*

602 *(Poster)*

Author: Roberto Cardarelli

Presenter: Roberto Cardarelli

Department: Family Medicine

Classification: Faculty

Roberto Cardarelli, DO, MPH; UNTHSC, TCOM, Department of Family Medicine, Fort Worth, TX 76107 Elizabeth Palmarozzi, DO; UNTHSC, TCOM, Department of Family Medicine, Fort Worth, TX 76107

OVERCOMING OBSTACLES TO IMPLEMENT A PRIMARY CARE RESEARCH FRAMEWORK

Purpose: Primary care departments are challenged to develop, conduct, and sustain a research program. We will present a successful framework that has been developed at the University of North Texas Health Science Center (UNTHSC), Texas College of Osteopathic Medicine (TCOM), Department of Family Medicine.

Methods: □Academia is an inter-related triad of education, patient care, and research. Research not only functions as a mechanism to new discovery, but is a framework to develop and implement new knowledge into medical practice. It is imperative for medical students to be knowledgeable about the various aspects of research methodology. This will enable them to appreciate, assess, and evaluate research when they are independent practitioners.

Results: The Department of Family Medicine of the UNTHSC, TCOM developed the Division of Education & Research (DEAR) in 1997. Since its conception, it has been successful in its scholarly activities and funding. Within DEAR, we have created a framework to ensure the viability and sustainability of research. The Center of Evidence Based Medicine (EBM) was developed to conduct research related to EBM and to teach medical students, residents, and faculty about the principles and practice of EBM. The North Texas Primary Care Practice Based Research Network was developed as a □laboratory to conduct primary care research. In addition, a predoctoral primary care clinical research fellowship was developed in 2003 to train future researchers. The fellows complete their D.O. and M.S. degree in clinical research in 4 years.

Conclusions: By creating an environment conducive to primary care research, primary care departments can be successful in primary care research.

Sponsor: *N/A*

603 *(Poster)*

Author: Rachel Miller

Presenter: Rachel Miller

Department: Physician Assistant Studies

Classification: TCOM MPAS Student

Rachel Miller, PA-S; Linda Reed, MEd, PA; Olive Chen, PhD UNT-HSC, Fort Worth, Texas 76107

A PROPOSED INTERACTIVE EDUCATIONAL PROGRAM AIMED TO ENCOURAGE PREGNANT ADOLESCENTS TO INCLUDE FOLATE IN THEIR DAILY DIETS

Purpose: The purpose of this study was to design a nutrition education program that intends to inform pregnant adolescents of their nutritional need for folate and interactively encourage them to obtain the recommended daily intake of 400 micrograms (mcg) folate from their diet, in order to prevent neural tube defects in their offspring.

Methods: The target population will be pregnant adolescents age 14-18 with computer access; and no prerequisite nutrition knowledge will be expected. The workshop portion aims to increase participants folate knowledge and influence attitude changes supportive of the desired behavioral change, which was to modify dietary choices in order to acquire 400 mcg folate daily. The interactive Folate Tracker, which is designed in a CD-ROM format, would provide a method of tracking daily folate consumption, and it would provide consistent individual encouragement for each participant.

Results: The proposed nutrition education program includes 2 portions□a 1.5 hour workshop and the personal utilization of the interactive Folate Tracker program. In an attempt to appeal to various learning styles, the workshop course content was organized into 4 unique teaching modules. Module 1 established a comfortable learning environment. Module 2, a classical lecture with visual aids, aimed to answer curriculum objectives. Through hands-on discovery and problem solving, Module 3 reinforced curriculum objectives. Module 4 concluded the workshop with an instructional demonstration of the Folate Tracker CD-ROM. The study participants would log in their daily food consumption, and the program would calculate and record the participants daily amount of acquired folate, tracking whether they were meeting the 400 mcg folate goal.

Conclusions: Clinicians can efficiently refer patients to nutrition education programs like this one, while still paying close attention to patient care follow-up. The effectiveness and validity of this program cannot be assessed, as it has not been implemented. Upon implementation, the cognitive, affective, and behavioral domains may be assessed and analyzed, revealing whether workshop participation and utilization of the Folate Tracker produced changes in those domains. Future recommendations are to implement this interactive nutrition education program, preferably more than once in order to lend more reliability and validity to the study. Additionally, the Folate Tracker program can be used as a model to create more extensive nutrition tracking devices.

Sponsor: *N/A*

700 *(Poster)*

Author: Shaoqing He

Presenter: Shaoqing He

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Shaoqing He, Ganesh Prasanna, Thomas Yorio. Dept. of Pharmacology Neuroscience, UNT Health Science Ctr, Fort Worth, TX

ENDOTHELIN-1-MEDIATED SIGNALING IN THE EXPRSSION OF MATRIX METALLOPROTEINASES AND TISSUE INHIBITORS OF METALLOPROTEINASES IN ASTROCYTES

Purpose: Remodeling of the extracellular matrix (ECM) of the optic nerve head and cupping of the optic disc are characteristics of glaucoma. Endothelin-1 levels are increased in aqueous and vitreous humor in glaucoma patients and animal models of glaucoma. Whether the elevated ET-1 induces ECM remodeling resulting in pathological changes in the optic nerve head is still unknown. In the present study, the regulation of MMPs and TIMPs and ECM remodeling in ET-1-activated astrocytes were determined.

Methods: Human optic nerve head astrocytes (hONAs) were exposed to ET-1 for 1 day and 4 days. Culture media and cell lysates were subjected to zymography and Western blot. A zymography assay was used for quantifying the activity of MMP-2, 3 and 9. Western Blot was employed to determine the expression of MMP-2, 3, 9 and TIMP-1, 2. siRNA was employed to knock down the expression of MMP-2, 3, 9 or TIMP-1, 2. Fibronectin and collagen IV were monitored by ELISA and immunofluorescent staining.

Results: ET-1 slightly increased the activity of MMP2, which was also increased in the presence of U0126 (a MEK inhibitor) and chelerythrine (a PKC inhibitor) in hONAs. The activity of MMP3 was detectable using casein zymography, but not Western blot. In addition, blockade of ERK-MAPK by U0126 and PKC by chelerythrine increased the activity of MMP3. Whereas, the significantly increased expression of TIMP-1 and 2 induced by ET-1 was abolished by U0126 and chelerythrine in hONAs. Furthermore, there were no apparent differences in the expression profile of MMPs and TIMPs in hONA cells from normal human and POAG patients. Knock-down of MMP2 and 3 using siRNA not only decreased the activity of MMP2 and expression of TIMP-1 and 2 but also increased the fibronectin concentration in the cell supernatant. Fibronectin deposition was also significantly increased and formed an ECM network in hONA at day 1 after cells were exposed to ET-1, but only slightly increased at day 4. Blockade of MAPK using U0126 did not alter the expression and deposition pattern of fibronectin in hONAs.

Conclusions: ET-1 increased the expression and activity of MMP2 and TIMP-1, 2. The ERK-MAPK and PKC pathways are involved in the regulation of MMP2 and TIMP-1, 2 expression. A balance of MMPs/TIMPs may be important not only to regulate the expression of MMPs and TIMPs but also to regulate ECM remodeling. Current data show that ECM remodeling is controlled in a temporal fashion.

Sponsor: *N/A*

701 *(Poster)*

Author: Kissaou Tchedre

Presenter: Kissaou Tchedre

Department: Select a Department

Classification: GSBS Student

K.T. Tchedre 1, R.Krishnamoorthy 2, T.Yorio 2. 1Biomedical Sciences, University of North Texas Health Sciences Center, Fort, TX, 76107; 2Pharmacology & Neuroscience, University of North Texas Health Science Center, Fort Worth, TX, 76107.

NEUROPROTECTIVE SIGMA LIGANDS AND THEIR EFFECTS ON GLUTAMATE AND KCL INDUCED CALCIUM CHANGES IN RETINAL GANGLION (RGC-5) CELLS

Purpose: Purpose: The purpose of these studies was to investigate the neuroprotective effects of sigma receptor agonists on cultured retinal ganglion cells, which offer a unique and convenient model to study the mechanism of retinal ganglion cell death.

Methods: Methods: Differentiated and undifferentiated retinal ganglion cells (RGC-5) were used to determine the expression of sigma receptors. RGC-5 cells calcium response was also measured by a ratiometric technique using Fura- 2/AM. The effect of sigma ligands on endothelin-1 receptor expression in both retinal ganglion cells and human breast cancer cells (MCF-7) was also determined. A DNA fragmentation technique was used to assess retinal ganglion cell apoptosis after treatment with 1mM glutamate for 24 hours.

Results: Results: Western blot and quantitative PCR have shown that both (+)-N-allylnormetazocine hydrochloride [(+) SKF10047]) and haloperidol down regulate endothelin 1 receptors A and B after 24 hours treatments. (+)-N-Allylnormetazocine hydrochloride [(+) SKF10047]) inhibited the retinal ganglion cell glutamate or KCL induced calcium influx. Haloperidol reversed the effect the (+) SKF10047 in RGC-5 cells. Endothelin-1 also potentiated KCL induced calcium influx in RGC-5 cells. Nimodipine was able to block the KCL induced calcium influx. Reverse transcriptase polymerase chain reaction (RT-PCR) demonstrated the expression of sigma receptors in both differentiated and undifferentiated RGC-5 and MCF-7 cells. In addition, we have shown that sigma 1 receptors were upregulated in retinal ganglion cells after endothelin 1, glutamate and (+)-SKF10047 treatments. DNA fragmentation studies have shown that undifferentiated RGC-5 cells were not sensitive to glutamate-induced apoptosis compared to differentiated RGC-5 cells, which were sensitive to glutamate. Quantitative PCR results show that sigma ligands down regulate both endothelin1 receptors A and B.

Conclusions: Conclusions: Sigma ligands (+) SKF10047, protected differentiated RGC-5 cells from apoptosis compared to haloperidol, which fails to protect differentiated RGC-5 cells from apoptosis induced by glutamate excitotoxicity. In addition, the calcium imaging results show that sigma 1 receptor ligands modulate intracellular calcium homeostasis by regulating voltage gated calcium channels, NMDA receptor, and endothelin A receptors. Thus Sigma 1 ligands may be neuroprotective and a target for potential glaucoma therapeutics.

Sponsor: *NIH EY 11979*

702 *(Poster)*

Author: Martha Stokely

Presenter: Martha Stokely

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

Stokely, M.E., Koulen, P. Univ. of N. TX Health Science Ctr., Dept. Pharm. & Neurosci., Ft. Worth, TX, USA

HISTOCHEMICAL ASSAYS TO ASSESS DISEASE SEVERITY IN A MOG-INDUCED MODEL OF OPTIC NEURITIS

Purpose: Develop standardized protocols for making quantitative comparisons between optic nerves from rats with myelin oligodendrocyte glycoprotein (MOG)-induced autoimmune optic neuritis and non-induce controls. This will permit our future evaluation of experimental treatments affecting the measured parameters and improve our understanding of the mechanisms that underlie pathogenesis in autoimmune optic neuritis and related diseases such as multiple sclerosis.

Methods: Synthetic MOG-peptide (35-55) is administered subcutaneously in Freunds complete adjuvant to induce autoimmunity in young female Brown Norway rats. Thirteen days post-immunization, optic nerves are harvested, fixed, cryoprotected, frozen, sectioned, and mounted on slides for histochemical analyses of the frozen tissue sections. Quantitative histochemical and immunohistochemical analyses are used to evaluate optic nerves for reduced levels of myelination and immune infiltration.

Results: We have successfully induced autoimmune optic neuritis in female Brown Norway rats, detected decreased levels of myelin, and can quantitatively assess severity of 4 additional pathologies in optic nerve that are characteristic of the multiple sclerosis family of diseases.

Conclusions: Standardized protocols will permit us to quantitatively assess the ability of experimental treatments to delay onset or decrease severity of markers for the wide variety of histological pathologies associated with optic neuritis and related diseases.

Sponsor: *NIH*

703 *(Poster)*

Author: Xinyu Zhang

Presenter: Xinyu Zhang

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

Xinyu Zhang, Cherie M. Ognibene1, Abbot F. Clark, Thomas Yorio Pharmacology & Neuroscience, University N Texas HSC-FT Worth, Fort Worth, TX.

DEXAMETHASONE INHIBITION OF TRABECULAR MESHWORK CELL PHAGOCYTOSIS AND ITS MODULATION BY GLUCOCORTICOID RECEPTOR BETA

Purpose: An alternative splicing variant of human glucocorticoid receptor gene, termed GR beta, has dominant negative activity on glucocorticoid receptor GR alpha and has been implicated in a variety of steroid-resistant diseases. Previously we reported that GRß mediated cellular response to dexamethasone (DEX) in the regulation of the expression of glaucomatous markers in trabecular meshwork (TM) cells. Currently we investigate the effect of GR beta in regulation of the functional changes by DEX treatment in normal and glaucomatous TM cell lines.

Methods: Transformed human normal NTM-5 cell line, which expresses relatively high amount of GR beta, and glaucomatous GTM-3 cell line, which has lower GR beta expression, were used. Alexa Fluor 488 conjugated Straphylococcus aureus bioparticles were used to track the abilities of the cells to phagocytose. Cells were treated with 100 nM DEX for 24 hours then incubated with bioparticles opsonized with rabbit IgG for one hour, followed by fixation and incubated with Alexa Fluor 633 conjugated goat anti-rabbit IgG to differentiate intracellular from extracellular bioparticles. DAPI nuclear staining was used to calculate cell numbers. A confocal microscope was used to visualize cells and bioparticles. Overexpression of GR beta by transfection of the GR beta expression plasmid was performed to study the inhibition of DEX-induced decrease in phagocytotic activity of NTM-5 cells.

Results: Normal NTM-5 cells ingested more bioparticles than GTM3 cells. DEX treatment significantly decreased the phagocytosis of bioparticles in NTM-5 and GTM-3 cells, while GTM3 cells were more sensitive to DEX, compared to NTM-5 cells. Transient transfection of pCMX-hGR beta plasmid increased the expression of GR beta and consequently retained the phagocytotic activity of NTM-5 cells in the presence of the challenge of DEX.

Conclusions: Our data demonstrate that the expression level of GR beta in TM cells can regulate the sensitivity to DEX in terms of the change of phagocytotic activity by steroid treatment. The lower expression of GR beta in glaucomatous TM cells could contribute to the damaged function of TM cells, and exaggerated aqueous humor outflow pathway in the presence of steroids.

Sponsor: *EY016242*

704 *(Poster)*

Author: Allison Heath

Presenter: Allison Heath

Department: Cell Biology and Genetics

Classification: GSBS Student

Allison K. Heath- UNT-HSC Fort Worth, TX 76107 Harold J. Sheedlo- UNT-HSC Fort Worth, TX 76107

MORPHOLOGICAL AND PROLIFERATIVE RESPONSES OF RAT RETINAL PROGENITOR CELLS FOLLOWING TREATMENT WITH RETINOIC ACID AND RETINAL PIGMENT EPITHELIAL CELL-SECRETED PROTEINS

Purpose: The principle objective of this research is to characterize virally-transformed rat retinal progenitor cells isolated from postnatal day 2 rats following exposure to retinal pigment epithelium-secreted proteins.

Methods: In these experiments, progenitor cells were cultured in retinoic acid, proteins secreted by neonatal rat RPE cells or serum for 3-7 days. The treated progenitor cells were analyzed by phase contrast microscopy, proliferation bioassays, and immunocytochemistry. The photopigment opsin immunolabeled differentiated, mature cells, specifically photoreceptor cells, while vimentin was used to label undifferentiated cells. For controls, progenitor cells were cultured in fetal bovine serum or media lacking serum.

Results: This study showed that retinoic acid caused a 4 fold increase in progenitor cell numbers after 3 days when compared to media lacking serum controls. Over 80% of the progenitor cells grown in retinoic acid were opsin immunopositive, while over 70% immunolabeled for vimentin, suggesting co-localization of mature and immature markers under these retinoic acid conditions. Rat progenitor cells cultured in RPE-secreted proteins proliferated 12 fold compared to controls, while almost 90% of the cells expressed opsin, while only 39% of the cells were immunolabeled for vimentin. Serum caused a 17 fold increase in progenitor cells, however, only 70% of the cells expressed opsin, while 55% were immunolabeled for vimentin. Interestingly, only process-bearing cells expressed vimentin in all culture conditions, while cells with and without processes expressed opsin.

Conclusions: In conclusion, this study showed that retinoic acid and proteins secreted by the retinal pigment epithelium alone can affect proliferation of rat retinal progenitor cells and drive these cells to become mature retinal cells, specifically photoreceptor cells. Furthermore, some cells grown in these factors maintained an immature characteristic, vimentin expression. (Project SCORE)

Sponsor: *SCORE*

705 *(Poster)*

Author: Tara Tovar

Presenter: Tara Tovar

Department: Cell Biology and Genetics

Classification: GSBS Student

T.O. Tovar, UNTHSC, Fort Worth TX; A.F. Clark, Alcon Research Ltd., Fort Worth TX; R.J. Wordinger, UNTHSC, Fort Worth TX.

CULTURED HUMAN TRABECULAR MESHWORK CELLS RESPOND TO EXOGENOUS BMP-4 VIA THE SMAD SIGNALING PATHWAY

Purpose: The bone morphogenetic proteins (BMP) are members of the TGF-ß superfamily of growth factors. We have previously demonstrated that trabecular meshwork cells (TM) are capable of secreting BMPs and that BMP-4 selectively counteracts the action of TGF-ß2 in TM cells with respect to synthesis of extracellular matrix proteins. BMPs can signal via the Smad canonical pathway or via non-canonical pathways (e.g. p38). In the canonical pathway, signaling is activated upon ligand binding through serine/threonine kinase type I and type II receptors. This signal then recruits intracellular Smad proteins. Following the recruitment of common Smad 4, the signaling complex translocates into the nucleus to activate gene expression. The purpose of this study was to determine if cultured human TM cells (a) express Smad pathway proteins and (b) respond to exogenous BMP-4 via the Smad pathway.

Methods: Human TM cells (N=3) were grown until approximately 80% confluent and treated in a time dependent manner or at 48 hours with BMP-4 (20ng/ml) in serum free media. Untreated cell lines acted as controls. Western Blot analysis was used to demonstrate the presence of phosphorylated Smad1, total Smad1, Smad4, and Smad 5. Intracellular localization of Smad5, Smad6, Smad7, Smad4, phosphorylated Smad1 (pSmad1), phosphorylated Smad1,5,8 (pSmad1,5,8) was studied via immunocytochemistry.

Results: Western blot analysis demonstrated the presence of all Smad signaling proteins in human TM cells. Immunocytochemistry demonstrated the presence and increased expression of Smad7 and pSmad1,5,8 following 48 hours of BMP-4 treatment. Immunocytochemistry also demonstrated the presence of pSmad1, total Smad1, Smad4, and Smad5.

Conclusions: These studies demonstrate that human TM cells express proteins for the canonical Smad pathway and respond to exogenous BMP4. Since we have previously demonstrated that human TM cells secrete BMP-2, BMP-4 and BMP-5, it is possible that secreted BMPs act on TM cells via an autocrine signaling mechanism. (Alcon Research Ltd, Fort Worth, Texas 76107).

Sponsor: *Alcon Research Ltd, Fort Worth, Texas 76107*

706 *(Poster)*

Author: Adnan Dibas

Presenter: Ming-Hui Yang

Department: Pharmacology & Neuroscience

Classification: GSBS Student

A. Dibas., M. Yang, J. Bobich, T. Yorio. Pharmacology, University of North Texas Health Science Center at Fort Worth, TX 76107, Chemistry, Texas Christian University, 2800 S University Dr, Ft Worth TX, 76129

NEURONAL AQUAPORIN IN RETINAL GANGLION CELL-LINE AND HUMAN OPTIC NERVE: CHANGES UNDER HYPOXIA AND APOPTOSIS

Purpose: To test the presence of aquaporin in retinal ganglion cell-line RGC-5 and human optic nerve tissue and study changes in expression under hypoxic insults.

Methods: Changes in cell volume was assessed following excitation of fura-2-labeled cells at 360 nm. Western blotting using anti-aquaporin-9 antibodies was used to test the presence of neuronal AQP9 in RGC-5 cells and human optic nerve. Real-time PCR was used for measuring changes in AQP9 and beta-actin under hypoxia. Hypoxia was initiated by flushing a mixture of 95% N2 and 5% CO2 for 15 minutes in a controlled atmosphere culture chamber. Apoptosis assay was performed by measuring the levels of released mitochondrial cytochrome c in the cytosol.

Results: RGC-5 cells subjected to a hypotonic solution showed a decrease in fluorescence and swelling as a result of water influx, a response that was blocked by known inhibitors of AQP such as phloretin or cyano-hydroxycinnamic (40 mM) acid pretreatment. Western blotting detected the presence of a doublet AQP9 protein bands (33 and 50 KDa) in the plasma membrane fractions of both RGC-5 cells and human optic nerve. Interestingly, under hypoxia, there was an initial decrease in AQP9 (1hr) then up-regulation at 3-6 hr post hypoxia as judged by Western blotting and RT-PCR. Up-regulation of AQP9 was accompanied by the release of mitochondrial cytochrome c in the cytosol as judged by Western blotting.

Conclusions: This is the first report showing that retinal ganglion cells have neuronal aquaporin-9. Changes in AQP9 expression correlated with apoptosis of retinal ganglion cells suggesting a novel role in retinal ganglion cellular death.

Sponsor: *NIH11979*

707 *(Poster)*

Author: Zhaohui Wang

Presenter: Zhaohui Wang

Department: Cell Biology and Genetics

Classification: GSBS Student

Zhaohui Wang, T.J. Bartosh, Neeraj Agarwal, Rouel S. Roque Department of Cell Biology and Genetics, University of North Texas Health Science Center, 3500 Camp Bowie Blvd., Fort Worth, Texas 76107.

INHIBITION OF NRH2 EXPRESSION BY RETINAL PROGENITOR CELLS PREVENTS OXIDATIVE DAMAGE TO CULTURED RETINAL GANGLION CELLS

Purpose: Purpose: Neurotrophin receptor homologue 2 (NRH2) is a member of the tumor necrosis factor receptor superfamily that exhibits substantial sequence homology to the intracellular domain (ICD) of p75 neurotrophin receptor (p75NTR). Previous studies localizing p75NTR and NRH2 to retinal ganglion cells (RGC), findings of increased levels of p75NTR in degenerating RGC of animals with elevated intraocular pressure, and reports showing overexpression of p75ICD or NRH2 promoted neuronal apoptosis—were all consistent with a role for NRH2 in RGC degeneration. In the following study, the effects of oxidative stress on the survival and expression of NRH2 in RGC were investigated. Moreover, the effects of trophic factors from human retinal progenitor cells (hRPCs) on NRH2 expression and RGC degeneration were established.

Methods: . Methods: A hydrogen peroxide-generating culture system utilizing glucose oxidase/glucose was used to test the effects of oxidative stress on the survival and expression of NRH2 in RGC-5 cells, a well-characterized transformed rat retinal ganglion cell line. RGC-5 cells were grown in the above culture system in the presence or absence of 48h-conditioned media (CM) from hRPCs isolated from donor neonatal retinas. RGC-5 cell survival was determined by MTS assay and fluorescent dyes (calcein AM and ethidium homodimer); while JC-1 was used to determine mitochondrial membrane integrity. NRH2 expression was determined using immunological assays.

Results: Results: Increased expression of NRH2 was observed in RGC-5 following oxidative stress. Glucose oxidase/glucose treatment of RGC-5 resulted in a dose-dependent increase in cell death and increased mitochondrial membrane depolarization. CM from hRPCs inhibited RGC-5 cell death and collapse of mitochondrial membrane potential due to oxidative damage. Moreover, the CM inhibited altered expression of NRH2 in RGC-5 cells.

Conclusions: Conclusion: Our study shows that oxidative stress to retinal ganglion cells promoted increased expression of NRH2, increased mitochondrial membrane permeability, and retinal ganglion cell death. Moreover, human progenitor cells isolated from neonatal retinas secreted anti-apoptotic molecules that inhibited NRH2 changes and protected RGC from oxidative damage in vitro. Our study suggests that putative hRPC-derived trophic factors and NRH2 inhibitors could prove useful in neuroprotection of RGC from oxidative stress such as in glaucoma.

Sponsor: *N/A*

708 *(Poster)*

Author: Oloruntoyin Mafe

Presenter: Oloruntoyin Mafe

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

O. Mafe, E. Gregg, H. Xin, P. Mitchell, P. Koulen Pharmacology & Neuroscience, University of North Texas, Fort Worth, TX 76106

DISTRIBUTION OF POLYCYSTINS IN MOUSE RETINAL GANGLION CELLS

Purpose: The polycystins family of transient receptor potential(TRP)channels includes three homologous proteins, polycystin-2 (PKD2), polycystin-2LI (PKD2L1) and polycystin-2L2 (PKD2L2) which are found in invertebrates, mammals and humans. These proteins form Ca2+ regulated cation channels and have distinct subcellullar localizations and functions. As part of a multiprotein complex, polycystins control intracellular Ca2+ signals. At the gene level, polycystins are potentially expressed in the retina but their expression in retinal ganglion cells (RGCs) has not been fully established. PKD2L1 is believed to be predominant in the retina while PKD2 has been cloned from retina. In the present study, the distribution of PKD2, PKD2L1 and PKD2L2 in mouse retinal ganglion cells was determined to identify molecular substrates of how these proteins interact and regulate polycystin mediated Ca2+ signaling in these retinal interneurons.

Methods: Primary RGC cultures were prepared using acute isolation of neurons from adult mouse retinae by enzymatic and mechanical dissociation. Immunocytochemical labeling of PKD2, PKD2L1 and PKD2L2 in vivo and of cultured RGCs was carried out using specific antibodies and detected with fluorescence microscopy. RGCs were identified with specific immunocytochemical markers, neurofilament 68kDa, Thy 1.1 and Thy 1.2.

Results: RGC morphology and immunoreactivity to neurofilament 68 kDa and Thy 1.1 or Thy 1.2 were identified in both retinal ganglion cell primary cultures and tissue cryosections. RGCs express polycystins-2, polycystin-2LI and polycystin-2L2. Immunoreativity of PKD2 revealed a stronger staining throughout the cell whereas PKD2L1 and PKD2L2 were less strongly expressed but also found throughout RGCs.

Conclusions: Expression of all polycystins by RGCs indicate that these homologous proteins potentially play a role in RGC signaling. Differential distribution of polycystins in RGCs may suggest essential physiological and functional activity in the regulation of intracellular Ca2+ signaling in distinct regions of the RGCs.

Sponsor: *NIH*

709 *(Poster)*

Author: Hua Xin

Presenter: Hua Xin

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

Hua Xin, Jo-Ann S. Yannazzo, R. Scott Duncan, Elaine V. Gregg, Meharvan Singh, Peter Koulen University of North Texas Health Science Center, Department of Pharmacology & Neuroscience, Fort Worth, Texas 76107-2699

AN ORGANOTYPIC CULTURE MODEL OF THE POSTNATAL MOUSE RETINA ALLOWS THE STUDY OF GLUTAMATE-MEDIATED EXCITOTOXICITY

Purpose: A novel organotypic culture method of mouse retina explants is being introduced and characterized to evaluate its usefulness in studying glutamate excitotoxicity and further pharmacological applications.

Methods: Retinal whole mounts were dissected from eyes of C57BL/6 mice aged P10-14 and transferred to poly-D-lysine/laminin coated round coverslips. After 7 days in vitro, retina explants were treated with varying concentrations of L-glutamate and cell death was accessed with TUNEL histochemistry. Neurofilament-68 kDa immunoreactivity was used to identify retinal ganglion cells (RGC) with immunohistochemistry. Additional cell markers were used to further characterize the cytoarchitecture of the organotypic retina cultures.

Results: Retina explants attached very well to the coated coverslips allowing for experimental manipulation and pharmacological access to the tissue. Hematoxylin-Eosin (HE) staining of vertical cryostat sections of retina explants demonstrated well preserved intact cytoarchitecture under organotypic culture conditions and PKCa, Calbindin, GABA, Rhodopsin, GFAP and Neurofilament immunoreactivities identifying rod bipolar, horizontal, amacrine, photoreceptor, glial, and retinal ganglion cells, respectively, were not different from freshly isolated mouse retina. Dose dependant glutamate toxicity and accompanying RGC apoptotic cell death, were determined by TUNEL histochemistry.

Conclusions: The described retina explant culture on glass coverslips allows for effective pharmacological manipulation including the study of excitotoxicity and RGC physiology.

Sponsor: *N/A*

710 *(Poster)*

Author: Mallika Valapala

Presenter: Mallika Valapala

Department: Molecular Biology and Immunology

Classification: GSBS Student

Mallika Valapala, Nirupama Sabnis, and Jamboor K Vishwanatha, Department of Molecular Biology and Immunology and the Institute for Cancer Research, University of North Texas Health Science Center, Fort Worth, TX 76107

ROLE OF ANNEXIN II IN PROLIFERATION AND MIGRATION OF RETINAL GANGLION CELLS

Purpose: The goal of our project is to understand the basic mechanisms that regulate migration and proliferation of retinal cells and potential role of annexin II in controlling these mechanisms.

Methods: Immunocytochemistry followed by confocal microscopy was done in RGC-5, ARPE 19 and RPE cell lines using anti-annexin II antibody. Western immunoblot was performed with cell lysates of RGC-5, ARPE 19 and RPE to check the annexin II expression. mRNA expression of annexin II was determined using RT-PCR. sh-AnnexIIpDrive construct was transfected in RGC-5 cells. Cell migration assay performed with the transfected cells.

Results: Immunocytochemistry and confocal microscopy indicated that annexin II is predominantly expressed in the cytosol of RGC-5, RPE and ARPE-19 cells. However some nuclear staining was also observed. Western blot analysis showed annexin II protein at 38kDa in all the cell lines. RT-PCR showed mRNA expression of annexin II in the retinal cells. Transfection of sh-annexIIpDrive construct resulted in down regulation of endogenous annexin II.

Conclusions: The down regulation of annexin II resulted in significant reduction of cellular migration in RGC-5 cells. Further studies are directed towards the role of annexin II in retinal cell migration and invasion.

Sponsor: *N/A*

711 *(Poster)*

Author: Gulab Zode

Presenter: Gulab Zode

Department: Cell Biology and Genetics

Classification: GSBS Student

G.S. Zode, UNTHSC,Fort Worth, Tx-76106 A.F. Clark,Alcon Research Ltd., Fort Worth, TX. 76134 and R.J. Wordinger,UNTHSC,Fort Worth, Tx-76106

EXPRESSION AND SECRETION OF THE BMP ANTAGONIST PROTEIN GREMLIN BY HUMAN OPTIC NERVE HEAD CELLS

Purpose: Primary open angle glaucoma (POAG) is the second leading cause of blindness in the world. Elevated intraocular pressure (IOP) is the major risk factor in development of glaucomatous optic neuropathy. The optic nerve head shows characteristic cupping and excavation which is associated with increased extracellular matrix synthesis and deposition. Recent reports indicate that transforming growth factor (TGF-ß2) is involved in the pathogenesis of POAG. TGF-ß2 expression has been reported to be elevated in the glaucomatous optic nerve head (ONH) and appears to be associated with alterations in ECM protein synthesis and degradation. Gremlin is a BMP extracellular antagonist which prevents BMP from interacting with the receptor complex. The BMP signaling pathway can modify TGF ß signaling in several adult tissues. Previously, we reported that in glaucoma, elevated gremlin expression inhibited BMP-4 antagonism of TGF-ß2 leading to increased ECM deposition and elevated IOP. In diabetic nephropathy, gremlin is an important modulator of fibrosis and it has been suggested that high levels of TGF- ß1 induces gremlin. Similarly, in glaucoma, elevated levels of TGF-ß2 may induce gremlin expression that blocks BMP leading to increased stimulatory effect TGF- ß2 on ECM synthesis and deposition in the ONH. The purpose of this initial study was to demonstrate that gremlin is expressed in human ONH cells and human tissues.

Methods: Well-characterized human ONH astrocytes (N=3) and lamina cribrosa (LC) cells (N=3) were utilized. RT-PCR was used to demonstrate mRNA expression of gremlin. Western blot analysis was used to demonstrate gremlin protein levels in cell lysate and conditioned media. Immunostaining was used to localize gremlin in the ONH cells and human tissues

Results: Optic nerve head astrocytes and lamina cribrosa cells express mRNA and also make protein for gremlin. Optic nerve head astrocytes secrete gremlin in the conditioned media. Gremlin is localized to nucleus and cytoplasm of optic nerve head astrocytes and lamina cribrosa cells. Immunostaining on human tissues demonstrated gremlin expression in the optic nerve head.

Conclusions: This study demonstrates that cells isolated from the human ONH are capable of synthesizing and secreting gremlin. In addition, gremlin is expressed in human tissues. Secreted gremlin may function to antagonize the inhibitory effect of BMP-4 on TGF-ß2 activity in the human ONH.

