THIRTEENTH ANNUAL

# RESEARCH Appreciation Day

APRIL 8, 2005

*Celebrating and encouraging the outstanding quality and range of research conducted at the University of North Texas Health Science Center at Fort Worth*

# TABLE OF CONTENTS

# 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 | **MORNING SESSION** | |
| | 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** | Luibel Hall (EAD-108) |

**Welcome and Overview of RAD 2005 Activities**
Thomas Yorio, Ph.D.
Vice President for Research and
Dean of the Graduate School of Biomedical Sciences

**Institutional Research Efforts**
Glenn Dillon, Ph.D.
Associate Vice President for Research and Biotechnology

**Introduction of Keynote Speaker**
Marc Hahn, D.O.
Dean of the Texas College of Osteopathic Medicine

***"NIH/NCCAM Five-Year Strategic Plan and Its Relevance to Osteopathic Medicine"***
Shan S. Wong, Ph.D.
Program Officer
National Center for Complementary and Alternative Medicine (NCCAM)
National Institutes of Health (NIH)

| | | |
|---|---|---|
| 2:00 - 5:00 PM | **AFTERNOON SESSION** | |
| | Poster Presentation Competition B | Center for BioHealth, 2nd Floor |
| | OCCTIC Oral Presentations | Center for BioHealth, 200 |
| | GSBS Oral Presentation Competition | Center for BioHealth, 201 |
| 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 |

# OCCTIC VI

University of North Texas Health Science Center is proud to welcome the sixth annual Osteopathic Collaborative Clinical Trials Initiatives Conference (OCCTIC) to our campus. Held on April 7-8, 2005, the goals of OCCTIC VI include developing a culture of clinical research in the osteopathic profession; developing a cadre of researchers able to secure significant funding for all types of clinical research; and fostering an interest in collaborative research projects, using tools such as the clinical research website and the clinical research database's collaboration center.

Funding for OCCTIC VI is provided by the National Institutes of Health, the American Association of Colleges of Osteopathic Medicine, the American Osteopathic Association, the Osteopathic Research Center and the American Academy of Osteopathy.

Continuing medical education credit will be provided by the University of North Texas Health Science Center Office of Professional and Continuing Education.

# KEYNOTE SPEAKER

**Shan S. Wong, Ph.D.**
Program Officer
National Center for Complementary and Alternative Medicine (NCCAM)
National Institutes of Health (NIH)

***"NIH/NCCAM Five-Year Strategic Plan and Its Relevance to Osteopathic Medicine"***

Shan S. Wong, Ph.D., oversees a research portfolio in cardiovascular, lung, and blood diseases, asthma, allergy, immunology, and small business innovation research (SBIR/STTR) programs. His expertise is in the area of clinical chemistry, biochemistry, and biophysics. Prior to joining NCCAM, he served as a Scientific Review Administrator at the National Institute of Diabetes and Digestive and Kidney Diseases. Before joining NIH, he was Chief of Assay Laboratory at Loma Linda University in California, Director of Clinical Chemistry Laboratory at Herman Hospital in Houston, Texas, Associate Professor of Laboratory Medicine at the University of Texas Health Sciences Center at Houston, and Professor of Biochemistry at the University of Massachusetts at Lowell.

Dr. Wong received a Ph.D. in Biochemistry from the Ohio State University and completed postdoctoral training at Temple University School of Medicine. He has conducted research in enzymology, protein chemistry, and biophysics and has developed diagnostic tests for cardiovascular, liver, lung, kidney, and bone diseases. His interest in complementary and alternative medicine is in the modality of energy healing.

# 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 12,200 individuals around the world. Total sales for 2004 exceeded $3.9 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 550,000 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 $2.1 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 both sessions of the basic science poster presentation competition.

The GSA Poster Presentation Awards are given to the top three student poster presentations in each session of 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 organization that serves as a forum for student concerns and activities. The purpose of the PHSA is to facilitate student-student and student-faculty communication and cohesiveness within the School of Public Health. The organization works on issues pertaining to curriculum revision, research opportunities, student participation, and alumni fellowship through social and professional activities.

The objectives of PHSA are: 1) to provide members with resources that will enhance their educational careers; 2) to foster communication among students, SPH faculty, staff, and administration; 3) to promote research opportunities through collaborative public health approaches to disease prevention and health promotion; 4) to foster a prosperous graduate school experience for its members; and 5) to encourage fellowship among alumni, SPH students, faculty, and staff.

The Public Health Student Association sponsors Research Appreciation Day student awards for the top two oral presentations and the top two poster presentations as determined 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.

# PROFESSIONAL AND CONTINUING EDUCATION AWARDS

Professional and Continuing Education (PACE) is pleased to announce the availability of two new research awards for outstanding poster presentations at the University of North Texas Health Science Center Annual Research Appreciation Day. PACE is the only accredited continuing education provider in the state of Texas for osteopathic as well as allopathic physicians, physician assistants, nurse practitioners, nurses, social workers, nursing faculty, administrators and certified health education specialists. PACE registers more than 10,000 healthcare professionals at more than 500 activities each year in 43 states.

The PACE Pre-doctoral Research Awards will be judged on the following criteria: quality of the research project and relevance of the research project to the field of professional and continuing education.

# 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

Tech Fort Worth
1150 S. Freeway, Suite 129
Fort Worth, Texas 76104
817.339.8968
817.332-6465 (F)
info@techfortworth.org

# 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 2005 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.

# LIST OF JUDGES

Graduate School of Biomedical Sciences judges are:

**Dennis Cheek, Ph.D., R.N.**
Texas Christian University

**Julie Crider, 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.

**Gerson Peltz, M.D.**
UT at Brownsville/Texas Southmost College

**Nancy Street, Ph.D.**
UT Southwestern Medical Center

**Patrick Cooke, Ph.D.**
Affymetrix

**Oswald D'Auvergne, Ph.D.**
Southern University

**Debra Fleenor, Ph.D. ('01)**
Alcon Research, Ltd.

**Lisa M. Hodge, Ph.D. ('01)**
Texas Wesleyan University

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

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

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

**Shivakumar Patil, Ph.D.**
Alcon Research, Ltd.

**Allan Shepard, Ph.D.**
Alcon Research, Ltd.

**Roberta Troy, Ph.D.**
Tuskegee University

Osteopathic Collaborative Clinical Trials Initiatives Conference judges are:

**Brian F. Degenhardt, D.O.**
Kirksville College of Osteopathic Medicine

**David Russo, D.O., M.S., M.P.H. ('02)**
Mayo Clinic

# LIST OF JUDGES

## Professional and Continuing Education judges are:

**Samuel T. Coleridge, D.O.**
UNT Health Science Center

**Carolyn Poirot**
Fort Worth Star Telegram

## School of Public Health judges are:

**Pat Fowler, M.S.**
City of Garland (formerly)

**Karen Wood, M.P.H. ('03)**
UNT Health Science Center

**Suzanne St. Clair, M.P.H. ('00)**
Lockheed Martin Missiles & Fire Control

## Texas College of Osteopathic Medicine judges are:

**Nasim Akhtar, M.D.**
Plaza Medical Center

**William Jordan, D.O.**
Texas Cancer Care

**Joane Baumer, M.D.**
JPS Health Network

**Robert W. Sloane, M.D.**
Harris Health System

## Tech Fort Worth judges are:

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

**Terry Wiernas, Ph.D. ('97)**
Alcon Research, Ltd.

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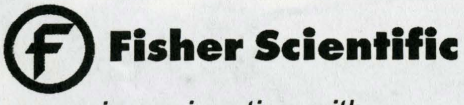


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# AGING/ALZHEIMER'S DISEASE

100 **Presentation Type:** Poster

**Author:** RICHARD VIRGILIO **Presentor:** RICHARD VIRGILIO
**Department:** FAMILY MEDICINE
**Classification:** Postdoctoral Fellow/Resident (Not for Competition)
*RICHARD F VIRGILIO, D.O.*
*Postdoctoral Clinical Research Fellow*
*Department of Family Medicine*
*University of North Texas Health Science Center*
*3500 Camp Bowie Boulevard*
*Fort Worth, TX 76107-2699*