Sponsor: *Alcon Research Ltd., Fort Worth, TX. 76134*

712 *(Oral)*

Author: Everett Nixon

Presenter: Everett Nixon

Department: Pharmacology & Neuroscience

Classification: GSBS Student

E. Nixon, A. Newsome, P. Koulen Department of Pharmacology and Neuroscience, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX

EXPRESSION OF CALCIUM SENSING RECEPTORS IN THE MOUSE RETINA

Purpose: Calcium Sensing Receptors (CaSR) are plasma membrane proteins and members of the family C of the G Protein Coupled Receptor (GPCR) superfamily. They have structural similarities to metabotropic glutamate receptors, GABAB receptors, and some putative pheromone/taste receptors. CaSR responds to changes in extracellular calcium (Ca2+) concentration and plays an important role in maintaining Ca2+ homeostasis. Ca2+ deregulation can lead to cell death, thus possibly playing a role in photoreceptor dysfunctions such as photoreceptor degeneration and/or age related macular degeneration. The release of neurotransmitter from neurons is triggered by Ca2+ entry in nerve terminals, while the intracellular signal transduction is regulated by Ca2+ release through the inositol 1,4,5-trisphosphate or the ryanodine receptor. CaSR may play a role in regulating these mechanisms by monitoring Ca2+ changes within the presynaptic region thus regulating the nerve terminals response to these Ca2+ changes. We hypothesized that CaSR is expressed by photoreceptors in their axon terminals, and that it may be co-localized with mGluR8.

Methods: Western blots of adult mouse retina tissue and immunohistochemistry of cryo-sectioned adult mouse retina was performed to determine the localization of mGluR8 and CaSR within the retina. Immunocytochemistry was also performed to show the co-localization of mGluR8 and CaSR in photoreceptor cells.

Results: Our results showed the expression of CaSR within the different layers of the retina, and indicate that mGluR8 and CaSR are co-localized in axon terminals of photoreceptor cells.

Conclusions: From these results we conclude that mGluR8 and CaSR can potentially interact functionally, and could play a role in photoreceptor physiology and neurotransmitter release within the retina.

Sponsor: *N/A*

713 *(Poster)*

Author: James Flynn

Presenter: James Flynn

Department: Cell Biology and Genetics

Classification: GSBS Student

James M. Flynn and Patrick R. Cammarata. Department of Cell Biology and Genetics, University of North Texas Health Science Center at Fort Worth. 3500 Camp Bowie Blvd. Fort Worth, Texas 76107

ESTRADIOL ATTENUATES MITOCHONDRIAL DEPOLARIZATION IN POLYOL STRESSED LENS EPITHELIAL CELLS

Purpose: Lens epithelium cultured in the presence of high extracellular aldoses convert these sugars, upon cellular uptake, to their respective sugar alcohols via the enzyme, aldose reductase (AR). This study examined the state of mitochondrial physiology subsequent to exposing lens epithelium to high ambient galactose (Gal), which upon conversion to galactitol (GalOH) and resultant intracellular accumulation thereof, leads to profound destabilization of mitochondrial membrane potential (MMP). Further, we determined whether the AR inhibitor, Sorbinil, or estrogen (17-beta-E2, and its isomer, 17-alpha-E2) added concomitant to Gal exposure might prevent loss of MMP.

Methods: Cultures of bovine lens epithelial cells (BLECs), as well as a human lens epithelial cell line (HLE-B3), were maintained in 40 mM Gal for up to 7 days in the presence and absence of either the AR inhibitor, 17-beta-E2 or 17-alpha-E2. Endogenous accumulation of reactive oxygen species (ROS) was assessed by loading cells with H2DCF-DA. To assess MMP, confocal microscopy was employed in conjunction with JC-1 staining. Polyol content was determined by gas chromatography.

Results: BLECs, more so than HLE-B3 cells, accumulate high intracellular levels of GalOH upon exposure to high ambient Gal. BLECs were significantly depolarized while HLE-B3 cells showed little to no depolarization. The addition of estrogen(s) to BLECs, over a dose range of 0.01 to 1.0 microM, completely prevented loss of MMP as did the addition of Sorbinil. Co-addition of Sorbinil prevented accumulation of GalOH; addition of either isoform of estrogen did not block GalOH synthesis. ROS accumulation of HLE-B3 cells from Gal exposure was negligible. Accumulation of ROS in Gal-maintained BLECs exhibited a marginal ROS increase and similar levels of ROS were generated irrespective of the presence of either Sorbinil or estrogen with Gal. Bolus addition of supraphysiological levels of H2O2 to Gal plus Sorbinil-maintained BLECs failed to induce a change in MMP.

Conclusions: This study establishes that polyol accumulation promotes MMP depolarization and that the loss of membrane integrity is prevented by addition of Sorbinil or estrogen with Gal. However, unlike Sorbinil, estrogens mode of action is not via the inhibition of AR activity. The failure of supraphysiological levels of hydrogen peroxide, added to Gal plus Sorbinil BLECs, to depolarize mitochondria indicates that polyol accumulation, not ROS generation mediates the stress.

Sponsor: *EY05570*

714 *(Poster)*

Author: Vidhya Rao

Presenter: Vidhya Rao

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Dr. Raghu Krishnamoorthy,UNTHSC,FortWorth,TX,76107 Dr. Thomas Yorio,UNTHSC, FortWorth,TX,76107

EXPRESSION OF ENDOTHELIN A AND ENDOTHELIN B RECEPTORS AND THEIR PHARMACOLOGICAL PROPERTIES IN HUMAN LAMINA CRIBROSA.

Purpose: Endothelin -1 (ET-1) is a potent vasoactive peptide. The aqueous humor and plasma levels of ET-1 are elevated in glaucomatous patients. Injection of endothelin-1 into rat eyes causes optic nerve damage similar to that seen in glaucoma. Previously our lab has characterized the expression of endothelin A (ETA) and endothelin B (ETB) receptors in human optic nerve head astrocytes. The purpose of this study was to determine the expression of endothelin receptors in GFAP negative Lamina cribrosa cells isolated from lamina cribrosa, the principle site of axonal transport block observed in POAG subjects.

Methods: Human lamina cribrosa cells were treated with 1nM, 10nM and 100nM of ET-1 for 24 hrs. Total RNA was isolated and cDNA synthesized. ETA and ETB receptor mRNA was analyzed using reverse transcription-polymerase chain reaction (RT-PCR). Total protein lysates of lamina cribrosa cells treated with 1nm, 10nM & 100nM for 24 hrs were separated on a 7.5 % SDS PAGE gel and expression of endothelin A and endothelin B receptors determined by Western blot using anti ETA and anti ETB receptor antibodies. ET -1 mediated intra-cellular calcium changes in the presence of 1, 10 & 100nM of ET-1, 1uM BQ788 an ETB selective antagonist and 1uM BQ123 an ETA selective antagonist were measured using Fura-2 calcium imaging. ET-1 mediated intra cellular calcium levels was also measured following ET-1(100nM) treatment for 24 hrs.

Results: Expression of both message and protein of ETA and ETB receptor were detected in human lamina cribrosa cells. The message and protein levels of ETA receptor were down regulated following treatment with ET-1 for 24 hrs. An upregulation of ETB receptor was observed following ET-1 treatment for 24 hrs. Increase in intracellular calcium was observed in a dose dependent manner with a greater increase at 100nM. The increase in intra cellular calcium was blocked by ETA specific inhibitor BQ123 but not by ETB specific inhibitor BQ788. The LC cells treated with ET-1 overnight failed to show an increase in intra cellular calcium levels when retreated with ET-1.

Conclusions: Human lamina cribrosa cells express functional ETA and ETB receptors and their expression and function can be altered in response to prolong exposure to ET-1. This may have an implication in the normal physiology of Lamina Cribrosa cells in POAG subjects where elevated plasma and aqueous humor levels of endothelin-1 have been detected.

Sponsor: *N/A*

715 *(Poster)*

Author: Amber Ondricek

Presenter: Amber Ondricek

Department: Cell Biology and Genetics

Classification: GSBS Student

Amber Ondricek, UNT Health Science Center, Fort Worth, TX, 76116

MECHANISMS OF MITOCHONDRIA ASSOCIATED RAT RETINAL GANGLION CELL DEATH: PRELIMINARY STUDIES

Purpose: Glaucoma exists in several etiologies, all of which include gradual neuronal degeneration and the eventual loss of vision. It is now widely believed that this loss of vision can be attributed to the apoptosis of retinal ganglion cells (RGC). The apoptosis of RGCs has been observed in rat and monkey laboratory models of glaucoma as well as in humans with primary open angle glaucoma. The actual stimulus for apoptosis of retinal ganglion cell death in glaucoma is currently not well understood. Iodoacetic acid (IAA) is a mitochondrial uncoupling agent. The purpose of this project is to create a suitable in vitro model of apoptosis in transformed cultured RGCs that would allow us to study the signaling pathways involved in apoptotic RGC death.

Methods: Transformed rat retinal ganglion cells (RGC-5) were grown in 24 well tissue culture dishes and treated with varying concentrations of IAA from 2 to 10 μM for a period of 24 hours. Antioxidants N-Acetyl Cysteine (2mM) and Thiourea (10mM) were administered along with IAA. Survival was assessed by the uptake of neutral red dye in two hours, which was quantified with spectrophotometry at 570 nm. Morphological changes were assessed by microscopy.

Results: There was a dose dependent loss of cell viability by IAA treatment of RGC-5 cells. IAA insult produces 50% cell death in RGC5s at 6 μM concentration of IAA. Antioxidants such as N-Acetyl Cysteine (2mM) and Thiourea (10mM) rescued RGCs from cell death.

Conclusions: IAA is cytotoxic to RGCs. The rescue by the presence of exogenous antioxidants from cell death of RGCs leads us to believe that IAA cytotoxicity involves oxidative stress, which activates mitochondrial dependent apoptotic pathways.

Sponsor: *N/A*

716 *(Poster)*

Author: Jwalitha Shankardas

Presenter: Jwalitha Shankardas

Department: Graduate School of Biomedical Sciences

Classification: GSBS Student

Jwalitha Shankardas,Graduate School of Biomedical Sciences,UNTHSC, Fort Worth,TX-76012 Dan.S.Dimitrijevich, Department of Integrative Physiology,UNTHSC, Fort Worth,TX-76012

DEFINING THE HUMAN CORNEAL EPITHELIAL STEM CELL NICHE

Purpose: Our harvesting and culture conditions provide putative corneal epithelial stem cells and partially preserve the proliferation capacity. Current objectives are to gain better understanding of the stem cell niche and implement of its defining factors in vitro. Specifically, understanding of the basement membrane requirements, cell-cell communications and the role of nutrients (EGF and calcium) is needed. Our corneal epithelial cell line that ectopically expresses hTERT is being used as a model of stem cell proliferation/ differentiation characteristics.

Methods: Cells(WT), from donor corneas, were cultured in serum free defined medium (EPILIFE). Cell proliferation (population doublings, pdl), on collagen type IV(CIV) and fibronectin(fnc) coated surfaces, and on plastic, were determined. The dose responses to calcium (0-1.6mM) and EGF (0-30ng/ml) were determined using SRB assay. Western blot analysis and Indirect immun-fluorescence were used to determine the expression of cell cycle related proteins (p53, pRb, p63, p16, p21, and hTERT) and differentiation markers (cytokeratins(CKs) 1-8, 9-20, CK3/12) in cultured cells and whole epithelium lysates. Cells were also subjected to FACS analysis to determine cell size.

Results: A higher pdl was obtained on CIV. p63 is expressed throughout the epithelium and the expression of its various isoforms varies with passage, but is uniform in hTERT cell line. WT cells express the CKs in groups 1-8 and 9-20. hTERT cells did not express CK 3/12. p16 expression increases and with passage in WT cells. P53 and pRb are intact in both the cell types. While calcium was mitogenic to wild type cells (up to 0.4mM), but not for hTERT cells, EGF had very little effect . The putative corneal stem cells are smaller in size than other cells present in the corneal epithelium.

Conclusions: CIV is a necessary basement membrane component for the preservation of □stemness. WT cells can undergo at least 16 population doublings on CIV but less on other surfaces; this correlates with the increased expression of p16. P63 is not a corneal epithelial stem cell marker. hTERT cells and the putative stem cells appear to be independent of EGF concentration and require very low extracellular calcium. hTERT cells are a good model of corneal limbal stem cells w.r.t size and expression of p53, pRb and and CKs. FACS sorting on the basis of cell size is an an easy method for isolating a pure population of stem cells from the adult corneal epithelium.

Sponsor: *Alcon Laboratories (JS), Global Medical Research (SDD), and American Eye Bank Association.*

717 *(Poster)*

Author: John Fuller

Presenter: John Fuller

Department: Cell Biology and Genetics

Classification: GSBS Student

John A Fuller 1, Abbot F. Clark1 2, Robert J. Wordinger 1 1Department of Cell Biology & Genetics UNT Health Science Center, Fort Worth, TX 76107 2 Alcon Research Ltd. Fort Worth, TX 76116

PRONEUROTROPHIN SECRETION AND PROCESSING IN THE RETINA AND OPTIC NERVE HEAD

Purpose: The mechanism for retinal ganglion cell (RGC) death in glaucoma is unknown. Recent studies have demonstrated that proneurotrophins are capable of elicting apoptosis via the p75NTR neurotrophin receptor, and are a possible cause of cell death in a variety of neurodegenerative conditions. We have previously demonstrated expression and secretion of neurotrophins from human optic nerve astrocyte cultures. We have also demonstrated that cultured ONH astrocytes are positive for the Trk A neurotrophin receptor, but are negative for p75NTR. However, immunohistochemistry of human retina has demonstrated intense staining p75NTR in the ganglion cell layer. The purpose of this study is to treat primary adult retinal ganglion cells with recombinant native and mutant proNGF to assess bioactivity and cell viability.

Methods: The open reading frame encoding human ß-NGF was inserted into the pIEX-3 insect expression system. Site-directed mutagenesis was used to disrupt the prodomain cleavage site by mutating the dibasic KR residues to AA or RG. Mutagenesis was confirmed by restriction digestion and sequencing. Protein expression was performed by cationic lipid transfection of Sf9 cells, and was purified from conditioned media 48 hrs later. Adult porcine retina obtained from a local abbatoir was triturated and cultured in modified Neurobasal-A supplemented with neurotrophic factors. Viability was assessed with a Calcein AM/SYTOX green stain 1 week after culture.

Results: Western blot analysis demonstrates that Sf9 cells are capable of secreting soluble rh proNGF into the conditioned media. Cultured adult porcine neurons are viable up to 1 week in culture

Conclusions: We have developed a method for producing soluble native and cleavage resistant proNGF. This method allows for a means of rapid transfection and downstream purification of bioactive neurotrophins which will be used in conjunction with a method of culture of adult retinal neurons for assessment of viability upon proneurotrophin treatment.

Sponsor: *N/A*

800 *(Poster)*

Author: Roberto Cardarelli

Presenter: Roberto Cardarelli

Department: Family Medicine

Classification: Faculty

Roberto Cardarelli, DO, MPH; Assistant Professor, and Executive Network Director, NorTex; Department of Family Medicine, UNTHSC, Fort Worth, TX 76107 Carol Knisley, Senior Network Editorial Assistant and Head of Membership and Communication, Department of Family Medicine, UNTHSC, Fort Worth, TX 76107

NORTEX: PRELIMINARY RESULTS OF THE PRIMARY CARE CLINICAL DEMOGRAPHIC SURVEY STUDY (CDSS)

Purpose: The primary descriptive study is the Clinical Demographic Survey Study that portrays the characteristics of the clinicians, population, and resources of NorTex members. This information is used for grant applications and to identify clinics and members that are suited for potential research projects.

Methods: Members continue to join on a daily basis and surveys are continually being received. This data represents characteristics of NorTex members and population from February 2005 to October 2005.

Results: In February 2005, the North Texas Primary Care PBRN (NorTex) was created to answer the need for a primary care research network in North Texas. Housed in the Department of Family Medicine of the Texas College of Osteopathic Medicine, NorTex has grown to involve 51 clinics and 105 members. Members continue to join on a daily basis and surveys are continually being received. This data represents characteristics of NorTex members and population from February 2005 to October 2005.

Conclusions: Practice-based research networks (PBRNs) have been in existence since the 1970s after the realization by Drs. Nutting and Green that research conducted in tertiary medical centers had limited application to the primary care setting. Obstacles to conduct research in the primary care setting include time limitations of the clinician, the length of time to collect sufficient data at one or few clinic sites, and the limited research experience of the clinician. To overcome these limitations and obstacles, a group of experienced research clinicians in Colorado recruited a coalition of clinics to conduct relevant primary care research. The focus was to conduct research without disrupting the clinical practice and to recruit patients in a timely manner so studies can be turned-over.

Sponsor: *N/A*

801 *(Poster)*

Author: Ana Chiapa

Presenter: Ana Chiapa

Department: Family Medicine

Classification: SPH Student

Ana Chiapa,MS, Department of Family Medicine, University of North Texas Health Science Center, Fort Worth, TX 76107; Roberto Cardarelli, DO, MPH, Department of Family Medicine, University of North Texas Health Science Center, Fort Worth, TX 76107, Kathryn Cardarelli, Department of Epidemiology, University of North Texas Health Science Center, Fort Worth, TX 76107

CLINICAL AND PSYCHOLOGICAL FACTORS AFFECTING MAMMOGRAPHY SCREENING IN HISPANIC WOMEN

Purpose: According to the National Healthcare Disparities Report, minority women are less likely to receive breast cancer screening services. Mammography screening is important because it reduces the chances of mortality by detecting breast cancer at an early stage and treatment is most effective. Although socioeconomic status, insurance status, and usual source of care account for much of the differences in minority women, Hispanic women who are less acculturated, and who are immigrants are less likely to receive these screenings. Although there have been studies that have reported a relationship between language and access to health care, few studies have looked at psychosocial factors affecting the decision-making process of the patient, specifically patient-provider communication, social support, and sense of control. The purpose of this study is to examine the differences in interpersonal processes of care, social support, and sense of control between English speaking and non-English speaking Hispanic women and analyze the relationship of these factors to obtaining a mammogram.

Methods: The design of this study is a cross-sectional survey. Participants for this study will be Hispanic women over the age of 40 who have received a mammography order from their physician, or who have ever received a mammogram. Participants will be recruited from University of North Texas Health Science Center Family Medicine clinics. Measurements: This study will use a demographic questionnaire, the Interpersonal Processes of Care measure by Stewart et al., and Social Support Scale, and Sense of Control by Mirowsky and Ross. The outcome variable for this study will be mammogram attainment dichotomized as yes/no responses.

Results: Univariate and bivariate analysis will be performed to assess for differences between the outcome measure and the independent variables of interest. A multivariate logistic regression will be performed controlling for age, education level, country of origin, and years of residency in the U.S. The regression will look at association between groups (English-speaking, vs non-English speaking) and mammography attainment outcome.

Conclusions: The results of this study can direct efforts in improvement of communication between Hispanic women patients and their doctors in order to have better health outcomes. The study will also provide an understanding of how psychosocial factors such as social support and sense of control impact Hispanic womens health.

Sponsor: *N/A*

802 *(Oral)*

Author: Jotam Pasipanodya

Presenter: Jotam Pasipanodya

Department: School of Public Health

Classification: SPH Student

Pasipanodya, J.G.1,2, Miller, T.L.1,2, Vecino, E.M.,1,3, Munguia, G.,1,3, Bae S., 2 Garmon R 1., Weis, S.E.,1,3 1. Department of Medicine, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX; 2. School of Public Health, University of North Texas Health Science Center at Fort Worth Fort Worth, TX; 3. Tarrant County Health Department, Fort Worth, TX

PULMONARY DYSFUNCTION SECONDARY TO TREATED TUBERCULOSIS

Purpose: Patients who complete TB treatment can be left with severe respiratory disability due fibro-cavitary lung disease. The frequency and extent of these sequalae have not been established, but their impact on TB patients is often apparent to clinicians. We conducted a prospective case/control study to measure residual lung impairment in pulmonary tuberculosis (PTB) patients completing standard therapy

Methods: A prospective case/control study was conducted on subjects with culture confirmed tuberculosis in Tarrant County, Texas. Pulmonary function tests were done after at least 20 weeks of treatment for patients with culture confirmed pulmonary tuberculosis. A case was defined as a patient with culture confirmed pulmonary TB. Persons with extra-pulmonary tuberculosis and randomly selected persons with latent tuberculosis served as controls. Pulmonary function test (PFT) was conducted in the normal fashion using Spirometry. A standard questionnaire was used to obtain demographic information, occupational, smoking, and medical history. Informed written consent was obtained, and the study was approved by the Institutional review Board.

Results: Sixty five consecutive patients with pulmonary TB who had 5 months or greater of treatment and 117 controls, with mean ages 46, and 43, respectively were evaluated between July 2005 and February 2006. Demographic characteristics of subjects with latent tuberculosis (LTBI), Extra-pulmonary TB and PTB were generally similar. There was no statistical difference in the proportion of smokers or pack-years between the cases and the controls. Fifty two percent of the cases had some impairment compared to only 16% among the control, p 25% loss of pulmonary function). Non-foreign born cases were 12.5 times more likely to be impaired than Non-foreign born controls. . After controlling for risk factors including smoking status, U.S born cases were 38.5 (7.35, 200) times more likely to have some pulmonary impairment than controls. There was no difference in impairment status for foreign cases versus controls after controlling for the risk factors. The dysfunction was obstructive and restrictive pattern.

Conclusions: Pulmonary tuberculosis results in frequent pulmonary dysfunction. This provides evidence that interventions designed to prevent tuberculosis have been undervalued relative to those intended to cure tuberculosis.

Sponsor: *N/A*

803 *(Poster)*

Author: Jotam Pasipanodya

Presenter: Jotam Pasipanodya

Department: Department of Health Management and Policy

Classification: SPH Student

Pasipanodya, J.G.1,2, Miller, T.L.1,2, Vecino, E.M.,1,3, Munguia, G.,1,3, Bae S., 2 Garmon R 1., Weis, S.E.,1,3 1. Department of Medicine, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX; 2. School of Public Health, University of North Texas Health Science Center at Fort Worth Fort Worth, TX; 3. Tarrant County Health Department, Fort Worth, TX

PULMONARY DYSFUNCTION SECONDARY TO TREATED TUBERCULOSIS

Purpose: Patients who complete TB treatment can be left with severe respiratory disability due fibro-cavitary lung disease. The frequency and extent of these sequalae have not been established, but their impact on TB patients is often apparent to clinicians. We conducted a prospective case/control study to measure residual lung impairment in pulmonary tuberculosis (PTB) patients completing standard therapy

Methods: Pulmonary function tests were done after at least 20 weeks of treatment for patients with culture confirmed pulmonary tuberculosis. A case was defined as a patient with culture confirmed pulmonary TB. Persons with extra-pulmonary tuberculosis and randomly selected persons with latent tuberculosis served as controls. Pulmonary function test (PFT) was conducted in the normal fashion using Spirometry. The American Medical Association guidelines were used to determine impairment. A standard questionnaire was used to obtain demographic information, occupational, smoking, and medical history. Informed written consent was obtained, and the study was approved by the Institutional Review Board.

Results: Sixty five consecutive patients with pulmonary TB who had 5 months or greater of treatment and 117 controls, with mean ages 46, and 43, respectively were evaluated between July 2005 and February 2006. Demographic characteristics of subjects with latent tuberculosis (LTBI), Extra-pulmonary TB and PTB were generally similar. The prevalence of HIV infection among the subjects with LTBI, EP-TB and PTB was 6.5, 15.8 and 10.9%. There was no statistical difference in the proportion of smokers or pack-years between the cases and the controls. Fifty two percent of the cases had some impairment compared to only 16% among the control, p 25% loss of pulmonary function). Non-foreign born cases were 12.5 times more likely to be impaired than Non-foreign born controls. After controlling for risk factors including smoking status, U.S born cases were 38.5 (7.35, 200) times more likely to have some pulmonary impairment than controls. The dysfunction was obstructive and restrictive pattern.

Conclusions: Pulmonary tuberculosis results in frequent pulmonary dysfunction. This is an important previously unmeasured sequelae of tuberculosis. This provides evidence that interventions designed to prevent tuberculosis have been undervalued relative to those intended to cure tuberculosis.

Sponsor: *N/A*

804 *(Poster)*

Author: Angela Brimhall

Presenter: Angela Brimhall

Department: Family Medicine

Classification: Dual Degree Student DO/MS

Angela K. Brimhall, Department of Family Medicine, Texas College of Osteopathic Medicine and Graduate School of Biomedical Sciences, University of North Texas Health Science Center, Fort Worth, Texas, 76107; Heidi Jacobe, Department of Dermatology, The University of Texas Southwestern Medical Center, Dallas, Texas 75390; Alan Menter, Chief of Dermatology, Baylor University Medical Center, Dallas, Texas, 75246; John Licciardone, Osteopathic Research Center, Texas College of Osteopathic Medicine, University of North Texas Health Sciences Center, Fort Worth, TX, 76107; Linda N. King, Gibson D. Lewis Health Science Library, University of North Texas Health Science Center, Fort Worth, TX, 76107, and Carlson Health Sciences Library, University of California, Davis, CA 95616.

META-ANALYSIS OF EFFICACY AND SAFETY OF ALEFACEPT, EFALIZUMAB AND ETANERCEPT FOR PSORIASIS

Purpose: This study is a systematic literature review using meta-analysis to analyze the efficacy and safety of three biologic therapies for psoriasis: alefacept, efalizumab, and etanercept. This work represents the first independent summary of industry sponsored clinical research that led to the recent approved of biologic treatments for psoriasis.

Methods: Systematic literature searches were performed independently for each biologic using structurally identical search strategies. The Cochrane Handbook for Systematic Reviews of Interventions 4.2.4 guidelines was utilized in searching MEDLINE and other databases. Thereafter, titles, abstracts and full reports were screened to select randomized, controlled, double-blind, mono-therapy trials. Reports were selected independently by the two senior authors.

Results: The results for both efficacy and safety are reported quantitatively as relative risk (RR) and graphically as Forrest Plots. Data from a total of 10 trials including 4,798 patients was compiled: 1,639 alefacept patients, 1,603 efalizumab patients, and 1,556 etanercept patients. The RR for achievement of 75% improvement in PASI (PASI 75) for alefacept was 3.83 (p=.001), for efalizumab 9.22 (p=.001), and for etanercept 13.83 (p=.001). Patients in the efalizumab treatment group reported at least one adverse event (AE) 148% more often than patients in the placebo group (p=.001). Similarly, serious adverse events (SAEs) were reported 334% more often in the efalizumab group compared to the placebo group (p=.017). AEs were not reported consistently across trials of alefacept and etanercept making conclusions difficult.

Conclusions: This analysis of 10 randomized controlled trials with a total of 4,798 patients further validates the efficacy of alefacept, efalizumab, and etanercept for the treatment of psoriasis. Concern regarding the omission of pertinent safety data from clinical trial reports of alefacept and etanercept and previously unreported statistically significant increases in SAEs and AEs in Efalizumab is raised. In the absence of head-to-head clinical trials, meta-analysis is a useful tool for indirect comparison and uncovering statistically significant low frequency safety events.

Sponsor: *N/A*

900 *(Poster)*

Author: Karen Meeks

Presenter: Karen Meeks

Department: Molecular Biology and Immunology

Classification: GSBS Student

Amy Sieve, Joshua Balch, and Rance Berg. Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, TX 76107.

LIVE VERSUS HEAT KILLED BACTERIA DIFFERENTIALLY STIMULATE THE SECRETION OF INFLAMMATORY CYTOKINES

Purpose: Interferon gamma (IFN-gamma) is a pro-inflammatory cytokine secreted by Natural Killer (NK) and T cells. Together, interleukin (IL) -12 and IL-18 are known to induce the secretion of IFN-gamma, which is critical for the host response against the gram positive bacterium, Listeria monocytogenes (LM). We hypothesize that IL-12 and IL-18 are secreted by macrophages (macs) and dendritic cells (DCs) that are infected with live LM.

Methods: B6 mouse bone marrow (BM) was cultured for 6-8 days in the presence of either macrophage colony stimulating factor (M-CSF) or granulocyte macrophage colony stimulating factor (GM-CSF). We found that BM cultured with M-CSF express a mac cell surface phenotype and BM cultured with GM-CSF express a DC cell phenotype. The cultured BM cells were stimulated with IFN-gamma and LPS (IFN-gamma + LPS) or infected with LM or heat-killed LM (HKLM). The BM cells were then stained intracellularly for IL-12 or co-cultured with B6 splenocytes. The splenocytes were stained for intracellular expression of IFN-gamma. IL-12 and IFN-gamma secretion was measured on an individual cell basis using flow cytometry.

Results: The macs and DCs were found to be capable of secreting IL-12 after infection with LM, HKLM, or after stimulation with IFN-gamma + LPS. Interestingly, after a co-culture with splenocytes, the HKLM and IFN-gamma + LPS stimulated macs and DCs failed to induce the splenocytes to secrete IFN-gamma. Both macs and DCs infected with LM were able to induce IFN-gamma secretion in the responding splenocytes. By adding back IL-18 or IL-12 into the co-culture, we were able to demonstrate that the addition of IL-18 was capable of inducing IFN-gamma in the splenocytes responding to the HKLM and IFN-gamma + LPS stimulated BM cells.

Conclusions: As demonstrated by our flow cytometry data, BM infected with HKLM are able to secrete IL-12. However, when co-cultured with splenocytes, the BM cells infected with HKLM or stimulated with IFN-gamma + LPS did not induce IFN-gamma secretion. We believe that the macs and DCs infected with live LM are able to secrete both IL-12 and IL-18 in response to the escape of the bacterium into the cytoplasm. On the other hand, HKLM do not escape the phagosome, which may explain why they are unable to induce IL-18 secretion. We postulate that the secretion of IL-12 and IL-18 are controlled in separate fashions; IL-12 can be induced by cell surface or phagosomal recognition, while the secretion of IL-18 requires cytoplasmic bacterial recognition.

Sponsor: *K22-AI064592-01*

901 *(Poster)*

Author: Evgenia Matveeva

Presenter: Anne Barnett

Department: Molecular Biology and Immunology

Classification: GSBS Student

*Evgenia Matveeva *+, Ignacy Gryczynski *,#, Anne Barnett *,^ Joseph R. Lakowicz +, Shashank Bharill*, and Zygmunt Gryczynski *. * UNTHSC, Dept of Molecular Biology and Immunology, Fort Worth, TX 76107 + Univ of Maryland at Baltimore, Dept of Biochemistry and Molecular Biology, Baltimore, MD 21201 # UNTHSC, Dept of Cell Biology and Genetics, Fort Worth, TX 76107 ^ Macquarie Univ, Dept of Physics, North Ryde, NSW 2019, Australia*

METAL PARTICLE ENHANCED FLUORESCENT IMMUNOASSAYS ON METAL MIRRORS

Purpose: To determine whether a mirror surface can improve the signal enhancement by SIFs for a surface immunoassay.

Methods: The following methods were required to successfully perform the experiments. Silver island films (SIFs) were formed on glass slides pre-coated with a thin metal (☐mirror) layer via chemical reduction of silver ions. A model immunoassay was conducted using rabbit IgG, non-covalently immobilized on the ☐sample (SIF) slide, or goat IgG on the ☐control (no SIF) slide. Dye-anti-rabbit IgG conjugate was added to the sample slide or control slide. Myoglobin immunoassays were performed using a ☐sandwich format . The slides were non-covalently coated with capture anti-myoglobin (anti-Myo) antibody. Myoglobin antigen (Myo) was added at various concentrations, and after incubation and washing a conjugate of the reporter anti-Myo antibody with one of two different fluorescent labels, Rhodamine Red-X or Alexa Fluor-647. Atomic Force Microscope (AFM) images were collected from dry slides.

Results: Our results showed that SIFs alone (on glass surface not coated with metal) enhance the immunoassay signal approximately 3 to 10-fold. Using a thin metal layer deposited on glass as support for SIFs leads to up to 50-fold signal enhancement.

Conclusions: Combination of SIF coating and metal mirror surface leads to improvement of the surface immunoassay, namely, further enhancement of the fluorescence signal (from labeled bound antibody) up to 50-fold if compared to non-SIF modified non-mirrored surface.

Sponsor: *N/A*

902 *(Poster)*

Author: Lisa Hodge

Presenter: Lisa Hodge

Department: Molecular Biology and Immunology

Classification: Faculty

Lisa Hodge, Arthur Williams, T.J. Belavadi, Jerry Simecka, Scott Stoll and Fred Downey. The University of North Texas Health Science Center

LYMPHATIC PUMP TREATMENT INCREASES LEUKOCYTE NUMBERS IN THORACIC DUCT LYMPHATIC FLUID

Purpose: Our long range goal is to evaluate the effectiveness of osteopathic manipulative therapy (OMT) at enhancing the immune response during immmunization and infection. In this study, the thoracic duct was isolated so the immediate effects of lymphatic pump on leukocyte output could be measured.

Methods: Five adult, mongrel dogs were anesthetized with sodium pentobarbital (30 mg/kg, i.v.). After intubation, the dogs were ventilated to maintain normal arterial blood gases. Arterial blood pressure was monitored through a catheter inserted into a femoral artery. A catheter was inserted into a femoral vein for administration of supplementary anesthetic and fluids. A left thoracotomy was performed, and the thoracic lymph duct was isolated, catheterized, and allowed to drain freely. Lymph flow was measured by timed collection and lymph was collected over ice under 1) resting (control) conditions, 2) during application of the osteopathic abdominal lymphatic pump procedure.

Results: Baseline leukocyte numbers were 1.7 x 10^6 cells/ml, while lymphatic pump manipulation significantly increased ($p < 0.05$) leukocyte numbers in the lymphatic fluid to 6.2 x 10^6 cells/ml. Flow cytometry and differential cell staining revealed macrophages, neutrophils, lymphocytes, T cells and B cells were significantly enhanced ($p < 0.05$) during LPT. In addition, LPT enhanced lymphatic flow rate approximately five-fold (2.7 ml/min) compared to the baseline lymphatic flow rate (0.5 ml/min). By combining the total cells per ml with the lymphatic flow rate per min, LPT significantly enhanced ($p < 0.05$) total cells from 0.75 x 10^6 total cells per minute to 17 x 10^6 cells per minute.