*JOHN C LICCIARDONE, D.O.*
*Professor*
*Department of Family Medicine*
*University of North Texas Health Science Center*
*3500 Camp Bowie Boulevard*
*Fort Worth, TX 76107-2699*

**PREDICTING ALZHEIMER'S DISEASE: A CASE-CONTROL STUDY**

**Purpose:** Alzheimer's disease affects millions of Americans. It is a devastating disease whose exact cause is unknown and for which there is no cure. A study was performed to determine what role, if any, several potential risk factors (age, gender, race, ethnicity, and level of education) have in the development of Alzheimer's disease.

**Methods:** A case-control study was performed on a convenience sample of 1390 subjects who presented to the University of North Texas Health Science Center at Fort Worth Geriatric Assessment and Planning Program for the evaluation and treatment of dysfunctions of cognition. Logistic regression analyses, stratified according to ethnicity, were performed using the variables age, gender, race, and level of education as independent variables and the variable Alzheimer's disease diagnosis as the dependent variable.

**Results:** The only variables included in the study that significantly predicted the non-Hispanic subjects' risk of developing Alzheimer's disease were age and level of education. The variable age had an OR of 1.036 (95% CI, 1.018 – 1.054; $p < .001$). As compared with the subjects having 8 or less years of education, those with 9 to 12 years of education were 34.4% less likely to develop Alzheimer's disease (OR = .656, 95% CI, .440 - .977; p = .038), and those with 17 or more years of education were 57.4% less likely to develop Alzheimer's disease (OR = .426, 95% CI, .225 - .805; p = .009). Study subjects with 13-16 years of education had a non-significant reduction in Alzheimer's disease risk (OR = 0.692, 95% CI, .439 - 1.092).

**Conclusions:** Increasing age is a well known and accepted risk factor for developing Alzheimer's disease. Greater education generally decreased the risk of developing Alzheimer's disease. The result for Alzheimer's disease risk in the group of subjects completing 13-16 years of education was not statistically significant possibly secondary to small sample size. Whether the effect of education on the development of Alzheimer's disease is independent or just a surrogate for other causative factors, is currently a matter of debate.

**Sponsor:** *None*

101 **Presentation Type:** Poster

**Author:** Patricia Cornett **Presentor:** Patricia Cornett
**Department:** FAMILY MEDICINE
**Classification:** GSBS Student
*Patricia F. Cornett B.S., University of North Texas, Denton, TX, 76202*
*James Hall, Ph.D., University of North Texas Health Science Center, Ft. Worth, Tx,76107*
*Susan Franks, Ph.D., University of North Texas Health Science Center, Ft. Worth, Tx,76107*
*Jerry McGill, Ph.D., University of North Texas Health Science Center, Ft. Worth, Tx,76107*

**RISK FACTORS FOR VASCULAR DEMENTIA**

**Purpose:** The purpose of the current study is to explore and identify risk factors for dementia. This information may aid in the future diagnosis, management, and treatment of persons at risk for or diagnosed with vascular dementia.

**Methods:** A sample of 481 participants were recruited from a list of all patients assessed or admitted to the GAP clinic at the University of North Texas-Health Science Center. Statistical analyses used included stepwise linear regression, multinomial logistic regression and proportional hazards regression (relative risk ratio analysis) using a polynomial independent variable. The second set of statistical analyses included logistic regression and odds ratio using a binomial independent variable.