Conclusions: Previous studies only measured leukocyte increases in peripheral blood. We have demonstrated that lymphatic pump manipulation increases leukocyte numbers in lymphatic fluid during treatment, suggesting that lymphatic pump increases leukocyte output via the lymphatic system, which then releases these cells into peripheral blood circulation.

Sponsor: *NIH grant U19 AT2023-01*

903 *(Poster)*

Author: Anthony Chuang

Presenter: Anthony Chuang

Department: Molecular Biology and Immunology

Classification: GSBS Student

Anthony Chuang, Xiangle Sun, and Jerry W. Simecka Department of Microbiology and Immunology, University of North Texas Health Science Center, Fort Worth, TX 76107

A QUANTITATIVE APPROACH TO EXAMINE CYTOKINE MRNA ASSOCIATED WITH DENDRITIC CELLS AND MACROPHAGES DURING MYCOPLASMA PULMONIS INFECTION

Purpose: The objective of this project is to establish a method to quantify the number of copies of cytokine mRNA associated with dendritic cells and macrophages during mycoplasma infection.

Methods: An assay will be developed that will consist of developing a standard curve which will be used to normalize data from real time polymerase chain reaction (PCR) studies of specific cytokines. The curve is generated by isolating messenger RNA (mRNA) from CD1 mouse cells and converting them to complementary DNA (cDNA) using the enzyme reverse transcriptase. PCR is then used to amplify the cDNA as well as the gene of interest. This gene is ligated into the Invitrogen pCR 2.1-TOPO vector and transformed into Escherichia coli (E. coli cells). Plasmids from specific colonies of E. coli are isolated and then digested using the restriction enzyme EcoRI, to confirm the presence of the gene. Once confirmed serial dilutions of the cloned DNA containing the desired gene are carried out to generate the standard curve. Cytokines that will be studied using this assay will include interleukin-4 (IL-4), interleukin-10 (IL-10_, interleukin-12 (IL-12), and gamma-interferon (IFN-y). In addition, the assay will quantify the number of copies of mycoplasma genome associated with these cytokines.

Results: A housekeeping gene, glyceraldehyde-3 phoshphate dehydrogenase (GAPDH), has been amplified, ligated into the Invitrogen pCR 2.1-TOPO vector, and transformed into E. coli cells. Colonies were selected and their plasmids isolated and digested using EcoRI to confirm presence of the GAPDH gene. The gene will be sequenced and serial dilutions will be carried out to create the standard curve for GAPDH.

Conclusions: Because the standard for the housekeeping gene GAPDH has been established, we expect to use this same assay to develop standards for the Mycoplasma pulmonis genome and cytokines IL-4, IL-10, IL-12, and IFN-y. The quantitative data obtained using this assay will ultimately aid in further understanding the role of dendritic cells and macrophages during mycoplasma infection. (Work supported for by a grant from NIH #1R01HI069431-01A2)

Sponsor: *NIH #1R01HI069431-01A2*

904 *(Poster)*

Author: Sheetal Bodhankar
Presenter: Sheetal Bodhankar
Department: Molecular Biology and Immunology
Classification: GSBS Student
Sheetal Bodhankar(1), Matthew D. Woolard(2)and Jerry W. Simecka(1) (1) Department of Microbiology and Immunology, University of North Texas Health Science Center, Fort Worth, TX 76107 (2) Department of Microbiology and Immunology, University of North Carolina, Chapel Hill, NC 27599

DEPLETION OF NK-LIKE CELLS PRIOR TO IMMUNIZATION RESULTS IN ENHANCED PROTECTIVE LYMPHOCYTE RESPONSES AGAINST MYCOPLASMA PULMONIS INFECTION

Purpose: A complex regulatory balance between the detrimental and beneficial effects of immunity determines the course of mycoplasma infection. On going studies suggest that IFN-gamma is critical in controlling the level of mycoplasma infection in the respiratory tract. NK cells are the major source of IFN-gamma, early in mycoplasma infection and NK-like cells have a novel role in generation of innate immunity. The purpose of this study was to identify the role of NK-like cells on the development of protective adaptive immunity against mycoplasma respiratory disease. We hypothesize that NK-like cells have a detrimental role in the development of protective adaptive immunity against mycoplasma infection.

Methods: The experimental mice were injected with rabbit anti-asialo GM1 antibody to transiently deplete NK-like cells prior to nasal-pulmonary immunization with mycoplasma membrane antigen. Sham immunized mice and mice receiving only anti-asialo GM1 antibody served as controls in this study. This treatment was repeated after 7 days and a week after second immunization, mice were challenged with 105 colony forming units (CFU) of M. pulmonis. CFU numbers in lungs and nasal passages were determined 3, 7 and 14 days later.

Results: There was a significant decrease ($p = 0.05$) in CFU numbers in the lungs and nasal passages of the NK-like cell depleted, immunized mice when compared to immunized and control mice at all time points. Correspondingly, there was a significant increase in the mycoplasma-specific serum IgG2a and IgG1 responses after immunization in NK-like cell depleted mice as compared to the other groups. However, after infection there were no differences in antibody titers. There were greater IFN-gamma and IL-4 mycoplasma specific responses from splenocytes collected from NK-like cell depleted mice in-vitro. To demonstrate depletion of NK-like cells prior to immunization resulted in enhance lymphocyte mediated protection, lung lymphocytes obtained from immunized mice were adoptively transferred to naïve mice and 14 days after infection, CFU numbers were determined. There was greater protection against mycoplasma infection in mice that received receiving lymphocytes from NK-like cell depleted, immunized mice.

Conclusions: In conclusion, NK-like cells dampen the generation of protective adaptive immunity in the lungs and nasal passages associated with nasal-pulmonary immunization, and this appears to be a lymphoid cell mediated response.

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905 *(Poster)*

Author: Marcia Spear
Presenter: Marcia Spear
Department: Molecular Biology and Immunology
Classification: GSBS Student
Marcia Spear, Xavier Gonzalez, Mark Pulse, and Harlan P. Jones Department of Microbiology and Immunology, University of North Texas Health Science Center, Fort Worth, TX 76107

RESTRAINT STRESS REDUCES HOST DEFENSES AGAINST STREPTOCOCCUS PNEUMONIAE INFECTION IN MICE

Purpose: The focus of this sutdy is to define how a stressfulevent influences the immune system's ability to defend against Streptococcus pneumoniae infection in mice. Our working hypothesis is that stress-induced changes in macrophage ability influences susceptibility to S. pneumoniae infection.

Methods: Female CD-1 strain of mice between 4-8 weeks of age was used in all studies. To elicit a stress response, mice were subjected to an approved restraint stress (RS) method previously shown in our laboratory to alter cellular immune responses in the lung. Specifically, group of mice (n=10) were placed in sterile well- ventilated 50 ml conical tubes for 3 hrs per day for 4 days. For comparision, similar groups of non-restraint stress (NRS) mice were similarly handled with the exception of being placed back into their home cage rather than undergoing RS. After each RS session, mice were returned to their home cage. One day following RS both RS and NRS mice were infected with prepared inoculums of S. pneumoniae (Strain #6301, ATTC) at doses ranging between 4-6 x 10^5 colony forming units (CFUs). As a control, a group of RS mice were sham-treated. After S. pneumoniae infection, the mice were monitored until death and survival analysis was calculated. The weight of each subject was recorded prior to stress, prior to infection, and post-mortem. In separate studeis, similarly treated mice were sacrificed 48 hrs after S. pneumoniae and the number of CFUs in lung, blood, and spleen was determined.

Results: Mice subjected to RS demonstrate a significant percent weight loss prior to S. pneumonia infection and their total percent weight loss is significantly ($p = 0.05$)greater than the percent weight loss observed among NRS infected mice at death. Whereas 30% of the NRS mice survived infection, all RS mice died within 72 hr after infection. Preliminary evidence also indicates that the number of CFUs in the lungs of RS-treated mice is greater than NRS mice, demonstrating an impairment of RS mice to prevent colonization of S. pneumoniae in the lungs.

Conclusions: Taken together, the results suggest that stress has a negative impact on the immune system ability to control S. pneumoniae infection in mice. This data serves as a springboard for future studies examining the role of macrophage and lymphocyte responses under stressed conditions.

Sponsor: *N/A*

906 *(Poster)*

Author: Nowland Bambard

Presenter: Nowland Bambard

Department: Molecular Biology and Immunology

Classification: GSBS Student

Nowland D. Bambard and Porunelloor A. Mathew, Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, TX 76107

FUNCTIONAL ROLE OF THE LLT1 RECEPTOR ON NATURAL KILLER CELLS

Purpose: NK cells are cells of the innate immune system that form the first line of defense against cancer and viral infections. NK cell functions are regulated by a balance between activating and inhibitory signals received through surface receptors. We have previously identified a lectin-like transcript 1 [LLT1] from a human NK cell cDNA library. LLT1 is expressed on NK cells, monocytes, B cells and T cells. Furthermore, Mathew et al. have shown that LLT1 ligation on NK cells is a potent stimulator of IFN-gamma secretion. LLT1 ligation has no effect upon the cytotoxic properties of NK cells. The natural ligand of LLT1 has recently been identified as NKRP1A, an important regulatory receptor on NK and T cells. A recent report shows that LLT1 is expressed on osteoclasts and it inhibits their formation and function. We hypothesize that LLT1 exhibits diverse functional roles on various cell types, and may employ multiple intracellular signaling strategies to accomplish this. Functioning as an immune modulator, LLT1 may possibly link a regulatory feedback loop between activated NK cells and macrophages.

Methods: A promonocytic cell line U937 was assayed for LLT1 expression by flow cytometry under multiple permutations, including incubation with IFN-gamma and anti-LLT1 IgG. A plasmid coding for a pSec□LLT1 and pSec-NKRP1A fusion protein was generated. This plasmid was transfected into the B16 cell line and the generated fusion protein was purified on a nickel column. Numerous cell lines were stained with these fusion proteins to analyze the expression and function of LLT1 and NKRP1A on various cell types.

Results: 100% of unstimulated U937 express LLT1. Activation of U937 cells by IFN-gamma induces a five-fold increase in LLT1 expression.

Conclusions: The expression and induction of LLT1 on U937 cells indicate that LLT1 may function as a link between innate and adaptive immune responses.

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907 *(Poster)*

Author: Byung-Jin Kim

Presenter: Byung-Jin Kim

Department: Molecular Biology and Immunology

Classification: GSBS Student

Byung-Jin Kim, Xiangle Sun, Harlan P. Jones and Jerry W. Simecka. Department of Molecular Biology and Immunology, University of North Texas Health Science Center, 3500 Camp Bowie BLVD, Fort Worth, Texas, 76107

DIFFERENTIAL MESSENGER RNA EXPRESSIONS OF CHEMOKINE/CYTOKINES IN PULMONARY ANTIGEN PRESENTING CELLS AFTER MYCOPLASMA PULMONIS INFECTION ON MICE.

Purpose: Mycoplasma pulmonis causes chronic lung disease in mice. Studies in our laboratory demonstrate that antigen presenting cell(APC)s can mediate pulmonary immune responses against M. pulmonis infection. The current focus of these studies is to examine the role of chemokine/cytokines and their receptors on APCs which are involved in immune cell recruitment and activation of other immune cells.

Methods: Real-time PCR was performed with RNA from 6-8 weeks aged C3H mice infected by M. pulmonis using cyber green method.

Results: Real-time PCR analysis showed that mRNA expression of FceR1-gamma, MIF (macrophage migration inhibitory factor) and CXCL10 (interferon-gamma inducible protein-10) were significantly increased in both dendritic cells and macrophages whereas mRNA expression of CCR1 and CCL4 (macrophage inflammatory protein 1-beta) were significantly increased only in dendritic cells after 14 days of infection. mRNA expression of CCL17 (ABCD2, thymus activation-regulated chemokine) showed no significant changes on each APC under the same conditions.

Conclusions: These data suggest that each APCs has unique patterns of chemokine/cytokine secretion and receptor expression after M. pulmonis infection. We hypothesized that these differences can trigger differential immune cell recruitment and interactions with APCs during mycoplasma disease pathogenesis. Future study, we will test our hypothesis that chemokine/cytokine mRNA expression patterns reflect differences in protein production and there factors play a role in the response to M. pulmonis infection.

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908 *(Poster)*

Author: Stephen Mathew

Presenter: Stephen Mathew

Department: Molecular Biology and Immunology

Classification: Faculty

Stephen O. Mathew1, Jong-rok Kim1, Swapnil V. Vaidya2 and Porunelloor A. Mathew1 1Department of Molecular Biology and Immunology and Institute for Cancer Research, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX, 76107. 2Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, 72205.

TRANSCRIPTIONAL REGULATION OF THE 2B4 GENE IN HUMAN NATURAL KILLER CELLS

Purpose: Natural killer cells are bone-marrow derived lymphocytes that function as key players in innate immunity by recognizing viral, bacterial and parasitic infections and neoplastic target cells. NK cell functions are regulated by specific receptors that, upon interaction with their respective ligands, may send stimulatory or inhibitory signals. We have previously identified and cloned a novel receptor 2B4 (CD244), which activates NK cells and T cells. 2B4 expression is upregulated on NK cells and CD8 T cells under various conditions, like viral infections (HSV) or cytokine stimulation (IL-2). This regulates the functions of these cells, stimulating cytotoxicity or cytokine secretion. Hence, understanding 2B4 gene expression and regulation will provide further insight into the regulation of immune response during viral infection. Earlier we had identified an Ets element that binds about 1kb upstream of the transcription start site of 2B4 and upregulates gene expression and is dependent on AP-1 for functional activity. In this study, we investigate the down regulation of 2B4 expression during NK cell activation.

Methods: In order to determine that the down regulation of 2B4 was due to a decrease in promoter activity, dual luciferase reporter assays were performed on YT cells after mAb C1.7 stimulation. YT cells were incubated with mAb C1.7 (200 ng/ml) at different time points and total RNA and nuclear extract were obtained. Electrophoretic mobility shift assay (EMSA) was performed with the YT nuclear extract and the labeled probe of human 2B4 promoter. The total RNA from YT cells were reverse transcribed and PCR amplified using gene specific primers. Flow cytometric analyses were also done with the stimulated YT cells.

Results: The results of the reporter assay show a decrease in 2B4 promoter activity by 60% after C1.7 stimulation. Similar results were obtained with the EMSA indicating that as a result of mAb stimulation, 2B4 down-regulates its own expression and this may be mediated by Ets.

Conclusions: Our study shows that the down-regulation of 2B4 could be a mechanism to attenuate the co-stimulatory signal from 2B4-CD48 interaction. Thus, 2B4-CD48 interaction among neighboring lymphocytes could help boost the initial immune response, which would then be limited by down-regulation of 2B4 on lymphocytes.

Sponsor: *NIH*

909 *(Oral)*

Author: Wees Love

Presenter: Wees Love

Department: Molecular Biology and Immunology

Classification: GSBS Student

Wees Love, Xiangle Sun and Jerry W. Simecka Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, TX 76107

TOLL-LIKE RECEPTOR 2 MEDIATES RESPONSES OF ANTIGEN-PRESENTING CELLS IN MURINE MYCOPLASMA PNEUMONIA

Purpose: We hypothesize that mycoplasmas stimulate antigen-presenting cells via toll-like receptors (TLR)

Methods: Mice were infected with 105 CFU of M. pulmonis, and 14 days later, pulmonary dendritic cells (DC) and macrophages were isolated from their lungs. As controls, lung cells from mice inoculated with mycoplasma broth were included. Total RNA was isolated from each of these cell populations, and TLR mRNA expression was determined via gene microarray and real-time PCR. In addition, human endothelial kidney cells (HEK293) stably transfected to express the human TLRs (TLR 2, 4, 4/MD-2) were stimulated with M. pulmonis components (whole organism, lipoprotein), LPS (TLR 4 agonist), or FSL-1 (TLR 2/6 agonist). Culture supernatants were then collected and subjected to sandwich ELISA to analyze IL-8 production.

Results: We found TLR 2, 3, 4 and 7 mRNA is expressed in DC and macrophages isolated from the lung. We also found that TLR 2 mRNA expression changes in macrophages and DC isolated from the lungs following infection with M. pulmonis. TLR2 mRNA levels were higher in macrophages isolated from infected mice, as compared to control mice. Interestingly, TLR2 mRNA expression was reduced, but still present, in DC from infected mice. Importantly, we found that TLR 2 expression mediated responses of the whole organism of M. pulmonis and its lipoprotein extract. There was increased IL-8 production in those HEK293 transfected with TLR 2, but not TLR 4 or 4/MD-2, when stimulated with the FSL-1 or with the whole organism or lipoprotein extract of M. pulmonis.

Conclusions: TLR 2, 3, 4 and 7 mRNA was expressed in pulmonary DC and macrophages, and there was differential expression of TLR 2 on these cells after mycoplasma infection. Furthermore, we determined that TLR 2 mediates responses to M. pulmonis in vitro. Thus, TLR 2 interactions with mycoplasma will likely play an important role in the host response to infection.

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910 *(Poster)*

Author: Jongrok Kim

Presenter: Jongrok Kim

Department: Graduate School of Biomedical Sciences

Classification: GSBS Student

Jong-Rok Kim, Stephen O Mathew and Porunelloor A. Mathew Department of Molecular Biology, University of North Texas Health Science Center, Fort Worth, TX 76107-2699

MOLECULAR BASIS FOR POSITIVE AND NEGATIVE SIGNALING BY THE 2B4 (CD244) RECEPTOR

Purpose: Natural killer cells are bone-marrow derived lymphocytes that function as key players in innate immunity by recognizing viral, bacterial and parasitic infections and neoplastic target cells. The activity of natural killer (NK) cells is regulated by a multitude of different surface receptors. NK cell recognition is regulated by specific receptors that, upon interaction with their respective ligands, may send stimulatory or inhibitory signals. Our recent studies have shown that the interaction between human 2B4 and its natural ligand CD48 leads to the functional activation of NK cells whereas in murine NK cells 2B4 (m2B4) functions as an inhibitory receptor rather than a stimulatory receptor. In order to understand the molecular basis of these two effects, we have generated chimeric human/mouse 2B4 molecules for functional analysis.

Methods: Extracellular(E) and transmembrane(Tm) regions of human and mouse 2B4 DNA were amplified by PCR. Similarly, cytoplasmic(C) domains of human and mouse 2B4 were also amplified. The PCR products were cloned into pGEM-T easy vector, and were restriction digested with SalI, PstI and XbaI. The human 2B4 E+Tm was ligated with mouse 2B4 C and similarly mouse 2B4 E+Tm was ligated with human 2B4 C and cloned into mammalian expression vector pEMCV.SR? by three way ligation method.

Results: 2B4 amino acid sequence comparison from different species shows that four cytoplasmic immunoreceptor tyrosine-based switch motifs (ITSMs) are well conserved. After three-way ligation, 6 colonies for mouse E+Tm/human C 2B4 and 10 colonies for human E+Tm/mouse C 2B4 were tested by the restriction endonuclease digestion analysis and DNA sequencing, and three colonies and one colony were correctly cloned, respectively.

Conclusions: The chimeric clone encoding human E+Tm and mouse C domain or mouse E+Tm and human C domain were successfully generated. Expression of these chimeric constructs in RNK-16 cells and functional studies should reveal the basis for positive and negative signaling by the 2B4 receptor.

Sponsor: *N/A*

911 *(Poster)*

Author: Nicole Dobbs

Presenter: Nicole Dobbs

Department: Molecular Biology and Immunology

Classification: GSBS Student

N. Dobbs, L. Hodge, L. Tabor, B. Kim, X. Sun, J. Simecka Department of Microbiology and Immunolgy, University of North Texas Health Science Center, Fort Worth, Texas 76262

MYCOPLASMA STIMULATION OF DENDRITIC CELL SUBPOPULATIONS AND CYTOKINE RESPONSES

Purpose: Mycoplasma pulmonis causes respiratory disease in mice and is an established animal model with similarities to human Mycoplasma pneumoniae infections. The adaptive immune response to mycoplasma in the lungs has shown to be protective and damaging. Dendritic cells may influence the adaptive response mycoplasma in the lungs. To understand these immune responses, we will identify what influence mycoplasma membrane antigen has on differentiated dendritic cells. We hypothesize that differentiated populations of dendritic cells (DCs) will have unique cytokine responses to mycoplasma and bacterial lipopolysaccharide (LPS).

Methods: Bone marrow-derived stem cells will be isolated from tibiae and femora of 6-8 week old Balb/c mice. The stem cells will be differentiated with cytokines for 4 days to produce three classes of bone marrow-derived dendritic cells (BMDCs) designated as DC0, DC1, and DC2. Once the DCs have matured and are differentiated, they will be stimulated with bacterial LPS (positive control), mycoplasma, and RPMI alone (negative control) to determine if the cytokine responses. The cytokine expression will be determined by examining DC mRNA expression through real time RT-PCR with primers specific for IL-4, IL-10, IL-12, IFN-? and enzyme-linked immunosorbant assays (ELISA) from the DC supernatants.

Results: DC differentiation will be identified through the comparison of morphological characteristics. In response to bacterial LPS, we expect the DC1 to show increased expression of Th1 promoting cytokines (IL-12 and IFN-?) and a decreased expression in Th2 promoting cytokines (IL-4 and IL-10). Whereas we expect the reverse to be observed with the DC2 class. The cytokine responses to mycoplasma may be similar to those indicated by LPS, but recent evidence from our lab suggests that the receptor recognition of mycoplasma are different than those of LPS. This would lead to unique cytokine expression for mycoplasma.

Conclusions: These studies will identify and characterize the cytokine response of these populations of DCs to mycoplasma in comparison to LPS. The differences will assist in the quest to identify components of mycoplasma disease pathogenesis. Future studies will test the ability of these APCs to specifically generate Th1 or Th2 responses, which will influence the immunoprotective versus immunopathologic responses during mycoplasma disease in vivo. This work was supported by a grant from the NIH grant number 1RO1HL069431-01A2

Sponsor: *NIH*

912 *(Poster)*

Author: Lisa Hodge

Presenter: Lisa Hodge

Department: Molecular Biology and Immunology

Classification: Faculty

Lisa Hodge, Hollis King and Scott Stoll.

LYMPHATIC PUMP MANIPULATION INCREASES ANTIGEN-SPECIFIC SERUM ANTIBODY.

Purpose: Our long range goal is to evaluate the effectiveness of osteopathic manipulative therapy (OMT) at enhancing the immune response against a variety of respiratory diseases. The objective of these experiments was to develop a rat OMT model to investigate the effectiveness of the lymphatic pump technique (LPT) at enhancing antigen-specific antibody responses during immunization.

Methods: Rats were divided into two groups, control and LPT treatment. Rats were then immunized with OVA antigen or PBS (control). Each animal in the treatment group was given 8 minutes of LPT under anesthesia daily for 3 consecutive days. The operators third and forth digits contacted the spine in close approximation of finger tips to provide a fulcrum during the rib lateral-cephalad expansion phase of the technique. A lateral-cephalad force sufficient to move the ribs was applied until resistance was reached. Then, medial-caudal pressure bringing the ribs toward the midline was applied until resistance was reached. No effort was made to exceed anatomic range of motion. The motion was a pump-handle type for the lower rib cage, and at the fullest extent of the medial-caudal excursion, the tips of the thumbs pressed cephalad on the respiratory diaphragm. This alternating lateral-medial pressure is applied approximately at the rate of 35-40 cycles per minute for eight minutes on each animal. Previously, this treatment was shown to increase lymph flow in healthy rats, a phenomenon similarly found in humans and dogs. Control animals were held (under anesthesia) for the same amount of time as treatment animals to not bias data. 7 days post immunization, serum was collected and analyzed for OVA-specific antibody responses.

Results: OVA-specific IgG titers were approximately 2-fold higher in rats given LPT, suggesting an enhanced antigen-specific adaptive immune response. This data is consistent with human studies showing increased vaccine-specific IgG titers in patients given LPT during immunization.

Conclusions: Current and future studies will determine the exact cellular immune mechanisms that are enhanced or affected by LPT.

Sponsor: *UNTHSC Osteopathic Research Center*

1000 *(Poster)*

Author: Roberto Cardarelli

Presenter: Roberto Cardarelli

Department: Family Medicine

Classification: Faculty

Roberto Cardarelli, DO, MPH; UNTHSC, TCOM, Department of Family Medicine, Fort Worth, TX 76107

RECURRENT AND PERSISTENT PAROTID ENLARGEMENT

Purpose: To present a case of parotid enlargement caused by the human immunodeficiency virus.

Methods: A case report will be presented utilizing a SOAP note format. The individual's history of presenting illness, past medical history, physical exam, and laboratory testing will be presented.

Results: This case report was published in the American Family Medicine Journal in 2005.

Conclusions: This case reminds physicians that the initial presentation HIV infection may be parotid enlargement.

Sponsor: *N/A*

1001 *(Poster)*

Author: Adam Odeh

Presenter: Adam Odeh

Department: Molecular Biology and Immunology

Classification: GSBS Student

Adam Odeh, Mark Pulse, and Jerry W. Simecka, Department of Microbiology and Immunology, University of North Texas Health Science Center, Fort Worth, TX 76107

ALPHA TOXIN IS IMPORTANT FOR BIOFILM FORMATION BY STAPHYLOCOCCUS AUREUS

Purpose: We hypothesized that S. aureus hla knockout (KO) strains would be impaired in their ability to form biofilm under in vitro and in vivo conditions as compared to wild type S. aureus strains.

Methods: Four S. aureus strains were used for this study: Two wild type parent strains (13, 83), and two hla KO strains (13-7, 373). In vitro testing was performed using Calgary devices, involving biofilm formation on standard 96 well plates, stained with crystal violet and measured for absorbance at 490 nm. Results were confirmed through counts of colony forming units (CFU). In vivo testing was performed by growing biofilm on plastic catheters which were then implanted subcutaneously into outbred mice. Catheters were removed at set time points, vortexed in phosphate buffered saline, and the solution used for spot plating and CFU counts.

Results: We found that hla KO strain 13-7 forms less biofilm than the wild type strains 13 and 83 after 48 hours in vitro. In addition, we also found that both hla KO strains, 13-7 and 373, form less biofilm as compared to the wild type strains after 72 hours in vitro. Finally, we observed that mice infected with hla KO strains 13-7 and 373 displayed less bacterial growth as compared to mice infected with wild type strains in vivo.

Conclusions: In this study, we determined that a-toxin is indeed involved in biofilm formation under in vitro and in vivo conditions. We observed that S. aureus hla KO strains were impaired in their ability to adhere to surfaces both in vitro and in vivo as compared to wild type S. aureus.

Sponsor: *Supported by Cumbre Pharmaceuticals, Inc., Dallas, TX 75235*

1002 *(Poster)*

Author: Xiangle Sun

Presenter: Xiangle Sun

Department: Molecular Biology and Immunology

Classification: Staff

Xiangle Sun, Jerry W. Simecka Dept. Molecular Biology and Immunology. University of North Texas, Health Science Center at Fort Worth. 3500 Camp Bowie Blvd, Fort Worth, TX 76107

DIFFERENTIAL CYTOKINE MRNA EXPRESSION AT LESION AREA AND NON-LESION REGIONS IN LUNGS FROM MICE WITH MYCOPLASMA DISEASE REVEALED BY LASER CAPTURE MICRODISSECTION

Purpose: Laser capture microdissection (LCM) makes it possible to select and capture certain regions or cells of interest on tissue based on light and fluorescent microscopy. The lung lesions in mycoplasma respiratory disease are often localized, and analysis of responses in the total lung may not reflect the event occurring at the lesion site. To investigate whether this is true, some cytokine and chemokines mRNAs were detected at lesion area and no-lesion regions which were captured by LCM.

Methods: Lungs were collected from BALB/c mice which were infected with 2x105 colony forming units (CFU) of Mycoplasma pulmonis or inoculated with broth as a control. The lungs were frozen sectioned at 15 um thickness. After hemotoxyline staining, the slides were viewed by LCM microscope. The region of lesions around airways showed inflammatory cell infiltrate were selected and captured. The similar region but without significant cell infiltration on the same slide and on broth control slide were also captured. The RNAs were extracted from these collected tissues. After reverse transcript reaction, cytokine and chemokines TNF-a, CCL4 and CCL8 mRNA levels on selected tissues were detected by real time PCR.

Results: The results showed that TNF-a, CCL4 and CCL8 mRNA levels are higher at lesion site as compared to relative normal region within the same tissue or from lungs control (broth inoculated) mice.

Conclusions: This results suggest that TNF-a ,CCL4 and CCL8 are closely related with lesion formation due to M. pulmonis infection. Furthermore, these studies demonstrate that LCM as a new technique will help us study genes and proteins involved in disease more precisely.

Sponsor: *NIH grant 1R01 AI 42075*

1100 *(Poster)*

Author: Contessa Majors

Presenter: Contessa Majors

Department: PHARMACOLOGY & NEUROSCIENCE

Classification: McNair/SMART Participant

Contessa Majors, James Simpkins, Andrew Wilson, Varun Goyal, Marianna Jung Department of Pharmacology and Neuroscience, University of North Texas Health Science Center at Fort Worth, TX 76107, USA

A NON-FEMINIZING ESTROGEN ZYC-26 PROTECTS AGAINST ETHANOL TOXICITY

Purpose: This study investigated mechanisms underlying potential protective effects of a non-feminizing estrogen ZYC-26 on ethanol toxicity in an Immortalized Hippocampal Cell line (HT-22). It was reported that ZYC-26 neither binds to estrogen receptors nor elicits a uterotrophic response. We tested the hypothesis that ZYC-26 protects against ethanol-induced cytotoxicity through antioxidant mechanisms in a manner that interacts with the GABA (?-Amino Butyric Acid) neurotransmission. GABA is the major inhibitory neurotransmitter and mediates some ethanol activity in the brain. Method: HT-22 cells were incubated with a media containing ethanol (0, 50, 100, and 200 mM) for 24 hours. Drugs (ZYC-26 or ZYC-26 + GABA-A antagonist) were simultaneously treated with ethanol to determine whether ZYC-26 attenuates ethanol toxicity and whether GABA-A antagonist bicuculline blocks the ZYC-26 protection. Following 24 hour ethanol exposure, three dependent variables were measured; 1) cell viability, 2) Lipid peroxidation, and 3) Protein oxidation.

Methods: Cell Viability: Cell viability was measured using a Calcein AM (Acetoxymethylester) assay. Cell treatments: Cells were exposed to ethanol concentrations of 0, 50, 100, and 200. Cells were then treated with zyc, bicuculline, zyc with bicuculline. Lipid peroxidation: Thiobarbituric acid reactive substances (TBARS) were measured. Protein oxidation: Carbonyls were measured.

Results: High doses of ethanol decreased cell viability, increased MDA (malondialdehyde) ? 4- HAE (hydroxyalkenals) (products of lipid peroxidation), and increased carbonyl contents (products of protein oxidation) in a manner that is prevented by ZYC-26. All ZYC-26 protection was inhibited by bicuculline.

Conclusions: These data suggest that ZYC-26 protects against ethanol-toxicity in part through normalizing oxidative imbalance associated with the GABA neurotransmission. Our findings may provide a potential therapeutic strategy for alcohol toxicity without feminizing side effects of estrogenecity.

Sponsor: *N/A*

1101 *(Poster)*

Author: Akiko Dohi

Presenter: Akiko Dohi

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Akiko Dohi, Cathy L. Bell-Horner, Quynh Nguyen, Glenn H. Dillon, Meharvan Singh Department of Pharmacology and Neuroscience University of North Texas Health Science Center at Fort Worth

THE MITOGEN-ACTIVATED PROTEIN KINASE PATHWAY REGULATES GABAA RECEPTOR FUNCTION

Purpose: The gamma-amino butyric acid-A receptor (GABAA receptor) is a ligand-gated chloride channel whose function can be modulated by phosphorylation of its various subunits. As such, we were intrigued to have found a consensus phosphorylation sequence for ERK, a key effecter of the mitogen-activated protein kinase (MAPK) pathway, within the intracellular loop of almost all ± subunits of the GABAA receptor. Thus, we hypothesized that extracellular-signal regulated kinase (ERK) may phosphorylate the GABAA receptor, thus regulating its function.

Methods: We tested our hypothesis in ±1²2³2-stably transfected human embryonic kidney (HEK) 293 cells and HEK293 cells that were transiently transfected with an ±1 subunit in which the putative ERK phosphorylation site, threonine (T) 375, was mutated to alanine (A)(±1(T375A)²2³2). GABAA receptor function was assessed using whole cell and perforated patch clamp electrophysiology in the presence or absence of a pharmacological inhibitor of ERK, U0126. The effect of U0126 on basal ERK phosphorylation was confirmed by Western blot.

Results: We found that U0126 reduced basal ERK phosphorylation and resulted in an enhancement of GABA-induced peak current amplitudes in ±1²2³2-transfected HEK293 cells. Further, the enhancement of GABA-gated currents required an intact intracellular environment as it was robust in perforated patch recordings (which preserves the intracellular milieu), but absent in conventional whole-cell recordings (which dialyzes the cytosolic contents), supporting the involvement of an intracellular signaling pathway. Interestingly, mutation of the ERK phosphorylation site (T375A) not only prevented the U0126-induced enhancement of GABA-gated currents, but now resulted in U0126-mediated inhibition of GABAA receptor function.

Conclusions: Our data demonstrate the presence of a novel mechanism for regulating the GABAA receptor, through activation of the ERK/MAPK pathway. Based on our results, we suggest that the effect of ERK on GABA-gated currents is due to a direct effect on the phosphorylation state of the alpha subunit, which in turn, influences receptor activity. The data also suggest that there may be sites other than T375 that serve as an important target of ERK in regulating GABAA receptor function. (NIH (AG23330, AG22550), National Alliance for Research on Schizophernia and Depression (NARSAD))

Sponsor: *NIH (AG23330, AG22550), National Alliance for Research on Schizophernia and Depression (NARSAD)*

1102 *(Oral)*

Author: Joshua Gatson

Presenter: Joshua Gatson

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Joshua W. Gatson and Meharvan Singh University of North Texas Health Science Center at Fort Worth, Department of Pharmacology and Neuroscience, Fort Worth, TX

ACTIVATION OF A MEMBRANE ANDROGEN RECEPTOR PROMOTES CELL DEATH IN GLIA

Purpose: Androgens, such as dihydrotestosterone (DHT), are involved in numerous biological functions including the regulation of cell viability. However, conflicting reports exist as to whether androgens are protective or damage-inducing. Since androgens may elicit their effects through activation of the □classical androgen receptor (AR) or alternatively, through a putative plasma membrane receptor, we proposed that this discrepancy may be attributed to differential activation of these two mechanisms. To test this hypothesis, we evaluated whether activation of the putative membrane AR in glia, suppresses the activity of survival pathways and increases in cell death during injury, relative to the effects mediated through the classical (intracellular) AR.

Methods: C6 cells were maintained in DMEM supplemented with 10% serum and the cells were treated at 90% confluency. Primary cortical glial cultures were isolated and plated on postnatal day 3 (P3) and treated on day 10 in vitro (DIV). The cultures were treated with iodoacetic acid (IAA; 10 ¼M) in the presence or absence of DHT (10 ¼M) or DHT-BSA (membrane impermeable form of DHT; 10 ¼M) for 12 hours. Indices of cell death included measurements of lactate dehydrogenase (LDH) release into the media and caspase-3/7 activity. In parallel, we assessed the phosphorylation of Akt, an important effector of the protection associated with the PI-3 kinase pathway.

Results: In both C6 cells and primary cortical glia, DHT protected against IAA-induced toxicity. In contrast, DHT-BSA treatment exacerbated IAA-induced toxicity. This effect was flutamide (intracellular AR antagonist) insensitive, suggesting that the mAR is distinct from the intracellular AR. In addition, activation of the mAR, led to a decrease in phospho-Akt levels and a correlative increase in caspase-3/7 activity. Interestingly, the damage promoting consequences of activating the mAR influenced other steroid hormones ability to protect, since DHT-BSA blocked estrogen-induced protection.

Conclusions: Collectively, these studies indicate that activation of the mAR during injury, leads to an increase in glial cell death. In contrast, activation of the intracellular AR protects. Thus, depending on the predominance of one receptor mechanism over another, the outcome of androgen treatment may be very different, and as such, could help explain existing discrepancies as to whether androgens are protective or damage-inducing.

Sponsor: *National Institutes of Health (NIH) Minority Supplemental Grant, Associate Fellowship, UNTHSC*

1103 *(Poster)*

Author: Andrew Wilson

Presenter: Andrew Wilson

Department: Pharmacology & Neuroscience

Classification: Staff

A.M. Wilson, J.W. Simpkins, M.E. Jung University of North Texas Health Science Center, Fort Worth, TX 76017.

A NONFEMINIZING ESTROGEN ANALOGUE PROTECTS AGAINST ETHANOL WITHDRAWAL TOXICITY IN IMMORTALIZED HIPPOCAMPAL CELLS

Purpose: The aim of this study is to investigate whether a cellular model of EW could be developed in a cultured hippocampal cell line (HT22) and whether an adamantyl-containing nonfeminizing estrogen analogue (ZYC26) protects against EW toxicity

Methods: HT22 cells were exposed to ethanol (0 - 500 mM) for 24 hours in the presence or absence of ZYC26 or E2. The ethanol solution was then removed from the cells for four hours to create EW. Samples were collected at the end of a 24 hour-ethanol exposure or at four hours of EW to assess 1) cell viability using a Calcein assay, 2) lipid peroxidation by measuring malondialdehyde (MDA), and 3) protein oxidation by measuring carbonyl contents.

Results: When tested, ethanol concentrations were constantly maintained during 24 hours of ethanol exposure and eliminated at four hours of EW. EW decreased cell viability and increased the levels of MDA and carbonyls more than ethanol exposure. ZYC26 reduced the cell death and MDA levels at a lower dose (1 μM) than E2 (10 μM). The increased carbonyl contents were reduced only by ZYC26 treatment.

Conclusions: These data suggest that EW can be created in HT22 cells in a manner that is more toxic than ethanol exposure and that ZYC26 is a more potent cytoprotectant than E2 against cell death and oxidative damage induced by EW. Therefore, ZYC26 can be a potential alternative estrogen therapy for a cellular and oxidative imbalance associated with EW

Sponsor: *NIAAA AA013864-01A1*

1104 *(Oral)*

Author: Scott Duncan

Presenter: Scott Duncan

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Scott Duncan, Sung-Yong Hwang and Peter Koulen, Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, 3500 Camp Bowie Blvd, Ft. Worth, TX 76107

DISTINCT NUCLEAR AND CYTOSOLIC CALCIUM SIGNALS MEDIATED BY DIFFERENTIALLY-DISTRIBUTED INOSITOL-1,4,5-TRISPHOSPHATE RECEPTORS IN HIPPOCAMPAL NEURONS

Purpose: The purpose of this work is to demonstrate the differential distribution and functional properties of inositol-1,4,5-trisphosphate (IP3) receptor (IP3R) isoforms in the hippocampal cell line HT22.

Methods: The murine hippocampal cell line HT22 was used for all experiments. Western blotting was conducted on cell lysates to detect the IP3R isoforms present while immunocytochemistry was done to identify their intracellular localization. Using optical imaging of intracellular Ca2+ concentration, Ca2+ release from intracellular stores was measured to determine the functional properties of IP3R isoforms in cytoplasmic and nuclear compartments.

Results: We demonstrate that IP3R1 and IP3R3 are predominantly expressed in cytosolic (endoplasmic reticulum) compartments while IP3R2 is concentrated in the nuclear envelope. We also show that nuclear IP3 responses mediated by IP3R2, which has a higher affinity for its ligand IP3 and a greater sensitivity to Ca2+ than IP3R1 and IP3R3, have faster kinetics than IP3 responses in the cytosol mediated by IP3R1 and IP3R3.

Conclusions: We conclude that differential distribution of biophysically distinct IP3Rs in HT22 cells leads to differential IP3 and Ca2+ signaling. We predict that this differential distribution is important for controlling Ca2+ homeostasis and signaling in cytosolic versus nuclear compartments.

Sponsor: *NIH / NIA grant AG10485*

1105 *(Poster)*

Author: Marianna Jung

Presenter: Marianna Jung

Department: Pharmacology & Neuroscience

Classification: Faculty

AGE EXACERBATES THE EFFECTS OF ETHANOL WITHDRAWAL ON BRAIN MITOCHONDRIA IN AN ESTROGEN REVERSIBLE MANNER
Marianna E. Jung, Ph.D., Andrew M. Wilson, Rajnee Agarwal, B.S. James W. Simpkins, Ph.D. Department of Pharmacology and Neuroscience, University of North Texas Health Science Center at Fort Worth, TX 76107, USA*

AGE EXACERBATES THE EFFECTS OF ETHANOL WITHDRAWAL ON BRAIN MITOCHONDRIA IN AN ESTROGEN REVERSIBLE MANNER

Purpose: The goal of this study was to provide a better understanding of the mechanisms underlying ethanol withdrawal (EW) toxicity as a factor of mitochondrial aging. Cytochrome c oxidase (COX) is a key mitochondrial enzyme that catalyzes an electron transfer to maintain respiratory homeostasis. We investigated whether EW alters the activity of COX in an age-dependent manner in both the presence and absence of endogenous estrogen [17ß-estradiol (E2)].

Methods: 5-, 12-, and 16-month-old ovariectomized rats with or without acute E2 replacement received a liquid ethanol (6.5%) or control dextrin diet for two weeks. They were then sacrificed either during ethanol exposure or at 24 hours of EW. Cerebellum and cortex were collected to assess 1) the activity of COX, 2) the levels of malondialdehyde (products of lipid peroxidation), and 3) rotarod performance. In a rotarod test, a shorter latency to fall from an accelerating rotarod indicates poor motor capacity.

Results: As compared to the control dextrin and ethanol exposure, EW decreased the activity of COX but increased the levels of MDA in both the cerebellum and cortex. The decrease in the activity of COX and the increase in the levels of MDA were more prominent in 12- and 16-month-old rats than 5-month-old rats, showing an age-dependent inverse relationship between the two variables. Estrogen treatment reduced all of the alterations induced by EW in all three age groups of rats. For a rotarod test, there was an age-dependent impairment after EW such that 12- and 16-month-old rats had a shorter latency to fall from the rotarod than control dextrin or 5-month-old rats in a manner that was prevented by E2 treatment.

Conclusions: These findings suggest that the combination of age and EW produces more toxic insults to mitochondria homeostasis than either condition alone or ethanol exposure per se. Estrogen appears to play a protective role against the deleterious interaction between age and EW.

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1106 *(Oral)*

Author: Maj Angarano

Presenter: Maj Angarano

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Maj Angarano Biology Department, University of Texas at Arlington Arlington, TX 76019 Robert F. McMahon Biology Department, University of Texas at Arlington Arlington, TX 76019 John A. Schetz UNT Health Science Center, Dept. of Pharmacology and Neuroscience Fort Worth, TX 76107

NOVEL NON-ORGANOMETALLIC COMPOUNDS FOR THE PREVENTION OF AQUATIC BIOFOULING BY ZEBRA MUSSELS (DREISSENA POLYMORPHA)

Purpose: Zebra mussels (Dreissena polymorpha) are a non-indigenous (invasive) species of mollusc that inhabit freshwater lakes and rivers and colonize industrial cooling ponds, irrigation systems and quarry reservoirs in massive numbers. They create a biofouling problem by obstructing the water intake structures and piping of water processing plants and other industries drawing raw water from a freshwater source. Current chemical control and mitigation strategies utilize primarily organometallic compounds and oxidizing agents that are toxic or create toxic by-products. The goal of our research is to discover an environment-friendly means for preventing the attachment of macrofoulers such as zebra mussels (Dreissena polymorpha) to aquatic substratum.

Methods: The ability of zebra mussel specimens to attach was assessed following exposure to one of 26 different compounds related to capsaicin, the natural product component of red hot chili peppers.. Following the initial exposure period, mussels were moved to untreated water and allowed additional time to reattach. The ability to reattach is a measure of the reversibility of any effect the compounds might have on attachment behavior.

Results: Several of the compounds show >70% inhibition of mussel attachment and significant reattachment following withdrawal of the treatment. All compounds also exhibit

Conclusions: The discovery of a non-toxic, yet potent class of zebra mussel antifoulants presents a potential alternative for current methods facing stricter federal regulations and moratoriums. Our findings demonstrate an initial proof of concept and will guide future research utilizing a green chemistry approach to develop a new generation of environment-friendly means to control aquatic biofouling.

Sponsor: *UNTHSC/UTA Joint Seed Grant Program (G67699) funds awarded to JAS & RFM; F&A funds (G67673)–JAS*

1107 *(Poster)*

Author: Xiaofei Wang

Presenter: Xiaofei Wang

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

X.Wang; R.Liu; S.Yang; J.W.Simpkins Pharmacology and Neuroscience, Univ. of North Texas HSC, Fort Worth, TX, USA*

CURCUMIN IS NEUROPROTECTIVE IN VITRO AND IN VIVO

Purpose: Oxidative stress is involved in many neurodegenerative diseases and the antioxidant effects of phenolic compounds are well documented. One commonly used natural phenolic compound is curcumin, a major yellow pigment in turmeric (the ground rhizome of Curcuma longa). Many studies indicate antioxidant and anti-inflammation activities of curcumin. Curcumin has been shown to protect neuronal cells against beta-amyloid insults, and in in vivo studies, curcumin protects against brain ischemia, reduced oxidative damage and amyloid pathology.

Methods: Cell viability was assessed using Calcein AM assay. A middle cerebral artery occlusion model was utilized to determine in vivo neuroprotective effects.

Results: Here, we evaluated neuroprotective effects of curcumin in both in vitro and in vivo models. In murine hippocampal HT-22 cells, curcumin protected against oxidative stress such as glutamate and iodoacetic acid (IAA) toxicity. Glutamate induced a 75% cell death after 18 h treatment at 40 mM. Curcumin dose-dependently enhanced cell survival at concentrations ranging from 2.5 micromolar to 10 micromolar. At the concentration of 10 micromolar, curcumin increased cell viability from 25% (vehicle) to 75%. Curcumin showed similar protection against IAA-induced toxicity. At the concentration of 7.5 micromolar, curcumin increased cell survival from 25% to 60%. Furthermore, we examined effects of curcumin in rat middle cerebral artery occlusion (MCAO) model. In ovariectomized female rats, curcumin was administered through IP injection at 300 mg/kg 30 min before surgery. Vehicle (DMSO) was given in control group. Compared to vehicle group, curcumin significantly reduced MCAO-induced infarct volumes from 347 +/- 32 mm3 to 68 +/- 35 mm3.

Conclusions: The present study indicates neuroprotective effects of curcumin in both in vivo and in vitro models.

Sponsor: *AG 10485 and AG22550*

1108 *(Poster)*

Author: April Confessore

Presenter: April Confessore

Department: Pharmacology & Neuroscience

Classification: Staff

April A. Confessore, Jaegwon Chung, Kun D. Yi, Andrew Wilson, and James W. Simpkins. Department of Pharmacology & Neuroscience, University of North Texas Health Science Center, Fort Worth, TX 76107

ESTROGEN PROTECTION AGAINST NITRIC OXIDE TOXICITY IN HIPPOCAMPAL CELLS

Purpose: Nitric oxide (NO) is a signaling molecule which plays an important role in neuronal injury associated with ischemia, neurodegenerative disease, and excitotoxicity. Estrogens are sex hormones that have been found to be neuroprotective in many areas against oxidative stress. We show here that 17?-estradiol can protect against NO induced death of HT-22 cells (a murine mouse hippocampal cell line), and NO induced death of HT-22 cells is mediated by an extracellular signal regulated kinase (ERK) pathway.

Methods: HT-22 cells were treated with kinase inhibitors before insult with sodium nitroprusside (SNP), a known NO donor. Cell viability was measured with by Calcein AM, a nonfluorescent, electrically neutral nonpolar analog of flourescein 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. Treatment with SNP (250?M or 500?M) caused a dose-dependent decrease in cell viability.

Results: Inhibition of p38 MAP kinase by SB203580 (20?M) did not protect HT-22 cells against NO-induced cell death, whereas inhibition of MEK with U0126 (20?M) was protective.

Conclusions: Our findings indicate NO-induced cell death of HT-22 cells is mediated by ERK activation and 17?-estradiol is able to protect against NO induced death of HT-22 cells. (Supported in part by NIH grants AG10485 and AG22550,)

Sponsor: *N/A*

1109 *(Oral)*

Author: Kathryn Gleason

Presenter: Kathryn Gleason

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Kathryn M. Gleason, Katalin Prokai-Tatrai, Laszlo Prokai, James W. Simpkins - University of North Texas Health Science Center, Fort Worth, TX 76107

LACK OF FEMINIZING EFFECTS OF CHRONIC TREATMENT WITH QUINOL PRODRUGS OF ESTRONE AND ESTRADIOL

Purpose: Estrogens are well documented as neuroprotective agents, however the side effects of feminizing estrogens can be undesirable and even detrimental. A nonphenolic quinol with no affinity for the estrogen receptor is produced by the capture of the hydroxyl radical by estrogen. The quinol is quickly converted back to the parent estrogen, acting as a prodrug for the active hormone. An acute dose of the estrone-quinol 2 hours prior to surgery is equipotent with its parent in reducing lesion volumes in a transient cerebral occlusion mode of stroke and proved to be non-feminizing in the estrogen-sensitive uterus. Because non-feminizing estrogenic compounds are desired but not currently available, we investigated the feminizing effects of chronic exposure to estrone-quinol as well as 17ß-estradiol-quinol.

Methods: Three groups of young adult Sprague-Dawley rats were ovariectomized and received subcutaneous injections of estrone, estrone-quinol, or vehicle (100µg/kg) every 48 hours for a period of 14 days. Forty-eight hours after the final injection, the rats were sacrificed and the uteri and anterior pituitary glands were collected and weighed. The same protocol was followed for three additional groups that received estradiol, estradiol-quinol, or vehicle.

Results: The uterine weights of the estrone group and the estradiol group were nearly three-fold higher than the estrone-quinol group and the estradiol-quinol group, respectively. There were no significant differences among the groups in anterior pituitary weight in the estrone study, however we saw a significantly lower anterior pituitary weight in the control group compared with the estradiol and estradiol-quinol groups. The estrone-quinol group and the estradiol-quinol group also had significantly higher body weights than the estrone group and the estradiol group, respectively.

Conclusions: Collectively, these data indicate that with chronic administration, estrone-quinol and estradiol-quinol are non-feminizing and that the compounds are not easily converted to the reduced estrogen in the periphery, or that this conversion occurs takes place in tissues that are not estrogen-sensitive. Further studies are necessary to better understand the actions of quinols in vivo, however these quinols have potential to serve as effective neuroprotective agents.

Sponsor: *NIH grants NS44765, AG 10485 and AG 22550*

1110 *(Poster)*

Author: Sara Taylor

Presenter: Sara Taylor

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

S.A. Taylor; J.F. Carroll ; N. Sumien*; K. Heinrich*; H.J. Taylor*; and M.J. Forster* * Department of Pharmacology and Neuroscience, Univ. of North Texas Health Science Center at Fort Worth, TX. Department of Integrative Physiology, Univ. of North Texas Health Science Center at Fort Worth, TX.*

THE EFFECT OF EXERCISE ON COGNITIVE DEFICITS IN AGING C57BL/6 MICE

Purpose: The ability of forced exercise training to ameliorate age-associated cognitive and psychomotor deficits was tested in aging C57BL/6 mice. It was the goal of this study to develop and assess an exercise training protocol for its ability to produce aerobically fit mice and to evaluate the effects of the training regimen on various psychomotor and cognitive tasks in aging mice.

Methods: 3 and 20 month old C57BL/6 mice were either subjected to 8 weeks of treadmill exercise followed by 3 weeks of concurrent exercise and behavior testing, or else they were age-matched, non-exercised controls. A citrate synthase assay was used to evaluate fitness levels in some of the mice in the study. Citrate synthase is a mitochondrial enzyme and skeletal muscle responds to exercise training by increasing its mitochondrial fraction so that citrate synthase levels can be used as a quantitative marker for increased fitness in exercised mice. Additional mice were tested on multiple behavioral tasks administered after 8 weeks of exercise training. The behavior testing included tasks designed to elucidate sensorimotor learning as well as tasks that required utilization of various components of cognitive learning.

Results: It is a finding of the study that moderate, short-term exercise initiated in aged C57BL/6 mice resulted in increased fitness in the aged mice to the same degree as observed in young mice, and it improved some but not all psychomotor skills, including bridge-walking, reaction time, swim speed, and it improved some aspects of age-impaired spatial memory performance.

Conclusions: The data presented in this project show that exercise has differentially beneficial effects on various behavioral tasks. Additionally it is shown that young and aged C57Bl/6 mice achieve similar increases in fitness with exercise.

Sponsor: *N/A*

1111 *(Poster)*

Author: James Simpkins

Presenter: Qing Liu

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

Qing Liu, Ran Liu, James W Simpkins, Shaohua Yang Deaprtment of Pharmacology & Neuroscience University of North Texas Health Science Center Fort Worth, TX 76107

IMPROVED FOCAL CEREBRAL ISCHEMIA INDUCED BY EMBOLIC MIDDLE CEREBRAL ARTERY OCCLUSION IN RATS

Purpose: We report the technical details and validation of the embolic middle cerebral artery occlusion (MCAO) rat model, which closely resembles clinical embolic stroke.

Methods: Focal cerebral arterial ischemia was induced by embolic MCAO in ovariectomized female rats. 0.6ml blood was mixed with 0.15ml thrombin (1mg/ml, Sigma), and injected into PE50 catheter (ID 0.58mm). The clots were removed and cut into small pieces (0.35X1.5mm) and trimmed under microscope. For clots injection, animals were anaesthetized with halothane (2%). The left external carotid artery (ECA) was canalized and 10 small clots were injected into the internal carotid artery (ICA) gently one after another over a period of 30s. Animals were sacrificed at 2 or 24hr after stroke, and brains were harvested and processed for inspection of Willis circle, 2,3,5-triphenyltetrozolium chloride (TTC) staining and immunohistological staining of tisse-type plasminogen activator(tPA).

Results: Right side weakness was evident in all rats after MCAO. In the rats sacrificed at 2hr after MCAO, clots were localized in the ICA close to MCA bifurcation and the proximal part of MCA, while no clots were found in Willis circle and the branching artery in the rats sacrificed at 24hr after MCAO. TTC staining demonstrated an evident ischemic lesion area in the MCA territory. Confocal microscopy of IHC staining of tPA showed a substantial increase of tPA immunoreactivity which was detected in both ischemic and non-ischemic side.

Conclusions: Our results indicate that the model produces reliable embolic occlusion of the proximal part of the MCA, and it results in the relatively consistent ischemic lesion in the MCA territory. This model resembles the complex pathophysiology of clinical embolic stroke closely and is well-suited for investigations of the specific pathophysiology of embolic stroke.

Sponsor: *NIH*

1112 *(Poster)*

Author: Angela Peterson-Ford

Presenter: Angela Peterson-Ford

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

Angela Peterson-Ford, Virgina Pearce, Peter Koulen Department of Pharmacology and Neuroscience University of North Texas Health Science Center at Fort Worth Fort Worth, Texas 76107-2699

INTRACELLULAR CELL SIGNALLING OF PROLIFERATING HIPPOCAMPAL PRECURSOR NEURONS

Purpose: Neuronal progenitor cells in the adult hippocampus may respond to proliferation and differentiation factors in order to renew. Therefore, we determined if specific culture media might facilitate renewal of cell types in adult primary hippocampal progenitor cells derived from C57/Bl6 mice. During renewal, IP3 receptors that mediate calcium signaling and neurite formation may be affected by cell signaling. Therefore, we used immunostaining and calcium signaling to determine phenotypes of cells with potential for renewal and differentiation.

Methods: Primary cultures of hippocampus were derived from C57/Bl6 mice. Immunostaining and calcium imaging were used to analyze the phenotype of derived progenitors. Antibodies to cell type specific markers were used to determine neuronal or glial phenotypes. IP3 receptor expression patterns were also identified using isotype-specific antibodies. Calcium (Ca2+) release was induced with 0.1 µM IP3-AM and monitored with Fluo-3 AM (Molecular Probes, Eugene, OR, USA). Changes in fluorescence as a measure of total Ca2+ release into the cytosol were determined.

Results: Cellular morphology of primary hippocampus cells changed within 6-24 hrs of culture, resulting in well defined and elongated processes in both neuronal and glial derived progenitor cells. Transgenic studies indicate that GFAP-expressing progenitor cells may be the predominate source for constitutive adult neurogenesis in mouse forebrain, and transient precursors of new neurons in the adult hippocampus may be derived from astrocytes. In vitro conditions can reprogram the neurogenic potential of cells. The activity of IP3-AM on primary hippocampal cultures was determined by the changes in the cytosolic Ca2+ concentration. In vitro, hippocampal precursors can differentiate into astroglia, oligodendroglia, and neurons, and are useful for studying the effects of growth factors on differentiation including proliferation of hippocampal neuronal progenitors in serum free media. During aging, the hippocampus exhibits diminished neurogenesis, possibly due to decreased levels of factors for cell proliferation. Proliferation factors act through their respective receptors to promote neurogenesis and self repair, and correspondingly these receptors are upregulated after cerebral ischemia.

Conclusions: Morphological changes in primary hippocampal cultures were observed including cell elongation and proliferation of precursor neurons and the potentiation of calcium release properties of neurons.

Sponsor: *NIH/NIA, Alzheimers Association*

1113 *(Oral)*

Author: Sung-Yong Hwang

Presenter: Sung-Yong Hwang

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Sung-Yong Hwang, Volodymyr Rybalchenko and Peter Koulen Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas 76107

EFFECT OF PRESENILIN-1 ON INTRACELLULAR CALCIUM SIGNALING

Purpose: RyRs interact with PS-1 and RyR-mediated Ca2+ signaling in neurons is altered by overexpression of PS-1 or mutant PS-1. However, it is unknown, which type of RyR is involved, and the binding site for PS-1 as well as the underlying mechanism of action for changes in Ca2+ signaling remain to be established. We hypothesize that specific regions of PS-1 interact with brain RyR type 2 leading to changes in channel activity.

Methods: In order to test our hypothesis, we used adult mouse CNS tissue and the neuronal cell line, SH-SY5Y. A cross-linking assay was used to identify the specific regions of PS-1 interacting with RyR type 2. Optical imaging of cytosolic Ca2+ concentration using Ca2+ sensitive fluorescent dyes, and single channel electrophysiology were used to measure changes in Ca2+ release in live cells and channel activity at the single channel level in the presence or absence of specific region of PS-1, respectively.

Results: Specific regions of PS-1 that interact with RyR type 2 were identified using a cross-linking assay. We found that specific PS-1 fragments enhance the activity of RyR type 2 at the single channel level by increasing the open probability of RyR2 channels. Optical imaging of cytosolic Ca2+ concentration was used to address effects of specific regions of PS-1 on intracellular Ca2+ signaling in living cells. SH-SY5Y cells overexpressing the PS-1 fragments showed elevated Ca2+ responses which were RyR specific as identified with specific pharmacologic inhibitors.

Conclusions: Our data demonstrate that the binding of specific regions of PS-1 to RyR type 2 leads to changes in RyR type 2 activity. Our results will allow us to understand the mechanism of action by which PS-1 modulates the activity of neuronal RyR type 2 and help develop new molecular and pharmacological tools to control Ca2+ dyshomeostasis, which is involved in the genesis of neurodegenerative diseases including AD.

Sponsor: *NIH/NIA, Alzheimers Association*

1114 *(Oral)*

Author: Ji-yeon Hwang

Presenter: Ji-yeon Hwang

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Ji-yeon Hwang, Meharvan Singh and Peter Koulen, Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, 3500 Camp Bowie Blvd, Ft. Worth, TX 76107

EFFECTS OF PROGESTERON ON CALCIUM SIGNALING IN HIPPOCAMPAL NEURONS

Purpose: The purpose of the present study is to identify the subcellular distribution of IP3Rs and other signaling proteins including Akt and phospho-Akt, in the primary hippocampal neuron and to test the hypothesis that P4 controls the gain of IP3R-mediated intracellular Ca2+ signaling in neurons.

Methods: All experiments were performed with cultured primary mouse hippocampal neurons. Immunocytochemistry was used to identify the subcellular distribution of proteins of interest. The effect of P4 on intracellular Ca2+ signaling was determined by optical imaging of intracellular Ca2+ concentrations using fluorescent Ca2+ indicator dyes.

Results: Primary hippocampal neurons express predominantly IP3R type 1 and 3. Their cellular distribution as well as that of Akt and phospho-Akt was altered by P4 treatment. P4-pretreated neurons showed potentiated IP3R-mediated intracellular Ca2+ responses. Acute application of P4 resulted in transient elevations of intracellular Ca2+ concentrations.

Conclusions: P4 increases the gain of IP3Rs in primary hippocampal neurons. Our results will contribute to establishing potential pharmacological approaches for the treatment of pathological conditions characterized by a dysregulation of cellular Ca2+ concentrations such as Alzheimers disease

Sponsor: *NIH/NIA*

1115 *(Poster)*

Author: Paramjit Kaur

Presenter: Paramjit Kaur

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Paramjit Kaur, Parmeet K. Jodhka, Wendy Underwood, and Meharvan Singh University of North Texas Health Science Center Dept. of Pharmacology and Neuroscience 3400 Camp Bowie Blvd. Fort Worth, TX 76107

PROGESTERONE PROTECTS AGAINST GLUTAMATE TOXICITY IN A MAPK AND PI-3K DEPENDENT MANNER IN ORGANOTYPIC EXPLANTS OF THE CEREBRAL CORTEX

Purpose: Women have a higher prevalence for Alzheimers disease than men, suggesting that the precipitous decline in gonadal hormone levels following the menopause may contribute to disease causation. While considerable attention has focused on the consequence of estrogen loss, it is important to recognize that the menopause results in a precipitous decline in progesterone levels as well. Thus, progesterone may also be an important hormone to consider in hormone therapies for post-menopausal women. Here we evaluated whether progesterone is neuroprotective, and further, determined if this protection required the activation of the pro-survival MAPK and PI-3K pathways.

Methods: Using organotypic explants (slice culture) of the cerebral cortex, we evaluated if progesterone protects cortical explants against glutamate toxicity. In addition, we evaluated whether such protection was dependent on activation of the MAPK and PI-3K pathways. Assessment of cell death was achieved by measuring the amount of Lactate Dehydrogenase (LDH) released into the media. An enzyme linked immunosorbant assay was used to detect and quantify cellular BDNF levels, a presumed surrogate marker of cell viability.

Results: Progesterone (100 nM) protected cortical explants against glutamate-induced LDH release. Pharmacological inhibition of both the MAPK pathway, using the MEK1/2 inhibitor (U0126, 10 μM), or the PI-3K pathway, using LY294002 (15 μM, 30 min) prevented progesterones protective effects, supporting the requirement of both the MAPK and PI3-K pathways in progesterone - mediated protection. In addition, progesterone elicited a two-fold increase in BDNF protein and a 70% increase in mRNA for BDNF, suggesting that progesterones protective effects could also be mediated by the pro-survival growth factor, BDNF.

Conclusions: Our data suggest that the protective effects of progesterone are mediated by rapid-□non-genomic signaling events (i.e., activation of the MAPK and PI-3K pathways), and is associated with an increase in the expression of the neurotrophic factor, BDNF

Sponsor: *The National Institutes of Aging (NIA) - 1 PO1AG22550-01 (Project 4) and 1 RO3 AG023330-01*

1116 *(Poster)*

Author: Nilka Rivera-Portalatin

Presenter: Nilka Rivera-Portalatin

Department: Molecular Biology and Immunology

Classification: Staff

Nilka M.Rivera-Portalatin (1,3), Jose L. Vera-Serrano (1), Katalin Prokai-Tatrai (2), Laszlo Prokai (1,3) (1)Department of Molecular Biology and Immunology, University of North Texas Health Science Center, Fort Worth, TX, 76107, USA (2)Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, TX, 76107, USA (3)Department of Medicinal Chemistry, College of Pharmacy, University of Florida, Gainesville, FL 32610-0485, USA

COMPARISON OF ESTROGEN-DERIVED ORTHO-QUINONE AND PARA-QUINOL CONCERNING INDUCTION OF OXIDATIVE STRESS

Purpose: Ortho-quinones formed from catechol estrogens are considered prooxidants due to the production of superoxide radical anions through redox cycling via semiquinones. Para-quinols have been identified as novel metabolites of and as the major products of hydroxyl-radical scavenging by estrogens. Cycling of these compounds has also been discovered, because they are converted back to the parent estrogen via reductive aromatization in vitro and in vivo. The purpose of this research is to demonstrate that, unlike ortho-quinones, para-quinols do not induce oxidative stress due to this cycling.

Methods: In order to prove our hypothesis, different tissue homogenates from ovariectomized rats were incubated with 17b-estradiol and 17b-estradiol-derived para-quinol (10b,17b-dihydroxyestra-1,4-diene-3-one). Negative control experiments were performed by incubating the tissues under study with a prooxidant compound, estra-1,5(10)-dien-3,4,17-trione (estrone 3,4-quinone). The amount of hydrogen peroxide produced was determined spectrophotometrically. Quantification of hydrogen peroxide was done by calibrating with serially diluted H2O2 standard solutions. The protein content of tissues was determined spectrophotometrically by the Bradford dye-binding method using serum albumin as a reference. Rates of H2O2 production were expressed as in nmol/h/mg protein (mean ± standard deviation). One way analysis of variance (ANOVA) followed by post hoc Dunnetts test was done to test for statistically significant differences (P

Results: Like the estrogen itself, 17b-estradiol-derived para-quinol did not induce oxidative stress, as the rate of hydrogen peroxide production during the incubations of the compounds in various tissue homogenates was not significantly different from that produced in the control experiments performed without the addition of a test compound. We also confirmed that the estrogen estrone 3,4-quinone was a profound prooxidant due to redox cycling, as the rate of H2O2 production increased substantially in its presence.

Conclusions: In conclusion, our studies have indicated that, unlike ortho-quinones, para-quinols do not induce oxidative stress. Consequently, para-quinols may be used as prodrugs for neuroprotectant estrogens

Sponsor: *NIH*

1117 *(Poster)*

Author: David Lim

Presenter: David Lim

Department: Pharmacology & Neuroscience

Classification: GSBS Student

David T. Lim; Parmeet Jodhka, PhD.; Meharvan Singh, PhD. -University of North Texas Health Science Center, Fort Worth, TX 76107

THE ROLE OF THE MEMBRANE PROGESTERONE RECEPTOR IN ERK/MAPK SIGNALING IN PRIMARY NEURONAL CULTURES

Purpose: Estrogens and progestins have been reported to promote cell survival in various experimental models and through different cell signaling pathways including ERK1/2. Recently, these steroid hormones have shown considerable promise as a neuroprotective agent. Estrogens and progestins can mediate neuroprotective effects by a classical genomic mechanism or by the recruitment of signal-transduction pathways like ERK/MAPK. Like others, we have shown that progesterone elicits ERK1/2 phosphorylation. We also wanted to know whether progesterone can elicit ERK5 phosphorylation, which has been shown to be important in neuronal survival. To further explore progesterones mechanisms in activating cell signaling, we determined whether the effect of progesterone on ERK/MAPK signaling is mediated by the classical intracellular/nuclear progesterone receptor (PR) or the newly cloned membrane progesterone receptor (mPR).

Methods: We used primary cortical cultures from postnatal day 3 (P3) mice to test our hypothesis. After 6 days in vitro, cultures were treated with progesterone (P4) or progesterone tethered to BSA (P4-BSA) in a time dependent manner. Individual cell samples were then collected and lysed. Western blots were performed using phosphopeptide-specific antibodies to assess relative phosphoERK1/2 and phosphoERK5 protein levels. Blots were then quantified using densitometric analysis.

Results: We found that P4 could elicit ERK1/2 and ERK5 phosphorylation in cortical primary cultures. We also found that P4-BSA could activate ERK1/2 phosphorylation in a time dependent manner.

Conclusions: Collectively, our data suggest that multiple members of the ERK family may be involved in progesterone-induced neuroprotection and implicate the novel membrane progesterone receptor as an important mediator of this effect.

Sponsor: *N/A*

1200 *(Poster)*

Author: Nicole Bereolos

Presenter: Nicole Bereolos

Department: Psychology

Classification: GSBS Student

Nicole M Bereolos, MPH, Susan F Franks, PhD, James R Hall, PhD, Susan Frensley, MS, Kelley Beck, BA, Sharon Yurvati, MS, German Berbel, DO and Adam Smith, DO. UNTHSC, Fort Worth, Texas, United States.

THE IMPACT OF STRESS MODERATORS IN INDIVIDUALS PRESENTING FOR BARIATRIC SURGERY WITH HIGH VERSUS LOW RISK EATING BEHAVIOR

Purpose: Candidates who presented for bariatric surgery were assessed on the stress moderator scales of the Millon Behavioral Medicine Diagnostic (MBMD) and psychological dimensions of eating assed via the Eating Inventory (EI). It is hypothesized that individuals who have maladaptive eating behavior will exhibit an increase in psychosocial stress.

Methods: Participants included 218 obese patients who presented for pre-operative evaluation and were primarily female (82%), Caucasian (78%), and married (58%). BMI ranged from 35 to 84 (M = 47.5). Prevalence scores for the MBMD stress moderator scales were compared to high versus low scores on the cognitive restraint (CR) and disinhibition (DI) scales of the EI via multiple ANOVAs.

Results: Significant group differences ($p < .05$) were found in 4 stress moderators (Illness Apprehension, Functional Deficits, Social Isolation, and Future Pessimism) with respect to DI. Therefore, those who have more problems losing control with respect to adaptive eating behavior have an increase in reported awareness of change in their bodies, are unable to carry out daily activities, have less social support, and do not anticipate a productive life secondary to their medical condition. Pain Sensitivity and Spiritual Absence were not significantly associated to DI. For CR, none of the stress moderators were significantly different for the high versus low scores on this dimension.

Conclusions: The hypothesis that differences in stress factors between those with high vs low risk eating behavior was partially supported. Individuals who are less likely to respond to behavior changes did not have a significant increase in stress, whereas those who are disinhibited with respect to eating behavior have more problems with illness apprehension, functional deficits, social isolation, and future pessimism. This information helps to provide insight into the role of psychosocial stress on eating behavior of those who are obese. Targeting these particular stressors may aid to alter maladaptive eating behavior.

Sponsor: *N/A*

1201 *(Poster)*

Author: Svetlana Serova

Presenter: Svetlana Serova

Department: Psychology

Classification: GSBS Student

Svetlana Serova, B.A., University of North Texas, Denton, TX 76209 Susan Franks, Ph.D., University of North Texas Health Science Center, Fort-Worth, TX 76109 James Hall, Ph.D., University of North Texas Health Science Center, Fort-Worth, TX 76109 Katherine Kaiser, B. A., University of North Texas Health Science Center, Fort-Worth, TX 76109

ASSESSMENT OF DEMENTIA: THE EFFECT OF ACQUIESCENCE RESPONSE BIAS ON THE WMS-III.

Purpose: Logical Memory Recognition (LMR) subtest of the Wechsler Memory Scale -III is commonly used in neuropsychological assessment to discriminate between Dementia of Alzheimer's type (AD) and Vascular Dementia (VD). To detect the effect of response bias in assessment of dementia, we evaluated item response bias to LMR. One common response tendency is the acquiescence response bias. People tend to respond affirmatively with a Yes than a No, regardless of the content of the questions they are asked (Blau & Katerberg, 1982; Ray, 1983; Zuckerman, Knee, Hodgins & Miyake, 1995). We hypothesized that due to the acquiescence response bias individuals would give significantly more affirmative responses than negative responses on LMR. In addition, we predicted that subjects would correctly answer more questions with Yes as an answer, compared to questions with No as an answer.

Methods: LMR was administered as part of the standard neuropsychological evaluation of dementia to 238 geriatric patients (167 women and 71 men). LMR consists of 30 recognition questions, with Yes as the correct answer to 15 of them, and No as the correct answer to the remaining 15.

Results: Subjects exhibited an acquiescence response set by providing more Yes (M = 20) than No (M = 10) answers. They correctly answered significantly more questions with Yes as an answer (M = 12.40) than questions with No as an answer (M = 7.49), $t(237) = -16.96$, $p < .001$.

Conclusions: We concluded that questions with Yes as the correct answer are affected by acquiescence response bias, and therefore, have lower diagnostic value than questions with No as the correct answer. Post hoc analysis revealed that complexity of the lexical structure of the questions on LMR effects their ability to discriminate between AD and VD. LMR items that discriminate best between AD and VD were identified. Qualitative analysis of LMR responses is suggested to yield useful clinical information in assessment of dementia.

Sponsor: *N/A*

1300 *(Poster)*

Author: Turner Slicho

Presenter: Turner Slicho

Department: Osteopathic Manipulative Medicine

Classification: Postdoctoral Fellow/Resident

Turner Slicho, DO, MS (1); Scott T. Stoll, DO, PhD (1,2); John C. Licciardone, DO, MS, MBA(1,2); des Anges Cruser, PhD (1,2) 1= UNTHSC-TCOM Department of Osteopathic Manipulatiove Medicine, Fort Worth, TX 76107 2= Osteopathic Research Center, Fort Worth, TX 76107

PLACEBO POTENCY IN MANIPULATIVE MEDICINE RESEARCH: A PILOT STUDY OF PATIENT ATTITUDES TOWARDS THE TREATMENT OF LOW BACK PAIN

Purpose: Placebo arms of Randomized Control Trials (RCTs) involving manual medicine research are often assumed by researchers to be equally efficacious in creating a placebo experience for the patient. Patient attitudes and expectations towards types of active therapies have a direct effect on the efficacy of the treatment administered in areas of research other than manual medicine. Because a placebo attempts to account for the suggestibility of the active therapy being investigated, attitudes towards the effectiveness of a manual therapy mimicked in the placebo treatment should affect the placebo response rate, or placebo potency. The principle objective of this research project is to determine if there is a bias for different types of non-surgical therapy for low back pain: 1) high-velocity, low amplitude musculoskeletal manipulation, 2) light touch musculoskeletal manipulation, 3) therapeutic ultrasound therapy, and 4) current standard of care treatment including muscle relaxants, anti-inflammatory medication, and home exercise stretching programs.

Methods: A survey of opinions towards the four therapies listed above was sent to a list of 300 random individuals from a purchased mail list from USAData.com, an independent mail-marketing firm. The survey defines each treatment and asks the respondent to mark the extent to which s/he believes each treatment would: 1) help them get better faster, 2) decrease pain, 3) increase functionality, and 4) be a logical approach for the treatment of low back pain.

Results: With 89 surveys returned, respondents had a more positive outlook on the described treatment if they had experienced them in the past. Respondents also agreed more that HVLA was a logical way to treat low back pain compared to standard of care and light touch manipulation.

Conclusions: Researchers must continue to takes steps towards standardization of the placebo in manual medicine research to further assist in scientific validation.

Sponsor: *ORC*

1301 *(Poster)*

Author: Bowlva Lee

Presenter: Bowlva Lee

Department: Cowtown Marathon

Classification: Dual Degree Student DO/MS

Samuel Coleridge, Principle Investigator, Fort Worth, Tx 76107 Bowlva Lee, First Author, Fort Worth, Tx 76107 Kim Fulda, Second Author, Fort Worth, Tx 76107

KNEE INJURIES IN MARATHON RUNNERS WHO WEAR BRACES VS NO BRACE

Purpose: Athletes are plagued with injuries at some points in their careers, and many will also wear some type of support device, brace, or orthotic to help compensate for their injuries. This outcome paper is going to try and look to see if there is any relationship specifically in marathon runners with knee injuries and whether or not they wear knee braces. My hypothesis is that marathon runners who wear knee braces are more likely to have associated sports related injuries than runners who do not wear knee braces.

Methods: Participants for the Cowtown Marathon in Fort Worth, TX were given a survey to fill out during the registration times of the race. The survey included a broad range of information ranging from demographics to injury history. Data collection was then based upon participants who completed the survey and returned it. The study population included runners who participated in the Cowtown marathon. Data was collected for 3 consecutive years for the marathon, and data is still being planned to be obtained in future Cowtown marathons. In this study, there was no intervention involved. The survey was merely a snapshot of the runners at that moment in time.

Results: The data that was collected from the surveys were added into a data base spreadsheet where statistical analysis can be conducted using SPSS. The beauty of the survey is that multiple research angles can be taken from this data since the survey covered such a broad range of topics. There were a total of 824 combined injuries from 2003-2005.

Conclusions: Due to the low population of participants in the study with knee problems, there was no significant correlation of knee injuries in marathon runners in relation to wearing knee braces.

Sponsor: *N/A*

1302 *(Poster)*

Author: Yamileth Cazorla-Lancaster

Presenter: Yamileth Cazorla-Lancaster

Department: Osteopathic Manipulative Medicine

Classification: Dual Degree Student DO/MPH

Yamileth Cazorla-Lancaster,B.A. Chau Pham, D.O., M.P.H. des Anges Cruser, Ph.D. Daisha Cipher, Ph.D. Texas College of Osteopathic Medicine University of North Texas Health Science Center Fort Worth, TX 76107

A CROSS-SECTIONAL STUDY OF SOMATIC DYSFUNCTION AND CHRONIC CONDITIONS IN OLDER ADULTS

Purpose: The purpose of this pilot study was to investigate the relationship between somatic dysfunction and chronic conditions in adults aged 65 and older who received Osteopathic Manipulative Treatment (OMT).

Methods: This was a cross-sectional study with information collected from medical records of patients seen for OMT in a Geriatric clinic at the University of North Texas Health Science Center between January 1, 2000-May 1, 2005. Data elements included demographics, Instrumental Activities of Daily Living (IADLs), Geriatric Depression Scale-Short Form (GDS-SF) scores, trauma history, chronic conditions, and somatic dysfunction.

Results: The sample included 139 adults, 83% of whom were females. In the sample, 118 (85%) subjects were White, 61 (44%) were married, and 112 (81%) were living at home. The average age was 77.4 years (SD = 8.44). The mean number of chronic conditions per subject was 6.49 (SD = 2.64). The most common areas of somatic dysfunction were the pelvis (84%), the sacrum (61%) and the ribs (60%). There were significantly more subjects with sacral somatic dysfunction that had GDS-SF cutoff scores above 5. IADLs were also significantly related to somatic dysfunction. Significantly more subjects that needed moderate assistance with meal preparation had somatic dysfunction in the upper thoracic (T 1-4) region (p=.039). Subjects with a history of motor vehicle accident (MVA) had significantly less lumbar somatic dysfunction (p=.031), but significantly more upper thoracic (T 1-4) somatic dysfunction (p=.012). Subjects with pulmonary/respiratory conditions had significantly more cranial somatic dysfunction (p=.016). Significantly more subjects with neurological/psychiatric conditions had somatic dysfunction of the diaphragm (p=.043).

Conclusions: The results of this study suggest several significant relationships between somatic dysfunction and chronic conditions (pulmonary/respiratory and neurological/psychiatric conditions) as well as trauma (MVA). Future research should be directed toward the prospective investigation of the onset of traumatic events and subsequent somatic dysfunction, depression, and associated medical conditions.

Sponsor: *N/A*

1303 *(Poster)*

Author: Arthur Williams, Jr.

Presenter: Arthur Williams, Jr.

Department: Integrative Physiology

Classification: Staff

Arthur G. Williams, Jr., Preethi Durgam, Linda Howard, Scott T. Stoll, and H. Fred Downey. Departments of Integrative Physiology and Manipulative Medicine, University of North Texas Health Science Center, Fort Worth, TX 76107

LYMPH FLOW IN THE THORACIC DUCT OF CONSCIOUS DOGS DURING OSTEOPATHIC MANIPULATIVE TREATMENT AND EXPANSION OF THE EXTRACELLULAR SPACE

Purpose: We have previously demonstrated that compression of the abdomen, as performed in osteopathic manipulative treatment (OMT), increases flow in the thoracic lymph duct (TDF) of conscious dogs. The study investigated the effects of expansion of the extracellular space (ECE) on TDF, and whether this expansion would enhance the action of OMT on TDF.

Methods: Eight mongrel dogs were surgically instrumented to measure TDF and other cardiovascular variables. After recovery, OMT was performed for 8 min before and after ECE with normal saline, i.v., 4.4±0.3 % of body weight.

Results: Pre-OMT baseline TDF was 1.7 ±0.5 ml/min, and OMT rapidly increased TDF to 5.0±1.1 ml/min at 1 min (P

Conclusions: In summary, expansion of the extracellular space increases flow in the thoracic lymph duct of conscious dogs. Osteopathic manipulative treatment increases flow in the thoracic lymph duct before expansion of the extracellular space and to a similar degree after this expansion. (Supported by NIH grant U19 AT2023-01)

Sponsor: *NIH CAM Grant*

1304 *(Poster)*

Author: Hollis King

Presenter: Heath White

Department: Osteopathic Manipulative Medicine

Classification: Postdoctoral Fellow/Resident

Heath D. White, D.O., Scott & White Memorial Hospital, Temple, TX 76505 & Texas A&M University Medical School Scott T. Stoll, D.O., Ph.D., TCOM, UNTHSC, Fort Worth TX 76107 des Anges Cruser, Ph.D., TCOM, UNTHSC, Fort Worth TX 76107 Rebecca Whitesell, MPH, UT San Antonio Medical School SA, TX 73107 H.H. King, D.O., Ph.D.

OSTEOPATHIC MANIPULATIVE MEDICINE FOR CARPAL TUNNEL SYNDROME: CHANGES IN NERVE CONDUCTION

Purpose: The goal of this clinical trial was to assess for physiologic and anatomic changes in CTS in response to OMT.

Methods: This prospective, randomized, controlled, clinical trial (RCT)included two experimental groups, OMT and placebo sub-therapeutic ultrasound. Adults were enrolled who were between 21 and 70 with a clinical diagnosis of CTS and increased conduction latency (slowed conduction) of the median nerve. Outcome measures were changes in median motor and sensory distal latencies measured by Nerve Conduction Studies (NCS). Subjects receive six treatments. NCS were taken at entry to the study (baseline), mid-point, and endpoint.

Results: Thirty-seven of a planned 50 subjects were randomized to groups. Thirty-one subjects were included in the final data analysis. Preliminary analysis found no significant difference in NCS values over the three testing intervals. Analysis of 15 subjects with a single treatment provider found significant improvements in some NCS for the OMT group.

Conclusions: The results of this study indicate possibility for improvement of CTS with OMT, but no conclusive statements about the efficacy of OMT can be made. This preliminary study enabled us to identify multiple areas in the research design and methodology that could be improved, and provides the framework for future studies. This study contributed to achieving a 3-year NIH-NCCAM R21 to study OMT for CTS in a larger number of subjects.

Sponsor: *N/A*

1305 *(Poster)*

Author: Daniel Clearfield

Presenter: Daniel Clearfield

Department: Osteopathic Manipulative Medicine

Classification: Dual Degree Student DO/MS

Daniel Clearfield, OMSIV, BS Co-investigator Pre-Doctoral Fellow, DO/MS Student Department of Osteopathic Manipulative Medicine John Licciardone DO, MS, MBA Principal Investigator Director of Clinical Research Graduate Advisor Osteopathic Research Center Scott Stoll, DO, PhD Co-Investigator and Graduate Committee Member Department of Osteopathic Manipulative Medicine Osteopathic Research Center Jay Shores, PhD Co-Investigator and Graduate Committee Member Assistant Professor School of Health Professions University of North Texas Health Science Center - Texas College of Osteopathic Medicine Fort Worth, TX 76107

ATTITUDES, KNOWLEDGE, AND USE OF OSTEOPATHIC MANIPULATIVE TREATMENT BY OSTEOPATHIC SPORTS MEDICINE PHYSICIANS:

Purpose: There is currently no literature supporting whether or not osteopathic sports medicine physicians (OSMP) use OMT on a regular basis. One might believe that all of these physicians would take advantage of the benefits OMT would have for their patients. If OMT is not being used by OSMPs, then their rationale for not employing such a valuable treatment must be further explored. This project aims to assess the frequency of OSMPs use of OMT. If there are OSMPs who choose not to use OMT, then this survey aims to discern the reasons why they are not. I will be analyzing whether the age, gender, geographical region, and/or practice is related to whether an OSMP uses OMT. I will be analyzing whether a residency in an AOA (American Osteopathic Association), ACGME (Accreditation Council for Graduate Medical Education), or dually-accredited program predicts the use of OMT by an OSMP. Finally, I will be analyzing if a sports medicine fellowship via the AOA vs. the ACGME predicts the use of OMT by an OSMP.

Methods: This study is a cross-sectional survey. Surveys will be mailed to a list of all available osteopathic sports medicine physicians in the United States made available by the American Osteopathic Association and the American Osteopathic Academy of Sports Medicine. In order to address specific aims 1-4, I have developed a 33-question survey instrument. The survey will be a self-reported instrument (with no subject identifiers) designed to be completed in approximately five minutes. Twenty-three of the questions are scored on a Likert scale graded from 1 to 5. A score of 1 will correspond to ☐strongly agree, a score of 3 analogous to ☐undecided, and a score of 5 corresponding to ☐strongly disagree. The ten remaining questions will request OSMP demographic and medical practice information. Survey data will be collected and analyzed using SPSSTM Version 11.5.

Results: Results for this study are currently pending.

Conclusions: The information from this project may provide support for policies that incorporate more OMT training in Continuing Medical Education (CME) or within post-doctoral Osteopathic Sports Medicine Fellowships.

Sponsor: *N/A*

1306 *(Poster)*

Author: des Anges Cruser

Presenter: Patricia Meyer

Department: Osteopathic Manipulative Medicine

Classification: Postdoctoral Fellow/Resident

Patricia Marie Meyer, D.O., MS, University of South Florida, Tampa, 33612 Scott T. Stoll, D.O., Ph.D., TCOM, UNTHSC, Fort Worth, TX 76107 des Anges Cruser, Ph.D., TCOM, UNTHSC, Fort Worth, TX 76107 Heath D. White, D.O., MS, Scott and White Memorial Hospital, and Texas A&M University, Temple, TX 75033 Rebecca Whitesell, MPH, UT San Antonio Medical School, SA, TX 73132

IMPROVING SYMPTOMS, PAIN, FUNCTIONING, AND STRENGTH FOR PERSONS WITH CARPAL TUNNEL SYNDROME

Purpose: The purpose of this study was to examine whether OMT could reduce symptoms, improve functioning, decrease pain and improve strength in persons with CTS. Hypothesis 1: OMT will decrease symptom severity and pain measured by the Levine Symptom Severity Questionnaire and the visual analog scale. Hypothesis 2: OMT will improve daily functioning and strength.

Methods: Subjects (N=32) between 21 and 70 with confirmed diagnosis of CTS based on Nerve Conduction Studies (NCS), who had none of the medical exclusions were consented and randomized to two groups (OMT and Control). OMT group received one treatment, Control group received one sub-therapeutic ultrasound treatment. Power analysis called for 19 subjects per group. Symptom severity and functional status were self-reported using the Levine scales for CTS. Pain was measured with the visual analog scale. Grip strength was tested using a Jamar Dynamometer. Based on the literature, the average of three scores taken at each visit for grip strength, key pinch strength, tripod pinch strength, and tip pinch strength was used for the analysis. Outcome measures were taken at entry to the study, mid point, and after the last treatment session.

Results: The OMT treatment group had complete data for 14 subjects, and the control group 18. The groups were similar in composition on gender, age, and body mass index (BMI). BMI correlated with symptom severity scores (r 0.392, p=.035) and functional status scores (r 0.379, p=.043). Baseline nerve conduction studies for median motor latencies (MML) differed significantly between groups (p=.047), and MML was related to symptom (r 0.437, p=.014) and function scores (r 0.418, p=.019). The OMT group reported significantly improved functioning at the end of the trial (p=0.019) but between group changes were not significant. For the OMT group grip strength changed significantly (p=.013). The control group made significant improvement in pinch and tripod pinch strength (p= .034).

Conclusions: This RCT was exploratory and preliminary; limited by a small sample size. These subjects continued in their normal standard care during the study which may have included stretching or splinting or other therapies, and this was not accounted for in the analysis. This study, however, provided statistical support for trends in the efficacy of OMT for CTS, and supported a successful R21 proposal to the NIH-NCCAM for a three year RCT for OMT in CTS patients.

Sponsor: *N/A*

1307 *(Poster)*

Author: Carolyn Pickett

Presenter: Carolyn Pickett

Department: Osteopathic Manipulative Medicine

Classification: Dual Degree Student DO/MS

Carolyn Pickett, Scott T. Stoll, D.O., Ph.D., des Anges Cruser, Ph.D., Daisha J. Cipher, Ph.D., TCOM, UNTHSC, Fort Worth, TX 76107

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): IMMEDIATE EFFECTS OF OSTEOPATHIC MANIPULATIVE TREATMENT ON EXERCISE TOLERANCE AND DYSPNEA

Purpose: Contribute to our knowledge of the effects of OMT on breating and exercise tolerance in patients with COPD. Hypothesis 1: One OMT intervention will have an immediate effect of improving dyspnea in a stable COPD subject, as measured by response to the Borg scale. Hypothesis 2: One OMT intervention will improve exercise tolerance in a stable COPD subject, as measured by distance in the six-minute walk test.

Methods: After obtaining informed consent, initial plethysmography and spirometry test were performed by a respiratory technician to verify that subjects met the pulmonary function test inclusion criteria. After acceptance into the study protocol, subjects were randomly assigned to either the Osteopathic Manipulative Treatment group or the no treatment (i.e. rest) group. Demographics were then recorded and questionnaires were completed. Subjects filled out the St. Georges Respiratory Questionnaire, The American Thoracic Society Dyspnea Index and Borg Scale. The entire study took place in the Internal Medicine Department at UNTHSC-TCOM.

Results: Exploratory data analyses revealed equal variances in all descriptive measures. Between group differences were not statistically significant for any demographics or for the Quality of Life measures. No immediate effects of OMT were statistically significant following exercise for any of the outcomes of interest. Examination of individual cases within the sample provides clinically important information to contribute to our knowledge of how OMT versus rest may affect the six minute walk and the Borg Scale for COPD patients.

Conclusions: Other challenges in OMT research are treatment dosage and frequency. In the clinical setting dosage and frequency of treatment is often based on subjective patient reports and physician reimbursement. Current OMT literature does not provide standards for dosage and frequency; therefore, this pilot study took the first step of looking at immediate affects. It is not possible to conclude appropriate dosage and frequency based on the findings of this study. Future studies with larger number of subjects and varying dosage and frequency will aid in determining these factors. Clinicaly important differences in the experimental groups provides information needed to design a larger study with improvements in design.

Sponsor: *N/A*

1308 *(Poster)*

Author: Damien Kinzler

Presenter: Damien Kinzler

Department: Select a Department

Classification: Dual Degree Student

Damien Kinzler, Jeffrey Siu and Michael L. Smith Universiy of North Texas Health Science Center and the Osteopathic Research Center Fort Worth, TX 76107

OSTEOPATHIC MANIPULATION CAN REDUCE PAIN-INDUCED ELEVATIONS OF SYMPATHETIVE NEURAL ACTIVITY

Purpose: Osteopathic Manipulative Treatment (OMT)has been shown to reduce pain secondary to musculoskeletal injury. As pain has been shown to produce a corresponding rise in sympathetic nervous activity (SNA), it is postulated that specific OMT techniques may exhibit sympatholytic effects. We hypothesized that an OMT technique known as "rib-raising" techniques will reduce SNA under a cold-pressor state.

Methods: Six naïve, healthy subjects by history and physical examination were recruited for this study. Each subject gave informed written consent. Each subject was then fitted with a 4-lead EKG, non-invasive beat-to-beat blood pressure monitor (photoplethysmograph) and measurement of sympathetic nerve activity using standard microneurography. All data were recorded continuously on a customized analysis system on a computer. After instrumentation, each subject was given an initial period of 20 min of quiet rest. They were then exposed to a two-minute intermittent cold-pressor stimulus at a bath temperature of 10° C. Data recording began two-minutes prior to the stimulus, during the stimulus and for a four-minute recovery period. After each recovery the subject was then allowed to rest for 12 minutes. This procedure was completed for a total of six stimuli (six sham and six OMT). During each stimulus either sustained inhibitory rib-raising or sham OMT was applied. Both conditions were performed by the same operator for all subjects. Sustained inhibitory rib-raising was performed by bilaterally placing the operators fingertips on the ipsilateral posterior rib heads at the most cephalic portion of the thoracic spine. The fingertips were then raised anterolaterally for 2 min in an attempt to inhibit the thoracic sympathetic chain ganglia. Sham OMT was performed by placing the hands in the same position without the concurrent anterolateral force.

Results: SNA activity was reduced in the 10° C state by simple nerve count, consistent with our hypothesis. A matched samples analysis revealed a significant reduction in the OMT vs Sham stimulus with $p<0.05$.

Conclusions: This study demonstrated that a sympatholytic effect of OMT can be invoked in healthy individuals with a pain-induced elevation of SNA. The reduction in SNA activity compared to the sham protocol supports the hypothesis that the effects of manual medicine are independent of a non-measurable operator dependent placebo effect and that significant physiologic effect can be derived from the appropriate use of OMT.

Sponsor: *NIH*

1400 *(Poster)*

Author: Anita Kurian

Presenter: Anita Kurian

Department: Department of Biostatistics

Classification: SPH Student

Anita Kurian, M.B.B.S, M.P.H. School of Public Health, University of North Texas Health Science Center, FW, TX; Tarrant County Public Health, Fort Worth, Texas - 76104; Sejong Bae, Ph.D School of Public Health, University of North Texas Health Science Center, FW, TX

HEAVY AND BINGE ALCOHOL USE IN TEXAS: BEHAVIORAL RISK FACTOR SURVEILLANCE SURVEY- 2003

Purpose: This study sought to assess the prevalence of heavy and binge alcohol use, and the factors predicting heavy and binge alcohol use by gender, in Texas using the 2003 Behavioral Risk Factor Surveillance Survey(BRFSS)data.

Methods: Crude and adjusted logistic regression analyses by gender, were performed to determine the relationship between each of the independent variable and being at risk for heavy and binge drinking. All analysis were performed using SUDAAN.

Results: Increasing age was found to have a statistically significant protective effect on binge alcohol use, in both men and women. Compared to never being married; being married or cohabiting had significantly lower odds of being at risk for heavy drinking in men. However, no such association between marital status and drinking pattern was seen in case of women. Current smoking status was significantly associated with higher odds of being at risk for heavy drinking and binge drinking in both men and women.

Conclusions: Although we did not find heavy and binge alcohol use to be a gender-specific behavior, based on prior research, it has been well established that significant gender differences do exist in the prevalence of heavy and binge alcohol use. Hence further efforts must be directed towards identifying variables that may interact with gender to help provide us with a more gender-balanced perspective of alcohol use. Furthermore, prevention and intervention strategies tailored to target the high risk groups such as smokers, younger age groups may particularly be required.

Sponsor: *N/A*

1401 *(Oral)*

Author: Anita Kurian

Presenter: Anita Kurian

Department: Department of Biostatistics

Classification: SPH Student

Anita Kurian, M.B.B.S, M.P.H School of Public Health, University of North Texas Health Science Center; Tarrant County Public Health, FW, TX-76104; Tyrone F. Borders, Ph.D. College of Public Health, University of Arkansas for Medical Sciences

RACIAL AND ETHNIC DIFFERENCES IN THE EFFECTS OF REGULAR PROVIDERS AND SELF-MANAGEMENT EDUCATION ON DIABETES PREVENTIVE CARE

Purpose: To examine the effects of having regular healthcare providers and diabetes self-management education (DSME) on the receipt of diabetes preventive care among all groups and by race/ethnicity, using the 2004 Behavioral Risk Factor Surveillance Survey (BRFSS).

Methods: Crude and adjusted logistic regression analyses were performed for the full sample, and also separately for blacks, Hispanics, and whites. All analyses were performed using SUDAAN.

Results: Among all persons, having at least one regular provider and DSME were significantly associated with higher odds of receipt of a HbA1c test, foot exam, and dilated eye exam in the past year. Among whites, having at least one personal provider was associated with higher odds of all three preventive services. Among blacks, having at least one personal provider was associated with higher odds of a HbA1c test; DSME was associated with higher odds of an HbA1c test and foot exam. Among Hispanics, having at least one personal provider was associated with higher odds of an HbA1c test and foot exam; DSME was not associated with any preventive service.

Conclusions: Access to personal healthcare providers should be promoted among whites, Blacks, and Hispanics to assure patients with diabetes receive recommended secondary preventive services. Diabetes self-management programs should also be expanded among whites and Blacks, but may need to be modified to benefit Hispanics.

Sponsor: *N/A*

1402 *(Oral)*

Author: Thaddeus Miller
Department: School of Public Health
Presenter: Thaddeus Miller
Classification: SPH Student

Thaddeus L. Miller, MPH, UNTHSC SPH; Department of Medicine Fort Worth Texas 76107 Peter Hilsenrath, PhD, UNTHSC SPH Fort Worth Texas 76107 Stephen E. Weis, DO, UNTHSC Department of Medicine, Tarrant County Public Health Department Fort Worth Texas 76107

THE HIDDEN BURDEN OF TUBERCULOSIS

Purpose: In the developed world tuberculosis is not considered to generate substantial loss of Quality Adjusted Life Years (QALYs). This assumption is based on enforced treatment, DOTS, and other strategies yielding a diminishing death toll, and the normally ambulatory, relatively limited course of treatment. This fails to consider sequelae of treated tuberculosis in terms of pulmonary function. Over 15,000 patients are treated for tuberculosis in the United States annually, with an unknown number left with reduced pulmonary function. Recognizing serious post illness loss of health quality is important to determining the full cost to society of tuberculosis, hence the value of prevention.

Methods: We used spirometry results of patients completing tuberculosis treatment to identify pulmonary dysfunction. Impairment was defined by American Thoracic Society guidelines. We assumed health quality lost to moderate to severe impairment in the cohort is similar to that known for chronic respiratory disease. We estimated remaining years of life, adjusted for region, and estimated QALYs lost to the cohort.

Results: Of 64 patients with treated tuberculosis, 17 (26.6%) experienced >25% loss of pulmonary function. Those 17 impaired patients can expect an adjusted cumulative 271.9 QALYs over their remaining lives. Never having had tuberculosis, this group would expect 468.8 QALYs, leaving a net loss of 196.9 QALYs to pulmonary disability. An additional 14.9 QALYs are lost to treatment, for a mean loss of 12.5 QALYs per impaired patient. Taken per tuberculosis patient, an average of 3.6 QALYs is lost to each.

Conclusions: The health utility lost to tuberculosis patients is much greater than previously estimated. Prior estimations of health quality include only that lost to treatment, or 0.45 QALYs per 6 month treatment course—3.6% of the health quality we found lost. An adjusted 14 QALYs has been estimated lost for each tuberculosis death. Consideration of health quality lost to pulmonary impairment reveals that those losses are even greater than those lost to death, emphasizing the value of prevention.

Sponsor: *N/A*

1403 *(Poster)*

Author: Yamileth Cazorla-Lancaster
Department: School of Public Health
Presenter: Yamileth Cazorla-Lancaster
Classification: Dual Degree Student DO/MPH

Yamileth Rosina Cazorla-Lancaster, B.A. Kristine Lykens, A.B., M.P.A., Ph.D. Fernando Treviño, Ph.D., M.P.H. Ximena Urrutia Rojas, Dr.PH University of North Texas Health Science Center School of Public Health Fort Worth, Texas 76120

DIFFERENCES IN HEALTHCARE UTILIZATION PATTERNS AMONG MEXICAN-AMERICAN, CENTRAL/SOUTH AMERICAN, PUERTO RICAN, CUBAN, AND DOMINICAN CHILDREN

Purpose: The purpose of this study was to investigate differences in healthcare access and utilization patterns among various subgroups of Latino children in the United States, specifically, Mexican, Puerto Rican, Dominican, Central/South American, Multi-Latino, and Cuban ethnic groups.

Methods: This is a cross-sectional study of deidentified public use data from the National Health Interview Survey from years 2001-2003 which was downloaded, merged and prepared by a research team at the University of North Texas Health Science Center, School of Public Health. Variables examined included demographic variables and indicators of access to and utilization of health care, such as where the child receives sick care and preventive care, whether the child had a well-child exam in the past 12 months and if the child had seen a specialist or a general doctor in the past 12 months.

Results: There were a total of 24,002 Latino children in the sample, including 17,088 Mexicans, 2,680 Central/South Americans, 1939 Puerto Ricans, 723 Multi-Latinos, 569 Dominicans and 563 Cubans. Over half of mothers of Mexican children had less than a high school diploma, while 21% of Cuban mothers had a bachelors degree or higher. Dominican (46.3%), Mexican (34%), and Puerto Rican (33.8%) children were most likely to have a ratio of family income to poverty threshold below .99. Those most likely to not receive preventive care anywhere were Mexicans (53.6%) and Central/South Americans (41.3%). Only 59.9% of Mexican, 70.9% of Central/South American, and 71.7% of Cuban children had a well-child checkup in the last 12 months compared to 84% of Puerto Rican and 82.5% of Dominican children.

Conclusions: These results suggest that there are significant within group differences among Latino children living in this country in terms of access to and utilization of health care. In general, Puerto Rican and Dominican children are among the poorest of Latino children, yet they are also the most likely to have preventive care. Mexican children were the most likely to not have a place to receive preventive care and not have had a check-up in the last 12 months. These differences have important implications for the delegation of public health resources and health care policy. In particular, more effort should be aimed at increasing the percentage of Mexican and Central/South American children receiving preventive care and greater attention needs to be paid to the needs of the emerging Central/South American and Multi-Latino groups.

Sponsor: *N/A*

1404 *(Poster)*

Author: Laura Gonzales

Presenter: Laura Gonzales

Department: Physician Assistant Studies

Classification: TCOM MPAS Student

Laura Gonzales PA-S; Suzanne Melville PA-S; Olive Chen, PhD; Laurie Hill, PA-C

WEIGHT LOSS AND ITS CORRELATION WITH PERCEIVED IMPROVEMENT IN COMORBIDITIES, PSYCHOLOGICAL WELL-BEING IN LAP BAND RECIPIENTS

Purpose: The purpose of this study was to investigate outcomes of Lap Band surgery focusing on recipients weight loss, their perceived improvement of five comorbid conditions and psychosocial wellbeing. The comorbidities included: high blood pressure, diabetes, high cholesterol, osteoarthritis and gastroesophageal reflux disease. Psychosocial wellbeing was measured using statements which gauged perceived improvements in self image, societal acceptance, and overall happiness.

Methods: A cross-sectional survey design was used in this study. Lap Band recipients who were =18 years at the time of surgery, and had their surgery between January 2002 and March 2005, were eligible to be included in this study. A total of 254 Lap Band recipients met the inclusion criteria and were invited to respond to the survey. A 10-question survey was developed by the researchers and pilot tested before mailing. SPSS (12.0) was used to perform statistical analyses.

Results: A total of 102 surveys were completed and returned (43.8% response rate). Most of the respondents were: Caucasian (90%), female (78%), between 36 and 55 (69%), and college educated (50%). Respondents on average lost 54.21% of their excess weight. Correlations between weight loss and perceived improvement in high blood pressure (r =.347, p

Conclusions: The results of this study showed that the extent of weight loss following Lap Band surgery is predictive of patients perceived improvement. The more weight respondents lost, the more improvement in blood pressure, cholesterol and psychosocial wellbeing they reported. Although, routine evaluation and progress notes from clinicians, as well as reduction or discontinuation of certain medications were events that likely contributed to the respondents perception of improvement in their comorbidities. The limitation of the study was that it relied heavily on self-reported data.

Sponsor: *N/A*

1405 *(Poster)*

Author: Christopher Mann

Presenter: Adib Asrabadi

Department: Family Medicine

Classification: Dual Degree Student DO/MS

Christopher R. Mann D.O., Department of Family Medicine, University of North Texas Health Science Center, Fort Worth, TX 76107; Adib Asrabadi DO/MS Student, University of North Texas Health Science Center, Fort Worth, TX 76107; Scott Hilborn MS, University of North Texas Health Science Center, Fort Worth, TX 76107

A SURVEY ANALYSIS OF TESTICULAR CANCER SCREENING AMONG SPORTS MEDICINE PHYSICIANS

Purpose: The purpose of this project is to evaluate the current practices of sports medicine physicians with respect to delivery of testicular cancer education and the practice of testicular cancer screening for young athletes. The specific objectives are to employ a survey to determine: (1) the prevalence of testicular cancer training during residency and fellowship, (2) the prevalence of practicing routine testicular examinations, (3) the prevalence of delivery of testicular health education.

Methods: A postal survey of approximately 1,800 sports medicine physicians nationwide was conducted. Eligible participants were physicians members of the American Osteopathic Academy of Sports Medicine. The initial survey questionnaires were mailed to a 50% random sample of the approximately 3600 physician members. Each questionnaire was accompanied by a cover letter stating the purpose of the survey as well as a self addressed and stamped envelope.

Results: A total of 741 returned questionnaires representing a response rate of roughly 41% were entered into SPSS. Descriptive statistical analysis characterizing the survey respondents and their reported beliefs, attitudes, and behaviors regarding testicular cancer screening were performed. Chi-square analysis was conducted to test for any overall statistical significance between categorical variables. We found that younger physicians (

Conclusions: Our findings demonstrate that physicians as a group are not comfortable with the medical training received on testicular cancer. Hopefully adjustments will be made to the medical education system to better train medical students, residents, fellows, and practicing clinicians. Also, our results indicated the need for further educational materials on testicular cancer screening. As a result, we aim to develop an "educational pamphlet" that can be used to increase patient awareness and promote self examination to screen for testicular cancer.

Sponsor: *N/A*

1406 *(Poster)*

Author: Lorena Gallegos

Presenter: Lorena Gallegos

Department: Family Medicine

Classification: McNair/SMART Participant

Lorena Gallegos, B.S. UNTHSC, TCOM, Dept of Family Medicine, Fort Worth, TX 76107; Roberto Cardarelli, DO, MPH, UNTHSC, TCOM, Dept of Family Medicine, Fort Worth, TX 76107 Kathryn Cardarelli, PhD, UNTHSC, SPH, Dept of Epidemiology, Fort Worth, TX 76107

PERCEIVED DISCRIMINATION AND STRESS

Purpose: The purpose of this study is to better understand the association between perceived discrimination and stress. Based on the potential findings, we hope to provide a guide for future investigators a concise understanding among the relationship between the discrimination and stress as mediators to poor health.

Methods: This was a cross-sectional study that used subjects enrolled in the Traditional and Emerging Risk Factors for Individuals Developing Diabetes, Metabolic Syndrome, and Coronary Heart Disease. Exactly eighty-two potential participants were approached and 80 agreed to participate in our study. Participants were administered a validated questionnaire, which assesses perceived discrimination and stress levels. Microsoft Office Access and Excel 2003 software were used for data collection and SPSS statistical software was used to analyze the data. All statistical analyses were performed at a level of significance of 0.05. Logistic regression was used to assess the association between perceived discrimination and stress. Information on age, gender, race/ethnicity, and socioeconomic status was also collected. Chi Square was used to evaluate differences among groups.

Results: Our results found that a person who indicated a very stressful lifestyle was 8 times more likely to have had an experience of discrimination in their life (p value = 0.01).

Conclusions: Stress and perceived discrimination are highly associated with each other. This may explain how perceived discrimination has been found to be a predictor to heart disease.

Sponsor: *N/A*

1407 *(Poster)*

Author: Nuha Lackan

Presenter: Nuha Lackan

Department: Department of Health Management and Policy

Classification: Faculty

Nuha Lackan, Ph.D., UNTHSC School of Public Health, Department of Health Management & Policy, Fort Worth, TX 76107. Walter McConathy, PhD. TCOM, Dept of Internal Medicine, Fort Worth, TX 76107. D.W. Lackan, M.D., Baylor Specialty Associates, Fort Worth, TX, 76104. John Menchaca, MD. Cooks Childrens Physician Network, Fort Worth, TX, 76104. Andras Lacko, Ph.D., UNTHSC, GSBS, Dept of Molecular Biology & Immunology, Fort Worth, TX 76107. Craig Spellman, D.O., PhD. TCOM, Dept of Internal Medicine, Fort Worth, TX 76107. Ximena Urrutia-Rojas, DrPH. UNTHSC School of Public Health, Dept of Social & Behavioral Sciences, Fort Worth, TX 76107.

RISK FOR TYPE 2 DIABETES AND CARDIOVASCULAR DISEASE IN A COHORT OF HISPANIC ADOLESCENTS.

Purpose: The purpose of the study was to assess the evolution of risk factors in a cohort of Hispanic adolescents previously identified at risk for T2DM and CVD.

Methods: Data from subjects enrolled in the Diabetes, Research, Education and Metabolic Studies Center (DREAMS) Project 1 was used for the study. Adolescents previously identified as at risk for developing T2DM (n=26; 15 males, 11 females) belong to a cohort of children who were Mexican American and study participants in both 2001 and in 2005. In both studies, enrolled children and their siblings risk factors were assessed by anthropomorphic and serum data, and administered surveys to obtain information about respondents eating habits and health behaviors. The at risk group was further divided into subjects whose risk category increased or whose risk category was maintained from 2001 to 2005.

Results: In the study cohort, 8 were in the normal category for waist circumference percentiles in 2001. By 2005, only 4 subjects remained in the normal category for waist circumference (WC) percentile. The mean age for each time point was 10.35 and 14.31 years, and mean Tanner stage 1.6 and 3.5 in 2001 and 2005 respectively. Mean BMI percentile increased from 67.1 in 2001 to 96.4 in 2005. Mean WC percentile increased from 69.4 in 2001 to 78.5 in 2005. All but two serum measures, mean values decreased from 2001 to 2005. Mean differences from 2001-2005 were not statistically significant. Subjects were divided into three categories based on the change in WC percentile from 2001-2005. There were 4 subjects who were normal at both time points, 8 whose WC percentile category increased and 13 who were at risk and remained in the same WC percentile category. Without exception, a trend was observed across risk categories. Risk factors values increased (decreased for LDL cholesterol) when moving from the normal category to the increased risk category and to the risk maintained category. In most cases, mean values in the risk maintained category were outside the normal range for at risk adults.

Conclusions: Despite small sample size, the findings indicate that this cohort of adolescents represents a population at high risk because of known ethnic risk factors for this ethnic group and their increased BMI/waist circumference. Larger prospective cohort studies should be carried out to ascertain the evolution of obesity related chronic diseases such as T2DM and CVD in Hispanic children.

Sponsor: *N/A*

1408 *(Poster)*

Author: Khiya Marshall
Presenter: Khiya Marshall
Department: Department of Social and Behavioral Sciences
Classification: SPH Student

Khiya Marshall, MPH., UNTHSC School of Public Health, Dept of Social & Behavioral Sciences, Fort Worth, TX 76107. Walter McConathy, PhD., TCOM, Dept of Internal Medicine, Fort Worth, TX 76107. John Menchaca, MD., Cooks Childrens Physician Network, Fort Worth, TX, 76104. Sejong Bae, Ph.D., UNTHSC School of Public Health, Dept of Bioestatistics, Fort Worth, TX 76107. Craig Spellman, D.O., PhD., TCOM, Dept of Internal Medicine, Fort Worth, TX 76107. Andras Lacko, Ph.D., GSBS, Dept of Molecular Biology & Immunology, Fort Worth, TX 76107. Ximena Urrutia-Rojas, DrPH. UNTHSC School of Public Health, Dept of Social & Behavioral Sciences, Fort Worth, TX 76107.

BODY MASS INDEX (BMI) AND WAIST CIRCUMFERENCE (WC) AS INDICATORS OF RISK FOR TYPE 2 DIABETES (T2DM) AND CARDIOVASCULAR DISEASE (CVD) IN HISPANIC CHILDREN

Purpose: To assess the hypotheses that elevated indicators of risk would be present at the 75thpercentiles of BMI and WC, and that WC would be more helpful in identifying elevated risk when contrasted with BMI.

Methods: To assess the hypotheses that elevated indicators of risk would be present at the 75thpercentiles of BMI and WC, and that WC would be more helpful in identifying elevated risk when contrasted with BMI.

Results: Systolic blood pressure consistently and significantly increased as the BMI/WC increased form 75th-95th percentiles, as well as the acanthosis nigricans (AN) prevalence. At WC 75thpercentile, AN was more than twice at BMI 75thpercentile. Fasting glucose was normal (75thpercentile compared to BMI as the BMI/WC increased form 75th-95th percentiles (4.7, 5.4, and 7.6mmol/L and 4.1, 5.2 and 6.8mmol/L respectively). Triglycerides, total cholesterol, and LDL-C mean values increased consistently and significantly at BMI/WC>75thpercentiles and were over the mean and/or at the 95thpercentiles for Hispanic children in the third National Health and Nutrition Examination Survey (NHANES III).

Conclusions: The findings indicated that elevated risk for T2DM and CVD were already present at 75thpercentiles of BMI and WC. In this group of children WC is a better predictor of risk than BMI.

Sponsor: *N/A*

1409 *(Poster)*

Author: Ximena Urrutia-Rojas
Presenter: Ximena Urrutia-Rojas
Department: Department of Social and Behavioral Sciences
Classification: Faculty

Ximena Urrutia-Rojas, DrPH. UNTHSC School of Public Health, Dept of Social & Behavioral Sciences, Fort Worth, TX 76107. Walter McConathy, PhD. TCOM, Dept of Internal Medicine, Fort Worth, TX 76107. Sejong Bae, Ph.D. UNTHSC School of Public Health, Dept of Bioestatistics, Fort Worth, TX 76107. John Menchaca, MD. Cooks Childrens Physician Network, Fort Worth, TX, 76104. Mary Luna Hollen, Ph.D.,RD. Maria Jimenez, MD, MPH., Khiya Marshall, MPH., Rosie Rojas, UNTHSC School of Public Health, Dept of Social & Behavioral Sciences, Fort Worth, TX 76107. Andras Lacko, Ph.D., UNTHSC, GSBS, Dept of Molecular Biology & Immunology, Fort Worth, TX 76107. Craig Spellman, D.O., PhD. TCOM, Dept of Internal Medicine, Fort Worth, TX 76107.

PRIMARY PREVENTION PROGRAM FOR HISPANIC FAMILIES AT RISK FOR T2DM, CVD, AND METABOLIC DISORDERS. DREAMS PROJECT 1.

Purpose: To decrease risk factors for Type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) related to overweight and obesity, and to promote physical activity and healthy diet in Hispanic families with overweight or obese children previously identified as "at risk" for T2DM.

Methods: Previously identified overweight Hispanic children (258), at risk of diabetes and cardiovascular disease, and their family members are enrolled in a randomized primary prevention intervention that aims to decrease risk for T2DM CVD, and metabolic disorders. T2DM was determined using the ADA guidelines to identify children that should be tested for T2DM. The 258 participating families completed the base line assessment of lifestyle, health history, physical assessment, and laboratory studies, and were randomized to a six month preventive educational intervention program utilizing Hispanic ☐Promotores de Salud, or to receive eduactional materials regarding healthy eating and physical activity by mail. Half of the families (129) were assigned to the intervention group and 129 to the control group.

Results: Update of Research Activities: The enrollment phase of the study was completed in October, 2005. The 258 overweight children at risk for T2DM and their nuclear families enrolled in the study completed the baseline assessment and were randomized to intervention/control. The 258 families include 853 individuals; 474 of those are children. Overall one half (54.9%) are females. Females constitute 65.2% of the adults and 46.6 % of children. The majority of adults were foreign born (88.8%) and most children (72.3%) were US born. Overall, the language of preference for about one half (52.9%) was Spanish. As of March 2006, 73% of the families completed the intervention phase and are undergoing the post intervention assessment. The program will be evaluated comparing the intervention and control groups after they complete the intervention phase, under the hypotheses that participants in the intervention group will be more likely engage in phisical activity and a healthy diet and would be less likely to be overweight, and to have decfeased the number of risk factors for T2DM and CVD.

Conclusions: This is one of the first studies that use ☐Promotores de Salud in the reduction of risk factors and prevention of T2DM and CVD in Hispanic children at risk and their nuclear families. Findings from this study will help to design future culturally appropriate interventions delivered by ☐Promotores de Salud.

Sponsor: *N/A*

1410 *(Poster)*

Author: Ximena Urrutia-Rojas

Presenter: Ximena Urrutia-Rojas

Department: Department of Social and Behavioral Sciences

Classification: Faculty

Ximena Urrutia-Rojas, DrPH., UNTHSC School of Public Health, Dept of Social & Behavioral Sciences, Fort Worth, TX 76107. .Sejong Bae, PhD., UNTHSC School of Public Health, Dept of Bioestatistics, Fort Worth, TX 76107. Maria Jimenez, MD, MPH., Khiya Marshall, MPH.& Mary Luna-Hollen, PhD, RD., UNTHSC School of Public Health, Dept of Social & Behavioral Sciences, Fort Worth, TX 76107. .Andras Lacko, PhD., GSBS, Dept of Molecular Biology & Immunology, Fort Worth, TX 76107. Craig Spellman, PhD., DO. & Walter McConathy, PhD., TCOM, Dept of Internal Medicine, Fort Worth, TX 76107.

RISK FOR TYPE 2 DIABETES (T2DM) AND CARDIOVASCULAR DISEASE (CVD) IN HISPANIC OVERWEIGHT CHILDREN WITH FAMILY HISTORY OF DIABETES. DREAMS PROJECT 1.

Purpose: Overweight and diabetes family history in children indicate increased risk for these diseases at an earlier age. The purpose of the study was to assess risk factors for T2DM and CVD in overweight Hispanic children with family history of diabetes.

Methods: Overweight Hispanic children with family history of diabetes (250) and their siblings (213), ages 7 to 17 years old, were examined for T2DM and CVD risk factors based on physical examination, family history, and laboratory studies. Data from children enrolled in the Diabetes, Research, Education and Metabolic Studies Center (DREAMS) Project 1, was used for the study.

Results: One half (53%) were female. Mean age was 11.1 and 11.4 years for females and males respectively. Three fourths (76.8%) were overweight/obese (BMI>85th%ile). One third of girls (31.6%) and 13.3% of boys exceeded the waist circumference values of 88cm. and 100cm. identified as the cutoff points for increased risk of obesity related co morbidities in adults. Although not in the hypertensive range, over one third had elevated systolic BP. Fasting glucose was elevated (>100mg/dl) in 6.8%, and 25.1% had elevated insulin levels (>15uU/mL). Close to 1/3 had elevated triglycerides (>150); 47.7% had total cholesterol>160mg/dl with 9.9% at>199. LDL-Cholesterol>90 and >129 was found in 48.7% and 6.6% respectively. Over two thirds (68.1%) had HDL-Cholesterol< 32. With one exception (girls were more likely to have elevated insulin levels), no significant differences were found between boys and girls.

Conclusions: These findings indicate that overweight and family history of diabetes can be markers of an increase in the severity of risk for T2DM and CVD in Hispanic children. The short and long term public health implications of these findings should guide the primary prevention of overweight and genetic related chronic diseases as early as possible in vulnerable groups.

Sponsor: *Centers for Disease Control and Prevention (CDC)*

1411 *(Poster)*

Author: Roberto Cardarelli

Presenter: Margaret Seater

Department: Family Medicine

Classification: Dual Degree Student DO/MS

Roberto Cardarelli, DO, MPH, UNTHSC, TCOM, Dept of Family Medicine, Fort Worth TX 76107 Kathryn M. Cardarelli, PhD, UNTHSC SPH, Dept of Epidemiology, Fort Worth, TX 76107 Margaret Seater, DO/MS Candidate, UNTHSC, TCOM Fort Worth TX 76107 Stephen Weis, DO Tarrant County Health Department/UNTHSC, TCOM Fort Worth TX 76107 Ana Chiapa, MS UNTHSC, TCOM, Dept of Family Medicine, Fort Worth TX 76107 Isabel Vecino, MD Tarrant County Health Department Fort Worth TX 76107

THE COMMUNITIES, COMMUNICATION, AND HEALTH STUDY

Purpose: Aim: To assess whether interpersonal processes of care, perceived discrimination, social support and/or sense of control influence HAART adherence among HIV/AIDS patients. Hypotheses: 1. Patients who experience poor or inadequate interpersonal processes of care are less likely to be adherent with their HAART regimen. 2. Patients who experience perceived discrimination are less likely to be adherent with their HAART regimen. 3. Patients who have low social support or a poor sense of control are less likely to be adherent with their HAART regimen.

Methods: A cross-sectional study that will use validated instruments to assess perceived discrimination, interpersonal processes of care, and social support and their relationship to HAART adherence. Charts will be reviewed to corroborate adherence information as well as HIV/AIDS associated illnesses (Toxoplasmosis, Mycobacterium Avium, TB, etc).

Results: Patient demographics and histories will be tabulated and within groups difference by medication adherence score will be assessed using appropriate bivariate analyses, including independent t-tests, analyses of variance, and chi-square tests. Univariate linear and logistic regression will be performed for continuous and categorical dependent variables, respectively, to assess for associations between HAART adherence and different independent variables, including interpersonal processes of care, perceived discrimination, social support, and sense of control.

Conclusions: Findings from this study will allow a better understanding of how aspects of the patient doctor relationship, specifically perceived discrimination, interpersonal processes of care, and social support, contribute to medication adherence among patients with HIV.

Sponsor: *N/A*

1500 *(Poster)*

Author: Darrin Jackson

Presenter: Darrin Jackson

Department: Pharmacology & Neuroscience

Classification: McNair/SMART Participant

Darrin Jackson, 934 Camellia Cove, Jackson, MS 39272 Mentor: Dr. Volodymyr Rybalchenko University of North Texas Health Science Center, Forth Worth, TX

INTRACELLULAR CALCIUM RELEASE OF RYANODINE RECEPTORS: EXPERIMENTAL IDENTIFICATION AND FUNCTIONAL PROPERTIES

Purpose: The focus of this research is to test the role of Ca2+ (calcium) metabolism in normal and oxidative stress induced cells. Ca2+ plays a pivotal role in exocytosis and secretion. The effects of variations in Ca2+ concentrations can be observed in lacrimal gland cells. In normal lacrimal gland cells, cytosylic Ca2+ concentration is influenced by receptors located on the membrane of the e.r. (endoplasmic reticulum).

Methods: We used an electrical recording device in order to measure the current and voltage accross the membrane. In order for us to determine whether a protein had been incorporated into the membrane, the experiment required KCl (potassium chloride). The determination of what protein(s) were present were evident after the addition of IP3 (inositol triphosphate) and ATP(adenosine triphosphate).

Results: Recent results show evidence of RyRs (ryanodine receptors) ability to operate differently at various Ca2+ concentrations. The activity was monitored from Ca2+ concentrations ranging from pCa 8 to pCa 7 (pCa=calcium concentrations). As Ca2+ concentration increased, the activity of these RyRs increased. After observing this, ruthenium red (20mM) was introduced, at pCa 7, and the activity of these receptors ceased.

Conclusions: Future studies will include analysis of these RyRs after being exposed to various levels of oxidative stress. Future research will be aimed in determining whether these receptors structurally change, and if so, what types of changes occur, and what measures could be taken in order for these receptors to retain their ability to work efficiently.

Sponsor: *N/A*

1501 *(Oral)*

Author: Lorie Gonzalez

Presenter: Lorie Gonzalez

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Lorie A. Gonzalez, Cathy L. Bell-Horner, Michael Gatch, Michael Forster, and Glenn H. Dillon, Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, TX 76107

EVIDENCE FOR THE BARBITURATE-LIKE ACTIONS OF CARISOPRODOL AT GABAA RECEPTORS

Purpose: Despite the emerging role of carisoprodol as a drug of abuse, its mechanism of action remains unclear. The sedative effects of carisoprodol are commonly attributed to its metabolite, meprobamate. However, case reports regarding the toxicity of these drugs suggest carisoprodol may elicit its own, equally dangerous effects. The aim of the current study was to investigate whether carisoprodol affects GABAAR function.

Methods: Whole-cell patch clamp electrophysiology was utilized to investigate carisoprodol-mediated effects on GABAAR function. In order to investigate the allosteric and direct effects of carisoprodol, currents were recorded from human embryonic kidney 293 (HEK 293) cells stably expressing either human ±1²2³2 or rat ±1²2 GABAAR. Currents were recorded from HEK 293 cells transiently transfected with GABAAR Á1 or glycine receptor ±1 subunits to investigate the effects of carisoprodol on barbiturate-insensitive receptors.

Results: Carisoprodol modulated GABA-gated currents in HEK 293 cells expressing human ±1²2³2 GABAAR. GABA-gated currents were potentiated and inhibited by micromolar and millimolar concentrations of carisoprodol, respectively. Co-application of GABA and millimolar concentrations of carisoprodol produced rebound currents upon termination of drug application; this phenomenon is consistent with the actions of barbiturates at high concentrations. In the absence of GABA, micromolar concentrations of carisoprodol produced inward currents that were rapid and reversible, indicating direct action at the receptor. In cells expressing rat ±1²2 GABAAR, carisoprodol, like barbiturates, did not require the ³ subunit to modulate GABA-gated currents. Furthermore, carisoprodol did not potentiate the GABA-gated currents of barbiturate-insensitive homomeric Á1 receptors or glycine ±1 receptors. When carisoprodol and isobarbital were co-applied, the resulting current amplitude was intermediate to that of either drug alone.

Conclusions: Our findings suggest the sedative effects of carisoprodol may not be due solely to its metabolite, meprobamate. Carisoprodol modulates GABAAR function in a barbiturate-like manner and may share a similar binding site with barbiturates. Its functional similarities with this highly addictive class of drugs may contribute to the abuse potential of carisoprodol. (NIH N01DA-2-8822)

Sponsor: *NIH N01DA-2-8822*

1502 *(Poster)*

Author: Walter McConathy

Presenter: Walter McConathy

Department: Internal Medicine

Classification: Staff

Walter J. McConathy, Sulabha Paranjape, Linda Mooberry, Sabitha Buttreddy, Maya Nair, and Andras Lacko Departments of Internal Medicinea and Molecular Biology & Immunologyb, University of North Texas Health Center, Fort Worth, TX 76107

DILAURYLFLUORESCEIN AS A PROBE OF HIGH DENSITY LIPOPROTEIN CORE COMPONENT METABOLISM

Purpose: Dilauryl fluorescein (DLF) is a lipid soluble molecule that becomes fluorescent when lauric acid is removed. Our objective was to develop high density lipoproteins (HDL) containing DLF as potential probes for metabolic studies of HDL hydrophobic core constituents.

Methods: Reconstituted HDL (rHDL) nanoparticles containing DLF (rHDL/DLF) were prepared by a modified sodium cholate dialysis procedure. Following dialysis and ultracentrifugation, the isolated rHDL containing DLF were used to study plasma exchange/transfer reactions and uptake of DLF by cells engineered to overexpress a HDL receptor (scavenger receptor,SR-B1). To monitor and compare the behavior of rHDL/DLF in serum, rHDL labeled with 3H-cholesterol esters (HDL/3H-CE) were also prepared. The rHDL nanoparticles containing DLF or 3H-CE were characterized by floatation, electron microscopy, and with regard to molecular weight.

Results: In transfer/exchange, the 3H-CE was transferred to LDL particles while DLF accumulated in the HDL1 region. Serum hydrolysis of free DLF was found to be lower than that of DLF, encapsulated in rHDL. Cellular uptake of DLF as well as its subsequent hydrolysis of DLF to fluoresceine was significantly higher in cells overexpressing SR-B1. These studies showed that DLF can be incorporated into reconstituted lipoproteins, remodeled in the plasma compartment, and hydrolyzed following cellular uptake

Conclusions: Based on these findings DLF appears suitable for studying the metabolism of hydrophobic core components associated with circulating HDL. These studies also suggest that DLF represents a useful probe to study the metabolism of hydrophobic drugs delivered by rHDL such as cancer chemotherapeutic agents.

Sponsor: *N/A*

1503 *(Poster)*

Author: Angela Chao

Presenter: Angela Chao

Department: Pharmacology & Neuroscience

Classification: Staff

Angela A. Chao, Willie E. Tays, and John A. Schetz Department of Pharmacology & Neuroscience, University of North Texas Health Science Center, 3500 Camp Bowie Blvd, Fort Worth, TX 76107-2699

MAPPING THE BINDING SITE OF BUTYROPHENONE ANTIPSYCHOTICS TO DOPAMINE RECEPTORS

Purpose: Dopamine receptors are essential targets in the treatment of various neurological and psychiatric disorders. Drugs that block dopamine receptors are useful for the treatment of ticks associated with Tourettes syndrome and psychosis related to schizophrenia. Although antipsychotic drugs of the butyrophenone class were some of the first to be developed, the orientation of the drugs in the dopamine binding-site crevice remains unclear. Both 3-fluorobenzylspiperone and N-(4-isothiocyanateophenethyl)spiperone (NIPS) are in the butyrophenone class and have similar structures and side chains. However, 3-fluorobenzylspiperone lacks the isothiocyanate moiety required for covalent attachment to the dopamine receptor. The idea is to utilize the isothiocyanate group to covalently attach the ligand to the D4 receptor and then determine the amino acid with which it interacts.

Methods: The cloned D4 dopamine receptor was transfected into CHO cells via calcium phosphate precipitation. The stable cell lines were then selected using the selection drug G418. Saturation radioligand binding was used to determine receptor expression levels in the stable cell lines. Affinity values for 3-fluorobenzylspiperone and NIPS were measured via a radioligand competition binding assay.

Results: A cell line was made that stably expressed high levels of the cloned D4 dopamine receptor. Both NIPS and 3-fluorobenzylspiperone were found to bind the D4 receptor with similarly high affinities. Even after repeated washings, NIPS could not be washed off the D4 dopamine receptor.

Conclusions: Washout experiments indicated that NIPS irreversibly binds to the receptor at a physiological pH. Both NIPS and 3-fluorobenzylspiperone were determined to have similar binding affinities for the D4 dopamine receptor subtype, indicating that the isothiocyanate group on NIPS does not drastically re-orient NIPS in the binding-site crevice. Localization of the site of covalent attachment of NIPS to the receptor by mass spectroscopy analysis should provide insight into how butyrophenone antipsychotics dock into the binding-site crevice.

Sponsor: *NIH/NIHM R01 MH063162 awarded to JAS*

1504 *(Poster)*

Author: Arthur Braden

Presenter: Arthur Braden

Department: Molecular Biology and Immunology

Classification: Postdoctoral Fellow/Resident

Arthur R. Braden, Erica Kafka, Jamboor K. Vishwanatha Department of Molecular Biology and Immunology University of North Texas Health Science Center 3500 Camp Bowie Blvd. Fort Worth, TX. 76109

POLYMERIC NANOPARTICLE MEDIATED INHIBITION OF ANNEXIN II LEADS TO A REDUCTION OF CELLULAR PROLIFERATION AND MIGRATION

Purpose: High levels of annexin II expression have been positively associated with cancers of lung, pancreas, breast and brain tumors. Prostate cancer is characterized by an absence of detectable annexin II expression during pre-neoplastic stages however in advanced malignant stages annexin II expression is regained. Thus, loss of annexin II modulation in prostate cancers indicates a potentially important regulatory role for this protein in prostate cancer development. We utilize a novel, □nanotechnology-based, non-viral controlled release delivery system for our investigation of the regulatory role of annexin II in prostate cancer. Our nanoparticles are formulated from an FDA-approved, biodegradable and biocompatible polymer, poly (DL-lactide-co-glycolide) (PLGA), which undergoes slow intracellular hydrolysis to release the therapeutic agent at a sustained rate.

Methods: Our particles are loaded with ABEK plasmid DNA. The transcriptional product of ABEK acts to inhibit transcription of annexin II within the cell nucleus. We have verified the reduction of cellular annexin II levels via western blot analysis. The impact of ABEK on cellular proliferation was determined through neutral red assays. Cellular migration was studied by agarose based cell motility assays.

Results: Upon transfection of the androgen insensitive prostate cancer cells lines PC-3 and DU-145 we have seen marked impact of annexin II down regulation from ABEK. Western blot analysis has shown a 40 percent reduction of annexin II levels in PC-3 cells and a 60 percent reduction in Du-145 cells at 4 days post transfection. We have also found that inhibition of annexin II leads to a reduction in cellular proliferation and cellular migration in vitro.

Conclusions: Nanoparticle mediated delivery of ABEK does inhibit intracellular annexin II levels. Inhibition of annexin II leads to a reduction in both cellular proliferation and cellular migration of the metastatic prostate cancer cell lines PC-3 and DU-145. These findings suggest a potentially therapeutic role for our nanoparticles in the mediation of metastatic prostate cancers.

Sponsor: *N/A*

1505 *(Poster)*

Author: David Cummings

Presenter: David Cummings

Department: Graduate School of Biomedical Sciences

Classification: Dual Degree Student DO/PhD

David F. Cummings, Shiuhwei Chen, Christina Z. Floresca, and John A. Schetz, Department of Pharmacology & Neuroscience, University of North Texas Health Science Center, 3500 Camp Bowie Blvd, Fort Worth, TX 76107-2699.

DISCOVERY OF A MUTATION IN THE D2 SUBTYPE OF DOPAMINE RECEPTOR THAT ELIMINATES ITS FUNCTIONAL RESPONSE TO QUINPIROLE

Purpose: Dopamine receptors are implicated in the pathology or treatment of numerous neurological and psychiatric disorders; however, current treatments have highly undesirable side effects due in part to their lack of functional selectivity for specific receptor subtypes. Our goal is to understand the molecular mechanisms inherent to the selective activation or inactivation of dopamine receptors. Comparison of two receptor subtypes, D2 and D4, revealed three subtype-specific amino acids on transmembrane segments two (TM2) and three (TM3). Previous work from our lab demonstrated that swapping one or more of these amino acids results in a D4 receptor with pharmacology mimicking the D2 receptor. While generating the reciprocal mutations in a D2 background we discovered that substitution of all three corresponding amino acids from the D4 receptor results in selective loss of functional activity.

Methods: Mutant receptors constructed by DpnI-based site-directed mutagenesis were transfected into HEK293 cells by calcium phosphate precipitation and stable cell lines were obtained after resistance drug selection. Receptor density and drug affinity were ascertained by [3H] methylspiperone radioligand binding studies. A fluorescence-based cyclic adenosine monophosphate (cAMP) assay was utilized to determine receptor function following activation by the agonist (-)-quinpirole.

Results: Radioligand binding revealed high receptor density and confirmed that wild type and all mutant receptors have similar affinity for [3H]methylspiperone and (-)-quinpirole. With the exception of the TM2 mutant receptor, affinity for the D4 selective antagonist L750,667 increases with the number of amino acid mutations eventually mimicking the D4 receptor in the TM2/TM3 mutant receptor. Although a cAMP response to (-)-quinpirole was observed in single TM2 or TM3 mutant receptors, it was abolished in the combined TM2/TM3 mutant receptor.

Conclusions: As evidenced by the TM2/TM3 mutant receptors high affinity for L750,667, mutation of all three amino acids results in a mutant D2 receptor with more D4-like pharmacology. Remarkably, the functional effects of the agonist quinpirole were only abolished in the TM2/TM3 mutant receptor. The TM2/TM3 mutant receptor provides a clear example of where receptor affinity can be dissociated from agonist function and implies that the interaction between TM2 and TM3 may be pivotal in the process of receptor activation.

Sponsor: *NIH/NIHM R01 MH063162 awarded to JAS*

1600 *(Poster)*

Author: Monica Campos

Presenter: Monica Campos

Department: SCHOOL OF PUBLIC HEALTH (SPH)

Classification: SPH Student

Monica Campos, MPH, University of North Texas Health Science Center -School of Public Health, Fort Worth, TX 76107 Brian Wittenmyer, University of North Texas Health Science Center- School of Public Health, Fort Worth, TX 76107

BIOFORTIFICATION IN CHINA: POLICY AND PRACTICE

Purpose: Hidden hunger, due to insufficient micronutrients in the diet, remains one of the most prevalent and, yet, preventable nutritional problems in the world today. More than one-third of the worlds population suffers from micronutrient malnutrition. Micronutrient malnutrition fosters reduced physical, cognitive, and reproductive growth and development, leading to lower societal productivity. Global efforts have increased to reduce the prevalence of these deficiencies via dietary modification, supplementation, and fortification.

Methods: A newer method, termed □biofortification, involves breeding plant varieties that increase the uptake of specific nutrients that are deficient in a population. Currently in China, despite supplementation and fortification efforts, stunting and underweight (symptoms of micronutrient malnutrition) remain high in the poor western provinces. Approximately 20% and 40% of rural areas are deficient in vitamin A and iron deficient, respectively.

Results: Agricultural programs have begun to implement the new strategy of biofortification, with help from government and international agencies. Specific policies need to be addressed and precautions put in place prior to and during implementation of these programs. This research addresses several policy issues that are vital for a fluid transition into the implementation and sustainability of biofortification. Policy issues involve seed disbursement, environmental affects, agricultural and commercial regulations, and property rights.

Conclusions: Biofortification efforts worldwide can prove to be fruitful but governments should recognize the benefits and consider providing structure through nutrition and agricultural policies to enhance effectiveness.

Sponsor: *N/A*

1601 *(Poster)*

Author: Kathryn Kaiser

Presenter: Kathryn Kaiser

Department: Psychology

Classification: GSBS Student

Kathryn A. Kaiser, B.S. MT(ASCP)-1, Susan F. Franks, Ph.D.-1, Joan F. Carroll, Ph.D.2 and James L. Caffrey, Ph.D.-2. 1-Psychology, University of North Texas HSC and 2-Integrative Physiology, University of North Texas HSC, Fort Worth, Texas, United States, 76107.

PSYCHOPHYSIOLOGICAL CORRELATES IN OBESITY: DISINHIBITION AND GHRELIN CHANGE IN RESPONSE TO A MEAL

Purpose: The gut peptide ghrelin has been investigated as a physiological mechanism of hunger regulation and meal initiation. Its relation to eating behavior in humans is not well defined. It was hypothesized that a decreased post-prandial ghrelin change may be related to subsequent abnormal eating. The purpose of this study was to determine whether the change in ghrelin levels in response to a meal was related to self-reported eating behavior in normal weight versus obese subjects.

Methods: The physiologically active form of ghrelin was measured in 42 obese (33 female, 9 male, BMI M=43.5, SD=9.23) and 33 normal weight (25 females, 8 males, BMI M=22.4, SD=1.96) subjects in a fasting state and 30 minutes after a liquid meal. The Eating Inventory (EI) was administered concurrently (Stunkard and Messick, 1985). The three EI subscales (Cognitive Restraint, Disinhibition, and Hunger) and fasting/post-prandial ghrelin ratio were each analyzed in a 2X2 ANOVA for gender and BMI effects.

Results: There were no gender main effects or genderXBMI interactions. Results indicate a significant difference between the two BMI groups for the EI subscale of Disinhibition [obese M=9.36,SD=3.38, controls M=4.7,SD=3.3; F(1,74)=19.9, p

Conclusions: The reduced fasting/post-prandial ghrelin ratio in obese subjects suggests a possible link between physiologic regulators of hunger and selected components of abnormal eating.

Sponsor: *Support provided by CDC grant H75/CCH224064*

1602 *(Poster)*

Author: Michael Gatch

Presenter: Michael Gatch

Department: Pharmacology & Neuroscience

Classification: Faculty

Michael B. Gatch, Elva Flores, and Michael J. Forster Department of Pharmacology & Neuroscience University of North Texas Health Science Center

CROSS-SUBSTITUTION OF NICOTINE AND METHAMPHETAMINE

Purpose: Nicotine and methamphetamine are both abused in similar settings, sometimes together. Because there are known interactions between central nicotinic acetylcholine receptors and dopamine receptors, it is of interest to characterize the nature of the interaction of these two compounds. The purpose of this study was to characterize the ability of these two compounds to modulate each others discriminative stimulus effects and to identify pharmacological mechanisms for their interactions.

Methods: Male Sprague-Dawley rats were trained to discriminate methamphetamine or nicotine from saline. First, the ability of methamphetamine and nicotine to cross-substitute in rats trained to the other compound was tested. Subsequently, the ability of a dopamine antagonist (haloperidol) and a centrally-acting nicotinic antagonist (mecamylamine) to block the effects of methamphetamine and nicotine was also tested.

Results: Nicotine and methamphetamine each partially cross-substituted (50-60% DAR). Further testing of methamphetamine-trained subjects revealed that some subjects consistently cross-substituted when given nicotine (42%), whereas others sometimes selected drug and other times selected saline (50%). A minority of subjects (8%) consistently showed no signs of substitution. In nicotine-trained rats, mecamylamine fully antagonized the discriminative stimulus effects of nicotine, but haloperidol had no effect. In methamphetamine-trained rats, mecamylamine failed to antagonize the discriminative stimulus effects of methamphetamine, but haloperidol fully blocked the methamphetamine cue.

Conclusions: These results suggest that nicotine and methamphetamine share subjective effects in some subjects. However, the behavioral data suggest that the two compounds do not act at the same site, but produce their interaction downstream from their respective receptors.

Sponsor: *NIDA*

1603 *(Poster)*

Author: Mark Flesher

Presenter: Mark Flesher

Department: Physician Assistant Studies

Classification: TCOM MPAS Student

Mark Flesher, PA-S II, Physician Assistant Class of 2007, Physician Assistant Studies Joshua Stoner, PA-S II, Physician Assistant Class of 2007, Physician Assistant Studies Olive Chen, Ph.D., Assistant Professor, Physician Assistant Studies Linda Reed, M.Ed., PA, Assistant Professor/Associate Director, Physician Assistant Studies

CAFFEINE CONSUMPTION, CALCIUM CONSUMPTION, AND STUDY-DEFINED PROTECTIVE FACTORS: CHARTING SIGNIFICANT DIFFERENCES WITH REGARD TO BONE MINERAL DENSITY (BMD) VALUES IN WOMEN BETWEEN THE AGES OF 45 □ 83

Purpose: To determine if a statistically significant difference exists between bone mineral density (BMD) values and caffeine consumption, calcium consumption, and other osteo- protective factors defined in the study as regular exercise, HRT, and oral contraception.

Methods: This is a cross-sectional study, using a question survey to collect data. Potential participants were first randomly selected from the database of the Rheumatology clinic of UNTHSC at Fort Worth. They were then assigned to three different BMD groups: 1). No osteoporosis group (NO); 2). Pre osteoporosis group (PO); 3). Active osteoporosis group (AO) according to their BMD values. SPSS (12.0) was used to perform Spearmans correlation, Chi-Square and ANOVA statistical tests.

Results: Eighty-seven (87) out of 300 total participants returned the survey. Statistical significance correlation was found concerning age among BMD groups ($p = 0.001$). No statistically significant differences were found on calcium consumption ($F= 0.083$, $p = 0.920$) or on caffeine consumption ($F = 1.884$, $p = 0.158$) among three BMD groups. Data showed a statistically significant relationship ($x2 =8.167$, $p = 0.017$) between the BMD groups and a history of oral contraception use, but did not reveal a statistically significant relationship between oral contraceptives and total calcium ($r= -0.147$, $p = 0.175$) or total caffeine ($r= -0.189$, $p= 0.080$) consumption.

Conclusions: The results of this study failed to show any statistically significant difference on caffeine consumption and calcium consumption with regard to BMD status. The lack of statistical significance when selecting for calcium and caffeine could be related to the study design. The BMD values were not individual, they were grouped, and this may have skewed the results. Furthermore the questions used in the survey may not have adequately portrayed each individuals complete consumption habits, thus the possibility of erroneous data exists. Also since this was a cross-sectional study, the possibility of reporting and recall bias exists. Furthermore, locations of patients were from one patient database at the UNTHSC in Fort Worth, Texas which does not extrapolate to the whole population. As for oral contraception, some studies are in agreement with the results of this study, but there is still conflicting data which warrants further investigation of the possible protective benefit from osteoporosis with oral contraceptive use.

Sponsor: *N/A*

1602 *(Poster)*

Author: Michael Gatch

Presenter: Michael Gatch

Department: Pharmacology & Neuroscience

Classification: Faculty

Michael B. Gatch, Elva Flores, and Michael J. Forster Department of Pharmacology & Neuroscience University of North Texas Health Science Center

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Sponsor: *NIDA*

1603 *(Poster)*

Author: Mark Flesher

Presenter: Mark Flesher

Department: Physician Assistant Studies

Classification: TCOM MPAS Student

Mark Flesher, PA-S II, Physician Assistant Class of 2007, Physician Assistant Studies Joshua Stoner, PA-S II, Physician Assistant Class of 2007, Physician Assistant Studies Olive Chen, Ph.D., Assistant Professor, Physician Assistant Studies Linda Reed, M.Ed., PA, Assistant Professor/Associate Director, Physician Assistant Studies

CAFFEINE CONSUMPTION, CALCIUM CONSUMPTION, AND STUDY-DEFINED PROTECTIVE FACTORS: CHARTING SIGNIFICANT DIFFERENCES WITH REGARD TO BONE MINERAL DENSITY (BMD) VALUES IN WOMEN BETWEEN THE AGES OF 45 □ 83

Purpose: To determine if a statistically significant difference exists between bone mineral density (BMD) values and caffeine consumption, calcium consumption, and other osteo- protective factors defined in the study as regular exercise, HRT, and oral contraception.

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Sponsor: *N/A*

1604 *(Poster)*

Author: Richard Virgilio, DO, MS
Presenter: Richard Virgilio, DO, MS
Department: Family Medicine
Classification: Faculty
RICHARD F VIRGILIO, DO, MS ASSISTANT PROFESSOR DEPARTMENT OF FAMILY MEDICINE UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH 3500 CAMP BOWIE BOULEVARD FORT WORTH, TX 76107 JOHN LICCIARDONE, DO DIRECTOR OF CLINICAL RESEARCH OSTEOPATHIC RESEARCH CENTER UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH 3500 CAMP BOWIE BOULEVARD FORT WORTH, TX 76107 KIMBERLY FULDA, MPH RESEARCH INSTRUCTOR OSTEOPATHIC RESEARCH CENTER UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH 3500 CAMP BOWIE BOULEVARD FORT WORTH, TX 76107 MARK SANDERS, DO, JD, MPH ASSISTANT PROFESSOR DEPARTMENT OF FAMILY MEDICINE UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH 3500 CAMP BOWIE BOULEVARD FORT WORTH, TX 76107

THE RELATIONSHIP BETWEEN CHEWING GUM, ATTENTION AND CONCENTRATION: A RANDOMIZED CONTROLLED TRIAL

Purpose: The purpose of this randomized controlled trial is to determine what relationship, if any, exists between the act of chewing gum and the study subjects score on a standardized test for attention and concentration. To achieve this goal, a convenience sample of 201 graduate students were randomly assigned to one of three study groups (gum containing sugar, sugarless gum, and no gum control) before taking a standardized test which measured various aspects of attention and concentration. There was no significant difference among subjects who chewed gum and those who did not chew gum with regard to the levels of attention and concentration measured by the standardized test taken during this study.

Methods: To obtain the study population for the randomized controlled trial, a convenience sample of 201 students (67 per group), 18 years of age or older, who were currently enrolled in any of the four schools that comprise the University of North Texas Health Science Center at Fort Worth was obtained by recruiting volunteers. The study subjects were randomly assigned to one of three groups (gum containing sugar, sugarless gum, and no gum control). A block randomization process was performed, consisting of 14 total blocks, in an attempt to obtain three equal sized groups. All study participants took the same standardized test, which measured their level of attention and concentration. Those subjects assigned to either of the two gum chewing groups were asked to start chewing the gum given to them by the study investigator, after which the standardized test was administered. Those in the gum chewing groups were asked to continue chewing their gum, as they would do normally, throughout the entire study period, namely until they completed the standardized test. Upon completion of the standardized test, the subjects participation in the study ended.

Results: There was no significant difference among subjects who chewed gum and those who did not chew gum with regard to the levels of attention and concentration measured by the standardized test taken during this study.

Conclusions: The results of the present study were unable to support the hypothesis that attention and concentration can be improved by the act of chewing gum. Instead of clearing the confusion regarding the effect that the act of chewing gum may or may not have on attention and concentration, the present study just adds to the current controversy. More studies are needed to further clarify this issue.

Sponsor: *N/A*

1605 *(Poster)*

Author: Kollier Hinkle
Presenter: Kollier Hinkle
Department: OB-GYN @ JPS Hospital campus
Classification: Postdoctoral Fellow/Resident
Kollier Hinkle, MD, Ralph Anderson, MD, Jackie Davis-Herr, MD, Philip Bailey, MD, Bonnie Parker Department of Obstetrics and Gynecology John Peter Smith Hospital, Fort Worth, Texas 76104

EVALUATION OF PREINCISIONAL ANESTHESIA ON POSTOPERATIVE PAIN AFTER LAPAROTOMY FOR GYNECOLOGIC SURGERY

Purpose: To evaluate postoperative pain in patients receiving 0.25% bupivicaine with epinephrine prior to abdominal and fascial incisions during laparotomy for gynecological surgery.

Methods: A double-blind, randomized, prospective trail was performed after IRB approval. Patients were randomized to a group that received 10cc of the study solution or normal saline prior to both skin and fascial incisions. All patients were placed on morphine PCA postoperatively for 24 hours. Additional doses of morphine were as needed. Pain control was evaluated using visual pain scales every four hours. Amount of morphine, time to discharge, 24 and 48 hour post-op averages were recorded. Students t-test was used to determine significance.

Results: Twenty-one patients were randomized to the study solution group and twenty to the saline group. No demographic differences were noted. The study group had an average post-op morphine usage of 67 mg compared to 64 mg in the saline group in the first 48 hours. Average pain scale values in the study group were 4.8 during the first 24 hours and 3.3 for the second 24 hours. The saline group had values of 4.6 and 3.3 for the first 24 and 48 hour periods respectively. The average hospital stay for the study group was 2.91 days and 3.26 day for the saline group.

Conclusions: Our results did not indicate a significant difference in post-operative pin control or length of hospital stay. We believe larger studies will need to be performed in order to suggest routine use of preincisional bupivicaine for our gynecological patients.

Sponsor: *N/A*

1606 *(Poster)*

Author: Kollier Hinkle

Presenter: Kollier Hinkle

Department: OB-GYN @ JPS Hospital campus

Classification: Postdoctoral Fellow/Resident

Kollier Hinkle, MD, Philip Abbott, MD, Ralph Anderson, MD Department of Obstetrics and Gynecology, John Peter Smith Hospital Fort Worth, Texas 76104

USE OF POLYETHYLINE TEREPHTHALATE SYNTHETIC GRAFT FOR VAGINAL VAULT PROLAPSE DURING SACROCOLPOPEXY

Purpose: To describe the efficacy and postoperative complications of polyethylene terephthalate as a graft material for sacroscolpopexy.

Methods: A 10-year chart review of women who underwent abdominal sacrocolpopexy was conducted. Specifically, women who had polyethylene terphthalate used as the vaginal cuff suspension graft material were identified. Data collected included each womans demographic information, operative procedures and technique, and all intraoperative and postoperative complications.

Results: Ninety-five women were identified. Grades II-IV prolapse was present in each case, with a mean pelvic organ prolapse quantification (POP-Q) score point Cof +4.6. Thirteen women underwent concomitant abdominal hysterectomy. All women were operated on by the same surgeon using the same technique. Mean age and parity were 61.6 and 2.4, respectively. Sixty-two percent were taking hormone therapy or premenopausal. The mean follow-up was 18 months.

Conclusions: There appears to be a low rate of complication associated with the use of polyethylene terephthalate as a graft material for vaginal cuff suspension during sacrocolpopexy. Polyethylene terephthalate appears to be a viable alternative to other graft materials currently in use. Complications n(%) Mesh extrusion 4 (4.2) Intraoperative 0 (0) Infection 1 (1) Recurrent prolapse 1(1) Return to operating room 2 (2.1)

Sponsor: *N/A*

1607 *(Poster)*

Author: Sean Rosenbaum

Presenter: Sean Rosenbaum

Department: OB-GYN @ JPS Hospital campus

Classification: Postdoctoral Fellow/Resident

Sean Rosenbaum, MD, Timothy Kremer, MD, Chad McCormick, MS Department of Obstetrics and Gynecology John Peter Smith Hospital Fort Worth, Texas 76104

THE UTILITY OF PREOPERATIVE CT SCAN IN PATIENTS WITH ENDOMETRIAL CANCER

Purpose: To evaluate routine preoperative CT scan of the abdomen and pelvis in patients with endometrial cancer.

Methods: A retrospective review of patients with endometrial cancer managed by a gynecologic oncologist was conducted. The age, presenting complaint, cell type, preoperative evaluation, operative report, and pathology report, was reviewed for each patient. A survey of the normal, abnormal, and incidental, findings on CT scan was compared to the surgical findings, histology, and grade.

Results: Of 103 patients, 64 had a preoperative CT scan. Of these 64 patients, histology included 46 adenocarcinomas, 2 adenosquamous, 3 adenosarcoma, 11 papillary squamous or clear cell, and 2 squamous cell carcinomas. Nineteen patients had grade 1 disease. Twenty-three had grade 2 disease, and 22 had grade 3 disease. Thirty-four patients had myometrial invasion less than 50%, and 11 had greater than 50% invasion. Fifteen patients had disease outside the uterus. Decisions made at staging laparotomy were not affected by preoperative CT scan results in any case. The remaining patients did not have a preoperative CT scan due to suspected low stage, low grade, prior to surgery or patient preference. In these patients no pathology was found at surgery that, if detected on a CT scan, would have altered the surgical approach.

Conclusions: While a larger study is needed, routine CT scan prior to staging laparotomy in patients with endometrial cancer may be an unnecessary expense regardless of histology, grade, or stage. In this small series, approximately forty-seven thousand dollars would have been saved.

Sponsor: *N/A*

1608 *(Poster)*

Author: Kollier Hinkle

Presenter: Kollier Hinkle

Department: OB-GYN @ JPS Hospital campus

Classification: Postdoctoral Fellow/Resident

Kollier Hinkle, MD, Joseph Pallone, MD, Lindsay McBride, DO, Vanessa Daros, MD, Ralph Anderson, MD, Bonnie Parker Department Obstetrics and Gynecology, John Peter Smith Hospital Fort Worth, Texas 76104

EVALUATION OF TERM FETAL WEIGHT IN AN URBAN HOSPITAL OVER TWENTY YEARS

Purpose: Obesity is major health problem in Texas affecting 23.6-27.4% of women. The incidence of gestational diabetes (GDM) has increased from 2.5% in the 1990s to 4% today. With a high body mass index (BMI) and increase in GDM, one would expect an increase in fetal birth weights. Our purpose was to evaluate trends in term birth weights over a twenty year period in our urban population.

Methods: Delivery logs from 1984, 1994 and 2004 were reviewed. Over a thousand deliveries were sampled from each year. Gestational age varied from 36 to 40+ weeks. Birth weight, maternal race, gravida and parity were recorded. Cesarean and vaginal deliveries were included. Students t-test was applied to determine significance.

Results: Demographic data was similar for each year examined. In 1984, 1025 newborns ranged between 1786 gm to 5046 gm. Mean weight was 3263 gm. 1178 newborns in 1994 ranged from 1672 gm to 5414 gm, with a mean birth weight of 3339 gm. In 204, 1250 newborns had a range from 1672 gm to 4904 gm with a mean birth weight of 3280 gm. Percentage of weighting more than 4500 gm was 3.8%, 2.7% and 2.6% for 1984, 1994 and 2004. No significant difference in average birth weight or percentage of 4500 gm newborns was seen.

Conclusions: Despite increased BMI and incidence of GDM, our population does not reflect an increase in average birth weight or newborns weighing at least 4500 gm. This supports the theory of environmental factors playing a leading role in obesity development.

Sponsor: *N/A*

1609 *(Poster)*

Author: Lowell Ku

Presenter: Ralph Anderson

Department: OB-GYN @ JPS Hospital campus

Classification: Postdoctoral Fellow/Resident

Lowell Ku, MD, Darren Tate, MD, Ralph Anderson, MD Department of Obstetrics and Gynecology John Peter Smith Hospital Fort Worth, Texas 76104

MANUAL VACUUM ASPIRATION: A VIABLE ALTERNATIVE TO SUCTION DILATION AND CURETTAGE

Purpose: To evaluate manual vacuum aspiration (MVA) compared with suction dilation and curettage (D&C) for uterine evacuation in early pregnancy failures.

Methods: Patients presenting with the diagnosis of early pregnancy failure before 12 weeks of gestation were offered MVA or D&C. Patients in whom missed abortion with a closed cervix had been diagnosed were managed with either Laminaria or misoprostol before MVA. Patients choosing D&C received only Laminaria for a closed cervix. Patient satisfaction surveys were obtained by phone or mail after each procedure. A cost analysis was performed comparing MVA with D&C.

Results: Mean gestational age, beta-hCG level, and blood loss were lower for patients receiving MVA than for D&C. One patient required D&C following aspiration. There were no patients requiring blood transfusion in either group. There were no cases of pelvic infection, cervical laceration, uterine rupture, or other significant complication. All patients surveyed reported that they would recommend the MVA procedure to someone else with a miscarriage diagnosis. No patients were dissatisfied with MVA. Cost analysis revealed significant savings to the hospital with aspiration over D&C. Savings per patient that received MVA instead of D&C amounted to $1,814.

Conclusions: MVA is a safe and a cost-effective alternative to D&C for the management of early spontaneous abortions. Further studies are warranted to confirm our findings.

Sponsor: *N/A*

1610 *(Poster)*

Author: des Anges Cruser

Presenter: des Anges Cruser

Department: Psychiatry

Classification: Faculty

des Anges Cruser, Ph.D., TCOM,UNTHSC, Fort Worth, TX 76107 Alan Podawiltz, D.O., M.S., TCOM, UNTHSC, Fort Worth TX 76107 Daisha J. Cipher, Ph.D., TCOM, UNTHSC, Fort Worth TX 76107

SERIOUS MENTAL ILLNESS AND EXPOSURE TO TRAUMA

Purpose: This study explored whether the quantity and types of traumatic experiences could differentiate three forensic sub-groups of persons with serious mental illness. Data is used to create plausible clinically coherent trauma factors and and test their relationships to other risk variables.

Methods: From a survey of all public system psychiatric outpatients in a West Texas university clinic, we classified 669 respondents (69.8% response rate) by amount of criminal justice system involvement. We collected trauma event data, psychosocial and forensic history, diagnosis, and demographics from 87 consented subjects. We factor analyzed the trauma items and tested for differences among forensic and diagnostic groups, and gender, and tested relationships between trauma factors, criminal history, and psychosocial risk variables.

Results: The forensic groups did not differ in age or primary diagnosis, but differed significantly on gender and race, and on Axis I Secondary and Axis II diagnoses. Factor analysis yielded six trauma factors (TF) explaining 53.939% of the variance. Forensic groups differed significantly in TFs Drug Culture ($F(2,84) = 9.82$, $p < .001$) and Extreme Violence, ($F(2,84) = 4.50$, $p = .014$). Male subjects scored higher on Drug Culture and Extreme Violence; women scored higher on Victim Abuse. Subjects with a substance use disorder scored significantly higher than those without, in Drug Culture; ($F(1,85) = 97.53$, p

Conclusions: Forensic sub-groups of persons with a serious mental illness appear to differ in exposure to traumatic events. Men and women seem to differ in the type of trauma exposure, as do certain diagnostic groups. More research in this area could produce testable trauma prediction models from psychosocial risk variables.

Sponsor: *N/A*

1611 *(Poster)*

Author: Evelyn Perez

Presenter: Evelyn Perez

Department: Pharmacology & Neuroscience

Classification: Postdoctoral Fellow/Resident

E.J.Perez 1; X.Wang1; R.Liu1; S.Yang1; Z.Cai2; D.Covey2; J.A.Dykens3; J.W.Simpkins1 1. Dept Pharmacol & Neurosci, Univ. of North Texas HSC, Fort Worth, TX, USA 2. Molocular Biology and Pharmacology, Washington Univ., St Louis, MO, USA 3. Migenix, San Diego, CA, USA

CORRELATION BETWEEN ESTROGENS NEUROPROTECTION AND PROTECTION OF MITOCHONDRIAL MEMBRANE POTENTIAL IN A NEURONAL CELL LINE

Purpose: The neuroprotective effects of estrogens have been demonstrated in in vivo and in vitro models. Oxidative stress is involved in neurodegenerative diseases. As the major subcellular organelle for energy and reactive oxygen species production, mitochondrial function is very important in neuronal survival against oxidative stress. Mitochondrial membrane potential collapse is a critical event in the life-death decision of neurons. To define the role of mitochondrial actions of estrogens in their ability to neuroprotect, we tested the relationship between the neuroprotective activity of estrogens and their ability to protect from mitochondrial membrane potential collapse induced by H202 in HT-22 cells.

Methods: Cell viability will be assessed using Calcein AM assay. Mitochondrial membrane potential will be assessed using a FRET-based assay.

Results: Eleven estrogen analogues that ranged in neuroptoective potency (EC50) from 12 nM to 8.6 M were selected for comparison. HT-22 cells were exposed to 4.0 mM H202 for 30 min to induce mitochondrial membrane potential collapse in the presence or absence of estrogens. The mitochondrial protective effects of estrogens were evaluated. The correlation between EC50 values of cytoprotection and EC50 values of mitochondrial protection was highly significant ($r2=0.64$, spearman $r=0.8000$, $p < 0.0047$). It is noted that one compound that failed to show cytoprotective activity also failed to stabilize mitochondria.

Conclusions: This strong correlation suggests that mitochondria play a central role in estrogen-induced neuroprotection.

Sponsor: *AG10485, AG22550 and the Texas Higher Education Coordination Board*

1612 *(Poster)*

Author: Britni McBryde
Presenter: Britni McBryde
Department: Physician Assistant Studies
Classification: TCOM MPAS Student
Britni McBryde PA-S Olive Chen PhD Linda Reed Med, PA Fort Worth, TX 76107

HOW KNOWLEDGE OF MEDICATION REGIMENS INFLUENCES ADHERENCE IN AMBULATORY GERIATRIC PATIENTS TAKING MULTIPLE MEDICATIONS

Purpose: The purpose of this study was to investigate geriatric patients knowledge about their medications and how their knowledge correlates with adherence.

Methods: This is a cross-sectional research study. The researchers used a survey, Mini-Cog, and chart review to collect the data. The Medication Knowledge and Compliance Survey was an 18 item survey developed by the researchers. The survey was pilot-tested on 5 seniors at a local senior center. A convenience sample of 61 geriatric individuals from two clinics located in Fort Worth, TX participated in this study. The patients knowledge of their medication regimens was measured by evaluating the consistency between patients responses regarding their prescription medications and chart data. Six areas of consistency were evaluated: 1) Chart matched medicine mentioned or patient knew medication, 2) Correct reason given for taking medicine, 3) Correct dosage given or patient knew dose, 4) Medicine listed in chart but not mentioned, 5) Medicine mentioned but not listed in chart, 6) Patient offered a reason for taking medication. Patients gained a knowledge score that ranged from 0 to 6. T-test and chi-square statistical analysis was performed using SPSS(11.5).

Results: A total of 50 subjects met the study inclusion criteria. The mean subjects age was 73.6 years, and 64% were female. Participants had 8.2 prescription medications on average. The mean knowledge score for subjects was 4.8 (SD=0.86). However, the scores of those subjects who reported never missing medications (M=4.79) and those who reported sometimes missing some of their medications (M=4.84) did not reach a statistically significant difference ($t=-0.201$, $p>0.05$). Likewise, the knowledge scores of those who reported having never stopped any medications (M=4.80) and those who reported having stopped taking a medication (M=5.10) did not reach statistical significance ($t=-1.138$, $p>0.05$). Other interesting findings were: 32.1% of the total medications that the subjects either did not know or did not match a medication in the chart; incorrect dosages were given for 31.2% of the total medications.

Conclusions: This study did not find a correlation between the geriatric patients medication knowledge and adherence. Knowledge may or may not play a role in how elderly individuals comply with medication regimens. Other possible influential factors, such as patients beliefs regarding the disease and its treatment, barriers to treatment, and social factors need to be further explored.

Sponsor: *N/A*

1613 *(Poster)*

Author: Christopher Mann
Presenter: Christopher Mann
Department: Family Medicine
Classification: Faculty
Christopher R. Mann, DO, UNTHSC, TCOM, Dept. of Family Medicine, Division of Sports Medicine: Michael Ellison PhD,TWU, Dept. of Psychology Consultant: Ronald C. Kessler PhD,Harvard Medical School, Dept. of Health Care Policy

SURVEY ASSESSMENT OF THE INCIDENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN ADULTS

Purpose: Adult-Form ADHD has only recently been accepted as a current pathology, to determine the incidence in the general population and particular populations previously shown to have a high incidence of symptoms related to this diagnosis.

Methods: A Survey Instrument of 85 questions that has no identifiers and will be voluntarily answered will be put before each subject. The pilot study will utilize a limited number of literate, English-speaking volunteers to allow for final improvement of the survey as required. The main study will have the survey placed into a Audio-Computer-Assisted Self-Administered Interviewing (A-CASI) system that will allow both English and Spanish translations. This system allows the subject to respond to the survey by either reading or hearing each question. The responses are recorded immediately in the lap-top programmed with the A-CASI format and allows for each subject to progress at their own pace with the ability to screen both literate and illiterate. This also allows for the difficult attention-span of the ADHD subject to not become as much of a barrier to responding accurately to the survey. Surveys will first be directed at what prior studies have identified as populations that have an unusually high set of symptoms similar to ADHD such as the drug-abuse and criminal populations.

Results: Univariate linear and logistic regression will be closely examined to screen for variables at a level of significance of

Conclusions: Findings from this study could confirm the existance of a high-percentage of Adults with ADHD, IED, and Mood Disorder. In particular, the study may show that the drug-abuse and criminal populations have an extraordinary high-incidence of ADHD pathology that should be properly diagnosed and treated. There is potential to significantly reduce recidivism and modify behaviour within the drug-abuse and criminal populations with appropiate discovery, diagnosis, and treatment plans.

Sponsor: *N/A*

1614 *(Poster)*

Author: Michael Nye

Presenter: Michael Nye

Department: Physician Assistant Studies

Classification: TCOM MPAS Student

Michael Nye PA-S II, Roxanne Simper PA-S II, Olive Chen PhD, Laurie Hill PA-C

PHYSICAL AND PHYSIOLOGICAL CHANGES OBSERVED FOLLOWING THE LAP-BAND SURGICAL PROCEDURE

Purpose: This study described specific physical and physiological changes found following the lap-band procedure. The changes evaluated were: blood glucose (BG), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), body mass index (BMI) and blood pressure (BP). Discontinuations or decreased dosages in any anti-hypertensive, anti-lipidemic, or diabetic medications were also observed.

Methods: The study was conducted as a retrospective chart review. The charts reviewed were taken from two surgery clinics in Fort Worth, Texas. Approximately thirty percent of the charts were randomly selected. The final group of fifty-one, was based on those meeting the inclusion criteria: at least one year post-op, over 18 years of age and the variables must have been completed during the perisurgical appointment as well as the six month and/or one year post-surgery. ANOVA was used to analyze the recorded data.

Results: The majority of the patients were middle-aged Caucasian females. Data showed that there were significant differences in BG, BMI and HDL. BG and BMI had reduced and HDL had increased. Data also showed that TG and SBP had decreased and that LDL and DBP had increased, but these variables did not show significant differences. The study also revealed reductions and discontinuations of anti-lipidemic, hypertensive, and diabetic medications. Data showed a 22% reduction or discontinuation in lipid lowering prescriptions, a 50% reduction or discontinuation in hypertensive prescriptions, and a 62% reduction or discontinuation in diabetic medications.

Conclusions: This project provides clinical and literary evidence that supports the lap-banding procedure for assistance in the management of the obese patient with co-morbidities such as diabetes, hypertension and hyperlipidemia. The results of this study showed that there were significant improvements in the levels of HDL, BG and BMI and that there were minimal changes in TG, LDL, and BP levels. However, it is important to recognize that reductions in medications will alter lab values masking or lessening the actual effect that the surgery had on these variables. The benefits of this procedure extend beyond one year. A future study could extend the data collection over a longer time span, perhaps two or more years.

Sponsor: *N/A*

1615 *(Poster)*

Author: Denise Marquez

Presenter: Denise Marquez

Department: Physician Assistant Studies

Classification: TCOM MPAS Student

Denise K. Marquez, PA Student, Fort Worth, TX 76107 Henry R. Lemke, MMS, PA-C Olive Chen, PhD

PREVALENCE OF NUTRITIONAL DEFICIENCY IN ELDERLY PATIENTS UNDERGOING MOHS MICROGRAPHIC SURGERY

Purpose: This study was conducted to 1) determine the prevalence of nutritional deficiency in elderly patients undergoing Mohs Micrographic Surgery, and 2) to evaluate the efficiency of the Mini Nutritional Assessment (MNA) tool in the dermatologic surgical/clinical setting.

Methods: This was a cross-sectional research. After obtaining IRB approval, the researchers used the MNA, which was developed and validated by Nestle®, to initiate screening for risk of and further assess for nutritional deficiency. The MNA included anthropometric measurements, global assessment, dietary questionnaire, and subjective assessment. A total of 102 elderly patients of DermSurgery Associates in Houston TX were solicited to participate in the study. Participants also were asked to rate the understandability of the MNA. The time required to complete each assessment was recorded. Descriptive statistical analysis was performed using the SPSS (12.0).

Results: A total of 100 patients participated in the study. Most participants were Caucasian (99%), male (64%), between the age of 61-80 (64%), and 79% had some level of college education. The prevalence of nutritional deficiency in this sample group was zero percent with a risk of being malnourished of 7%. The MNA was easy to use as determined by 100% of the study participants. Time required to complete the assessment averaged less than 3 minutes per encounter.

Conclusions: Previous studies have shown that malnutrition can lead to problems or delays in wound healing. Correcting these deficiencies promises to enhance wound healing. If malnutrition is suspected in an elderly patient about to undergo surgery, nutritional status should be assessed and can efficiently be done with the MNA. This study did not find the expected prevalence of nutritional deficiency in the elderly patient as predicted by Nestle® when using the MNA. This may be due to the inadequate survey size and unique demographic characteristics of the study population. Other studies found that elderly, black, immigrant or persons who have a lower education level or socioeconomic status are at higher risk for malnutrition; whereas, the study population was mostly an affluent Caucasian subset of the general elderly. The results of this study were limited due to short duration of data collection and a lack of homogeneity in comparison to the United States elderly population at large. Recommendations for future research are to allow for adequate sample size and diversity of the clinic sites.

Sponsor: *N/A*

1616 *(Poster)*

Author: Claudia Coggin

Presenter: Claudia Coggin

Department: School of Public Health

Classification: Faculty

Claudia S. Coggin,PhD,CHES,Doug Mains,DrPH*,Clifton Cage,DO**, Patti Pagels,PA**, Shawn Jefferies,PhD**, and Susie Quintana***, *School of Public Health, **Texas College of Osteopathic, ***Founders Activity Center Medicine,University of North Texas Health Science Center*

PATCH: A MULTI-MODE SMOKING CESSATION PROGRAM

Purpose: Tobacco use has been cited as the single, most avoidable cause of disease and death. The harmful effects of nicotine dependence and habitual smoking represent one of the largest social and medical problems in the United States. A voluntary worksite smoking cessation program, Positive Attitudes Toward Changing Habits (PATCH) was developed and implemented at a United States academic health science center to assist faculty, staff, students and their insurance-eligible dependents quit smoking.

Methods: . Program participants were surveyed on their readiness to stop smoking, smoking behavior, nicotine tolerance, readiness for physical exercise and provided with pre and post fitness assessments. The PATCH Program used a unique multi-mode intervention model that utilized nicotine replacement patches, education and behavior modification, social support, and an optional exercise program over a period of 12 weeks. Participants were called twice monthly to reinforce the decision to quit smoking. Participants smoking/non-smoking was assessed at 12 weeks, 6 months and 12 months.

Results: . Participants in the first iteration (PATCH 1) had a 12 month quit rate of 23.5% and those in PATCH 2 (second group) had a 12 month quit rate of 54.5%. No statistically significant differences were found between quitters and non-quitters.

Conclusions: Overall the results of PATCH 1 and 2 are positive. Continued evaluation and modification of the PATCH program could increase the efficacy of the program. This multi-mode intervention may be replicated at other work site locations.

Sponsor: *N/A*

1617 *(Poster)*

Author: Erin Donovan

Presenter: Erin Donovan

Department: Cell Biology and Genetics

Classification: GSBS Student

Erin W. Donovan (1), Glynis N.R. Price (1), Joseph Warren (1), John Planz (1), Brant Cassidy (2) (1) Department of Cell Biology and Genetics, University of North Texas Health Science Center, 3500 Camp Bowie Blvd., Fort Worth, Texas 76107. (2) DNA Solutions Inc., 840 Research Parkway, Suite 551, Oklahoma City, OK 73104

MAMMALIAN SEX DETERMINATION PROJECT ☐ SENSITIVITY AND OPTIMIZATION

Purpose: Non-phenotypic sex identification of meats from supermarkets, hunted game, and forensic samples for use in forensic cases where other methods of sex determination are unavailable.

Methods: DNA extractions of samples were done using organic extraction, then quantified using both UV Spectrophotometry and a SYBR Green I® assay methods. Both 6-FAM and unlabeled universal primer sets targeting sex determining regions were applied and PCR was performed under specified conditions. Gel electrophoresis was done on the unlabeled products followed by visual analysis. Capillary electrophoresis of the labeled products was carried out followed by software analysis using GeneMapper® ID.

Results: Quantification methods indicated large amounts of DNA requiring additional dilutions. Testing of samples where the sex was known indicated correct sex determination. Further testing on samples of unknown origin indicated a sex in all samples. The expected bands and base pair numbers, 244bp and 445bp, were present in males while only the anticipated 445bp was present in the females.

Conclusions: Our findings suggest that these sex determining markers will be useful in a forensic setting, either alone or in conjunction with an autosomal marker panel. Further investigation is planned using different species, including some non-domestic species such as tiger, cougar, bear, and coyote depending on availability of samples from zoological parks.

Sponsor: *N/A*

1618 *(Poster)*

Author: Nykiconia Preacely

Presenter: Nykiconia Preacely

Department: Department of Epidemiology

Classification: SPH Student

Nykiconia Preacely,MPH,UNTHSC,Fort Worth,TX 76107; Melicia R. Brown,MPH,Denton County Health Department,Denton,TX 76209;Antonio Rene,PhD,Texas A&M Univ School of Rural Health,College Station,TX 77843

LEAD CONTAMINATION IN WEST DALLAS AND CADILLAC HEIGHTS

Purpose: This case study was conducted to provide a historical account of the some of the factors that may have affected residents of the West Dallas and Cadillac Heights neighborhoods due to smelter operations. Several factors which may have contributed to the residents exposure to lead included: breathing contaminated air,occupational exposures,and ingesting soil contaminated with lead. It has been postulated by some of the residents that exposure to the smelters may have lead to certain adverse health effects experienced in their communities.

Methods: Documentation used as units of analysis for the current study was obtained from archival records including site histories dating from 1855-2004. Health indicators including disease specific mortality rates,birth outcomes,and lead screening data were extracted from community assessment reports,and past environmental pollutant screening studies. Epigrammatic semi-structured interviews were conducted in June,July,and August of 2005 with 11 key informants. Each informant was asked several items from an open-ended questionnaire to assess their experiences of the environmental health situation related to industrial pollution in West Dallas and Cadillac Heights.

Results: There have been no direct links to the residents health problems and lead exposure. While many residents want specific answers to why they are experiencing certain health problems these answers are not always readily available. Future studies are needed to determine if there is an association between certain health problems experienced that have been thought to be associated with lead exposure from the smelters. Currently,the blood lead levels of the residents of these two communities are lower than other racial,age-group matched comparison Texas residents according to NHANES III data. Yet,the impact of the years of lead exposure still affects the communities in various ways.

Conclusions: The efforts of the USEPA,TCEQ,the City of Dallas Environmental Quality Air Control Board,Parkland Hospital,and the advocacy of West Dallas and Cadillac Heights residents has assisted in the identification of the contamination problem,remediation efforts,and to discovering possible solutions to this problem.

Sponsor: *Parkland Health and Hospital System*

1619 *(Poster)*

Author: Navin Rauniyar

Presenter: Navin Rauniyar

Department: Molecular Biology and Immunology

Classification: GSBS Student

Navin Rauniyar, Nilka M. Rivera-Portalatin, Jose L. Vera-Serrano, Katalin Prokai-Tartrai, Laszlo Prokai Department of Medicinal Chemistry, College of Pharmacy, University of Florida; Department of Molecular Biology and Immunology and Department of Pharmacology and Neuroscience, University of North Texas HSC, FortWorth, Texas,

MICROWAVE METHOD: A NOVEL APPROACH IN SYNTHESIS OF ESTROGEN QUINOL

Purpose: It has been demonstrated that estrogens mediates neuroprotective effect against various oxidative insults. It serves as a free-radical scavenger. During an antioxidant cycle, capture of hydroxyl radical produces nonphenolic estrogen quinols, which are rapidly converted back to parent estrogen without the production of reactive oxygen species. Here we describe a novel method for the synthesis of estrogen quinols by the use of microwave technology.

Methods: In contrast to traditional methods that involve reaction at room temperature for twenty-four hours or more and requires excess of reagent, we investigated the effect of microwave heating on the synthesis of E1Quinol (10ß-Hydroxyestra-1,4-dien-3,17-dione) using estrone (3ß-Hydroxyestra-1, 3,5(10)-trien-17-one), and lead acetate. Our procedure used microwave irradiation at 60°C for merely 15 minutes. The product obtained is identified and confirmed by LC/APCI-MS.

Results: We got a significant reduction in the time of reaction with considerable satisfactory product yield.

Conclusions: We found that the microwave approach is simple, offers cleaner synthesis and an impressive acceleration of reaction time (minutes compared to hours) while increasing the product yield and purity.

Sponsor: *N/A*

1620 *(Poster)*

Author: Scott Emerson

Presenter: Scott Emerson

Department: Texas College of Osteopathic Medicine

Classification: TCOM DO Student

Scott S. Emerson: The University of North Texas Health Science Center-Texas College of Osteopathic Medicine, Fort Worth, Texas 76107 Dong-Hoon Hyun: Laboratory of Experimental Gerontology/Laboratory of Neuroscience, National Institute on Aging, GRC, NIH, 5600 Nathan Shock Drive, Baltimore, Maryland 21224

COENZYME Q10 AND ?-TOCOPHEROL LEVELS DURING DIFFERENT MEAL FREQUENCY PERIODS

Purpose: At present, there has been little data generated defining the effects that different meal frequencies have on antioxidant levels in human plasma. Current belief suggests that 3 meals per day (3m/d) may overall be better to individuals. Consequently, the purpose of our study was to determine, on an antioxidant level, whether 3 meals (vs. 1 meal per day [1m/d]) are in fact healthier.

Methods: Subjects were placed on a meal frequency plan: 3m/d vs. 1m/d; total caloric intake equal for both groups. The administration, content, and schedule of meals was monitored at a government facility. Blood was drawn before the study and at intervals throughout. A break midway was given to accommodate two holidays. After the break, the subjects switched groups: those that were on the 3m/d went to 1m/d, and vice versa. When the clinical study was complete, the blood plasma samples were prepared for High-Performance Liquid Chromatography (HPLC) identification of Coenzyme Q10 (CoQ10) and a-Tocopherol levels by hexane:methanol extraction.

Results: The levels of CoQ10 are initially greater in the 3m/d vs. those that were on the 1m/d. The early increase of this antioxidant is seen at the onset of the study and after the break/switch period. With time, though, the CoQ10 levels in those of the 3m/d group essentially □equilibrated to levels seen in the 1m/d diet. The levels of antioxidant a-Tocopherol indicates that 1 meal, irregardless of group switching, is increased initially and overall

Conclusions: Initially we thought that 3m/d would be healthier at an antioxidant level. However, the resulting data is limited by the amount of variables within the study and, therefore, makes it difficult to interpret. Despite these short-comings, the results suggest that for human plasma levels of CoQ10 and a-Tocopherol, 1m/d (of similar caloric intake as 3 meals) may be more advantageous over the long run. Levels of CoQ10 in the 3m/d diet group were initially increased above amounts found at the onset of the study and after the break. This early increase was independent of whether the individual started in the 3m/d group (which switched to 1 meal after the break) or ended on the 3m/d diet (those that initially were on 1 meal but switched to 3 after the break). In time, however, the levels of CoQ10 were seen to be greater, without decline, and possibly increasing in the 1m/d group. The production of antioxidant a-Tocopherol was seen to be greater throughout the study in the 1m/d diet group.

Sponsor: *N/A*

1621 *(Oral)*

Author: Shashank Bharill

Presenter: Shashank Bharill

Department: Pharmacology & Neuroscience

Classification: GSBS Student

Shashank Bharill, Volodymyr Rybalchenko and Peter Koulen Department of Pharmacology and Neuroscience University of North Texas Health Science Center Fort Worth, Texas 76107

EFFECT OF PRESENILIN-2 ON RYANODINE RECEPTOR ACTIVITY

Purpose: The purpose of this study is to determine the effect of interaction between presenilin-2 and ryanodine receptor (RyR) type 2 on RyR channel activity.

Methods: We recorded RyR channel currents using bilayer lipid membrane single channel electrophysiology. The receptors were isolated in SR vesicles and monitored for degradation and concentration by Western blotting.

Results: We demonstrate that mouse cardiac RyR type 2 gets inhibited in the presence of presenilin-2 protein and that RyRs isolated from mouse cerebellum are less tightly controlled than their cardiac homologs.

Conclusions: We conclude that RyR type 2 gets inhibited by Presinilin-2 and may remain in this state in the SR membrane until activated. These receptors get activated in presence of high calcium concentrations. RyR from cerebellum are less tightly regulated than cardiac RyR. This observation is physiologically significant in that such tight control in the heart might contribute to the avoidance of cardiac hypertrophy and might give us indications regarding potential intervention strategies for cardiac hypertrophy.

Sponsor: *N/A*

1622 *(Poster)*

Author: Linda Davis

Presenter: Linda Davis

Department: Rheumatology

Classification: Faculty

Linda Davis, MHS, PA-C, UNT-HSC Natasha Cha, MPAS, PA-C,UNT-HSC Rahul Patel, MD, UNT-HSC Raymond Pertusi, DO, UNT-HSC Bernard Rubin, DO, UNT-HSC

EARLY RHEUMATOID ARTHRITIS CLINIC - UPDATE

Purpose: Due to a nationwide shortage of rheumatologists and evidence that shows the efficacy of ealy evaluation and treatment of patients with early rheumatoid arthritis(RA), this model clinic was developed to help explore and address these issues.

Methods: Patients referred to rheumatology clinic who met screening criteria for early RA may be seen in 1-2 weeks; whereas the average wait time to be seen by a rheumatologist has been 2-6 months. A process (previously reported) was developed that allowed referring physicians to schedule these patients sooner. Area physicians were notified that the clinic was implemented. Two Physician Assistants were utilized to screen these patients, with close communication with the three rheumatologists. At the first visit, the patient completes specific forms providing insight into the way they view their health status and ability to perform daily activities. Then a complete joint examination is performed and specific blood tests drawn. A return visit to review these results is scheduled within 2 weeks. A diagnosis of RA or other inflammatory rheumatologic disease triggers a visit with a rheumatologist. If not, then the patient is asked to return to the referring physician and a follow-up leter is sent with the outcome of the visits.

Results: The clinic has been ongoing for 30 months, beginning in August 2003, and 193 patients have been screened. Of those, 56% had RA, 6% had another inflammatory rheumatic disease, and 38% were referred back to the physician who referred them, generally the primary care physician,(PCP).

Conclusions: This model clinic was developed and implemented in a busy academic rheumatology department. Access to care was improved, by reducing wait time to be seen by the rheumatologist, from 6 months to 1 month. In addition, the patients who had early RA were seen and treatment begun earlier. Since data indicates that delay in diagnosis of RA correlates with a worsened radiographic and functional outcome, this ERAC clinic will hopefully improve longterm outcomes - which will be the topic of future research.

Sponsor: *N/A*

1623 *(Poster)*

Author: Natasha Cha

Presenter: Natasha Cha

Department: Rheumatology

Classification: Faculty

Natasha Cha, MPAS, PA-C, Instructor, Division of Rheumatology; Linda Davis, MHS, PA-C, Instructor, Division of Rheumatology; Rahul Patel , M.D. Assistant Professor of Medicine, Division of Rheumatology; Raymond Pertusi, D.O.; Associate Professor of Medicine, Division of Rheumatology; Bernard Rubin, D.O. Professor of Medicine, Department of Internal Medicine, Chief-Division of Rheumatology. University of North Texas Health Science Center at Fort Worth, TX 76107, USA.

METHOTREXATE: IMPROVING COST EFFECTIVE MEASURES FOR UNTHSC RHEUMATOID ARTHRITIS PATIENTS

Purpose: Our objective was to look at cost effective measures for treating Rheumatoid Arthritis (RA) at UNTHSC.

Methods: We reviewed the pharmaco-economics of MTX treatment by comparing costs associated with oral therapy, and clinical and self administration of injectable MTX. We also reviewed studies on the efficacy and bio-availability of MTX in tablet and injectable formulations.

Results: While the use of injectable MTX is one cost effective method of treating RA, UNTHSC and patients can further improve on these costs. We found that patients, if taught to self administer injectable MTX, will need less visits to the clinic. As a result, the cost of treating RA will be reduced for both patients and UNTHSC.

Conclusions: Although visits to the clinic will be reduced, proper monitoring of patients will still be required and follow up visits remain vital.

Sponsor: *N/A*

1624 *(Poster)*

Author: Natasha Cha

Presenter: Natasha Cha

Department: Rheumatology

Classification: Faculty

Sharon Natasha Cha, MPAS, PA-C, Instructor, Division of Rheumatology Department: Internal Medicine; Linda Davis , M.H.S., P.A.-C Instructor, Division of Rheumatology, Department: Internal Medicine; Rahul Patel , M.D. Assistant Professor of Medicine, Division of Rheumatology Department: Internal Medicine; Raymond Pertusi , D.O. Associate Professor of Medicine, Division of Rheumatology, Department: Internal Medicine; Bernard Rubin , D.O. Professor of Medicine, Department: Internal Medicine, Chief, Division of Rheumatology. University of North Texas Health Science Center at Fort Worth, TX 76107, USA

METHOTREXATE: ALTERNATIVE METHODS OF DELIVERY OFFERED TO UNTHSC PATIENTS

Purpose: Our objective was to develop protocols for instructing patients on preparing injectable Methotrexate (MTX) for self-injection or as a solution for oral ingestion as a cost effective alternative in the treatment of Rheumatoid Arthritis (RA).

Methods: We reviewed the pharmacokinetics of MTX and sought studies on modes of delivery, guidelines for administering and handling injectable MTX for self-injection and preparing an oral solution of injectable MTX. We also reviewed guidelines for monitoring MTX and safety precautions, and the bio-availability and efficacy of MTX in its injectable formulation and tablet format. Based on these findings, we developed protocols for UNTHSC patients to self inject MTX or prepare injectable MTX for oral ingestion.

Results: We developed brochures providing separate instructions for patient self administration of injectable MTX as an injection or as an oral solution.

Conclusions: Patients should be carefully evaluated for likelihood of compliance and ability to follow instructions for at-home administration of MTX. This may therefore not be suitable for all patients. In addition, patients will need to be properly monitored while on MTX therapy.

Sponsor: *N/A*

1625 *(Poster)*

Author: Eunmi Kim

Presenter: Eunmi Kim

Department: Graduate School of Biomedical Sciences

Classification: GSBS Student

Eunmi Kim, Jinjun Gong and Wolfram Siede Biomedical Sciences, Cell Biology and Genetics University of North Texas Health Science Center at Fort Worth, 3500 Camp Bowie Blvd., Fort Worth, Texas 76107

ANALYSIS OF THE FUNCTION OF SRL3, A SACCHAROMYCES CEREVISIAE PROTEIN AFFECTING DNA REPAIR AND SPONTANEOUS MUTABILITY

Purpose: It is known that Saccharomyces cerevisiae Srl3 is a suppressor of rad53 null mutation lethality when overexpressed. However, its detailed function is unknown. The purpose of our research is finding out the function of Srl3. Rad53 (Chk2 in mammals) is an essential protein kinase in DNA damage and DNA replication checkpoint pathway. Rad53 can arrest cell cycle progression in G1, S and G2/M phases, stabilizes stalled replication forks, regulates repair gene expression and increases dNTP pools. There are reports that a higher ribonuclotide reductase level suppresses rad53 lethality. We initially identified the srl3 deletion mutants by its elevated spontaneous mutation rate and some sensitivity to DNA damaging agents compared to wild type. Based on these facts, we explored hypotheses. Hypothesis 1: Srl3 is a checkpoint protein. Hypothesis 2: Srl3 is related to dNTP pool regulation. Hypothesis 3: Srl3 has a role in repair of DNA damage.

Methods: Hypothesis 1: Isogenic wild type and srl3? strains were synchronized in G1 or S phase with ?-factor or hydroxyurea and UV-irradiated. Hypothesis 2: Spontaneous mutation rates and sensitivity to UV light of rnr1?, rnr3?, rnr4? , as well as srl3 strains were measured. Hypothesis 3: Epistasis of SRL3 with several repair pathway genes (RAD14, RAD6 and RAD5) was studied.

Results: Hypothesis 1: srl3? showed delayed resumption of cell cycle compared to wild type after UV irradiation. Hypothesis 2: Spontaneous mutation rate of rnr? strains are slightly elevated at best, but that of srl3? strain is 11.3 fold of wildtype control. rnr? strains do not exhibit any UV sensitivity but srl3? strain is UV sensitive. Hypothesis 3: SRL3 is epistasis with RAD5.

Conclusions: Hypothesis 1 is wrong. If Srl3 is a checkpoint protein, srl3? will not be able to arrest cell cycle after DNA damage. Hypothesis 2 is under investigation. The phenotypes of rnr? and srl3? strains proved to be different. However, we cannot firmly conclude that srl3 is not related to the regulation of dNTP pool, because of functional redundancy among the various forms of RNRs. Hypothesis 3 is correct. Rad5 is epistatic with Srl3, supporting a role of Srl3 in the error-free TLS damage tolerance mechanism. Recently, the Rad5 helicase has also been shown to play a TLS-independent role in double-strand break repair and a role of Srl3 in this pathway still needs to be analysed.

Sponsor: *N/A*

1626 *(Poster)*

Author: Fang Wang

Presenter: Fang Wang

Department: Rheumatology

Classification: Postdoctoral Fellow/Resident

Fang Wang, DO, Rahul Patel, MD, Raymond Pertusi, DO, Bernard Rubin, DO, Rheumatology Division, Internal Medicine Department, University of North Texas Health Science Center, 3500 Camp Bowie Blvd., Fort Worth, Texas 76107; Plaza Medical Center of Fort Worth, 900 8th Avenue, Fort Worth, Texas 76104.

FEBUXOSTAT, A NOVEL NONPURINE SELECTIVE INHIBITOR OF XANTHINE OXIDASE, IS A POTENTIAL NEW MEDICATION TO TREAT PATIENTS WITH HYPERURICEMIA AND GOUT

Purpose: To compare Febuxostat with Allopurinol for the ability of reduction in serum urate concentration in patients with chronic hyperuricemia and gout.

Methods: The Rheumatology Department of UNTHSC was one of the 112 participating medical centers in the United States and Canada. After the evaluation of the safety, pharmacological properties, and urate-lowering efficacy of febuxostat, 762 patients who met the criteria for gout and with the serum urate concentration of at least 8.0 mg per deciliter were randomly assigned to receive either febuxostat (80 mg or 120 mg) or allopurinol (300 mg) once daily for 52 weeks. Serum urate concentration of less than 6.0 mg per deciliter for the last three monthly measurements and/or reduction in the incidence of gout flares and tophus size were viewed as study end points.

Results: 53 percent of patients receiving 80 mg of febuxostat, 62 percent of those receiving 120 mg of febuxostat, and 21 percent of those receiving allopurinol ($P < 0.001$) achieved serum urate concentration less than 6.0 mg per deciliter. The median percent changes of tophus size were -87.0%, -72.5% and -28.7% in febuxostat 80 mg, 120 mg and allopurinol 300 mg groups, respectively ($P < 0.05$).

Conclusions: Febuxostat, at a daily dose of 80 mg or 120 mg, was more effective than allopurinol at the commonly used daily dose of 300 mg in lowering serum urate level. Similar reduction in tophus size occurred in all treatment groups. The result of further phase three febuxostat study is under FDA review.

Sponsor: *N/A*

1627 *(Poster)*

Author: Tristan Tayag

Presenter: Slobodan Dimitrijevich

Department: Integrative Physiology

Classification: Faculty

: 1Tristan J. Tayag, 1R. Stephen Weis, 1M. Cullen Johnson, 2S. Dan Dimitrijevich, Department of Electrical Engineering, Texas Christian University, Fort Worth Texas 76110, 2 Department of Integrative Physiology, UNTHSC, Fort Worth Texas 76107

OPTIMIZATION OF CELL AGGREGATION IN ROTATING WALL VESEL BIOREACTORS

Purpose: Rotating Wall Vessel Bioreactors (RWVBs) were developed at NASA to study the effects of simulated micro gravity on biological systems. The existing RWVBs lack continuous speed control that correlates with the size of the cell aggregate/tissue. The goals of this project are: (1) to develop a real time non-invasive imaging system that continuously monitors cellular /tissue functions in the high aspect rotating vessel (HARV) bioreactor and (2) to optimize cell aggregation/tissue growth vai an imaging feed-back loop that will continuous adjust of the rotation speed.

Methods: The position of particles (ie. cells or micro-tissues) within the RWVB, are described by a coupled set of differential equations. These equations that define the gravitational and centrifugal forces, and the drag of the medium, were solved numerically using the Runge-Kutta technique. A low cost commercial CCD camera was used to image glass micro-spheres (150-200 micron diameter), a model of cells and small aggregates. Off-line image processing was performed to reduce the data sets and generate binary images that represent the motion of particles in the HARV-RWVB. These image pre-processing steps are critical for real-time operation of the feedback loop.

Results: Computer simulation model of the RWVB dynamics shows that cell aggregates of increasing size follow a trajectory of increasing radius. However, the speed of rotation adjustment of the RWVB, will maintain the particles with a mass density smaller than that of the culture medium, at a position toward the center of the bioreactor. Captured images of cells, cell aggregates/tissues that are hundreds of microns in size, after pre-processing, can determine the position and approximate size of particles within the RWVB. A computer operating near 1 GHz clock rate is satisfactory for real-time operation required for the feedback control.

Conclusions: Our preliminary studies show that at constant rotational speed, the cell aggregates/tissues of increasing size will eventually collide with the vessel wall and be subjected to forces, which disrupt their integrity. Continuous non-intrusive adjustment of the rotational speed will prevent such events, and keep the growing aggregate in a simulated state of free fall close to the center of the RWVB. The digitized images can be captured and processed in real-time to monitor the growth of cell aggregates/tissues in the RWVB and provide feedback control of the speed of rotation.

Sponsor: *N/A*

BIOMEDICAL SCIENCES ORAL PRESENTATIONS SESSION A

2:00 PM	**Vaibhav Pawar** CHRONOLOGICAL LIFESPAN OF SACCHAROMYCES CEREVISIAE: A SIGNIFICANT MODEL TO STUDY AGING OF POSTMITOTIC CELLS IN HIGHER ORGANISMS?	**Abstract# 110**
2:20 PM	**Kun Yi** PP2A IS INVOLVED IN NEUROPROTECTIVE EFFECTS OF 17?-ESTRADIOL	**Abstract# 112**
2:40 PM	**Arti Sharma** PYRUVATE THERAPY DURING CARDIOPULMONARY RESUSCITATION PROTECTS POST-ARREST NEUROLOGICAL FUNCTION	**Abstract# 307**
3:00 PM	**Dongmei Lu** ANTI-APOPTOTIC SIGNAL OF PROTEIN KINASE C-EPSILON	**Abstract# 400**
3:20 PM	**T.J. Bartosh** CARDIAC STEM CELL COMPARTMENT-SPECIFIC DIFFERENCES IN GROWTH AND DIFFERENTIATION	**Abstract# 403**
3:40 PM	**Everett Nixon** EXPRESSION OF CALCIUM SENSING RECEPTORS IN THE MOUSE RETINA	**Abstract# 712**
4:00 PM	**Wees Love** TOLL-LIKE RECEPTOR 2 MEDIATES RESPONSES OF ANTIGEN-PRESENTING CELLS IN MURINE MYCOPLASMA PNEUMONIA	**Abstract# 909**

BIOMEDICAL SCIENCES ORAL PRESENTATIONS SESSION B

2:00 PM	**Joshua Gatson** ACTIVATION OF A MEMBRANE ANDROGEN RECEPTOR PROMOTES CELL DEATH IN GLIA	**Abstract# 1102**
2:20 PM	**Scott Duncan** "DISTINCT NUCLEAR AND CYTOSOLIC CALCIUM SIGNALS MEDIATED BY DIFFERENTIALLY-DISTRIBUTED INOSITOL-1,4,5-TRISPHOSPHATE RECEPTORS IN HIPPOCAMPAL NEURONS"	**Abstract# 1104**
2:40 PM	**Maj Angarano** NOVEL NON-ORGANOMETALLIC COMPOUNDS FOR THE PREVENTION OF AQUATIC BIOFOULING BY ZEBRA MUSSELS (DREISSENA POLYMORPHA)	**Abstract# 1106**
3:00 PM	**Kathryn Gleason** LACK OF FEMINIZING EFFECTS OF CHRONIC TREATMENT WITH QUINOL PRODRUGS OF ESTRONE AND ESTRADIOL	**Abstract# 1109**
3:20 PM	**Sung-Yong Hwang** EFFECT OF PRESENILIN-1 ON INTRACELLULAR CALCIUM SIGNALING	**Abstract# 1113**
3:40 PM	**Ji-yeon Hwang** EFFECTS OF PROGESTERON ON CALCIUM SIGNALING IN HIPPOCAMPAL NEURONS	**Abstract# 1114**
4:00 PM	**Lorie Gonzalez** EVIDENCE FOR THE BARBITURATE-LIKE ACTIONS OF CARISOPRODOL AT GABAA RECEPTORS	**Abstract# 1501**
4:20 PM	**Shashank Bharill** EFFECT OF PRESENILIN-2 ON RYANODINE RECEPTOR ACTIVITY	**Abstract# 1621**

PUBLIC HEALTH ORAL PRESENTATIONS

9:00 AM **Anita Kurian** **Abstract# 1401**
RACIAL AND ETHNIC DIFFERENCES IN THE EFFECTS OF REGULAR PROVIDERS AND SELF-MANAGEMENT EDUCATION ON DIABETES PREVENTIVE CARE

9:20 AM **Thaddeus Miller** **Abstract# 1402**
THE HIDDEN BURDEN OF TUBERCULOSIS

9:40 AM **Jotam Pasipanodya** **Abstract# 802**
PULMONARY DYSFUNCTION SECONDARY TO TREATED TUBERCULOSIS

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