**Results:** Relative Risk Ratio analyses indicate that a history of hypertension (RRR= 1.80, p = .009) and a history of hypercholesterolemia (RRR = 1.85, p = .016) are robustly significant risk factors for Alzheimer's disease. A history of tobacco use (RRR = 2.18, p = .01) is a robust significant risk factor for vascular dementia. Multinomial logistic regression analyses produced similar results as the Relative Risk Ratio analyses. Stepwise regression analyses indicate that hypercholesterolemia is an independent risk factor for dementia (b = -.113, p = .009). The analysis of hypercholesterolemia (b = -.104, p = .018) and hypertension (b = -.094, p = .031) together indicate a cluster risk factor effect. Participants who presented with no specific medical or memory concern who were not demented were found to be statistically at a greater risk of developing dementia if they had a history of tobacco use (RRR = .543, p = .036) and a history of hypercholesterolemia (RRR = .474, p = .012)

**Conclusions:** The results of this study have provided some insight into the etiology of dementia. They indicate that cardiovascular risk factors, such as hypercholesterolemia, hypertension, diabetes, and smoking need to be considered for the etiology for the diagnosis of dementia. Thus, the findings of this study indicate that some factors that are common between cardiovascular disease and dementia do exist. In fact, this study found that some cardiovascular risk factors are not independent risk factors for dementia, but the combination or cluster of the included risk factors viewed together become significant risk factors.

**Sponsor:** *None*

102 **Presentation Type:** Poster

**Author:** Evelyn Perez **Presentor:** Evelyn Perez
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**Classification:** Postdoctoral Fellow/Resident (Not for Competition)
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*UNTHSC, Fort Worth, TX76107*

**ESTROGEN RECEPTOR KNOCK-DOWN INCREASES THE RESISTANCE TO OXIDATIVE STRESS IN HT-22 CELLS**

**Purpose:** Estrogen receptor beta (ERbeta) has recently been shown to localize to the mitochondria of many cell types. The reason for this localization is unclear. In an effort to elucidate this question, ER beta was knocked down utilizing RNA interference in a murine hippocampal cell line, HT-22.

**Methods:** We utilized siRNA technology to knockdown estrogen receptor beta, fluorescence and confocal microscopy to visualize cell morphology and mitochondrial membrane potential, calcein AM assay to determine cell viability, and ATP levels to determine mitochondrial function.

**Results:** There was a >90% decrease in ERbeta protein as detected by Western blot and immunohistochemistry. A drastic change in morphology occurred in these ERbeta knockdown cells (siERbeta), as they displayed a more stellate appearance with longer processes. The growth characteristics did not change as compared to their vector controls. However, siERbeta cells were more resistant to various oxidative stressors including hydrogen peroxide, iodoacetic acid, and glutamate toxicity. Estradiol (E2) protection against IAA was not altered by ERbeta absence and the potent ER antagonist, ICI 182780, did not inhibit E2 actions. ATP levels in siERbeta were more resistant than vector cells to hydrogen peroxide. Furthermore, siERbeta cells maintained mitochondrial membrane potential against hydrogen peroxide application.

**Conclusions:** In summary, knock-down of ER beta resulted in a resistance to oxidative stress and maintenance of mitochondrial function.

**Sponsor:** *NIH grant AG10485 and AG 22550*

103 **Presentation Type:** Poster

**Author:** Christopher de Fiebre **Presentor:** Christopher de Fiebre
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**Classification:** Faculty (Not for Competition)
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**MOUSE STRAIN DIFFERENCES IN SUSCEPTIBILITY OF PRIMARY NEURONAL CULTURES TO ?-AMYLOID1-42 NEUROTOXICITY**

**Purpose:** Although it is clearly established that genetic variability in the cleavage of amyloid precursor protein (APP) to form ?-amyloid1-42 (A?) influences the propensity of an individual to develop Alzheimer's disease, little work has been done to ascertain if genetic variability exists in the modulation of susceptibility to the neurotoxic properties of this peptide. Inbred strains of mouse have often been used in an initial assessment of whether genetic variability may influence a particular trait (e.g., susceptibility to A?-induced neurotoxicity). In the current study, primary neuronal cultures of cerebral cortical tissue derived from neonates of 3 inbred mouse strains, C57BL/6J, C58/J and DBA/2J, were used to test the hypothesis that genetic factors can influence the neurotoxic properties of A?.

**Methods:** Tissues were collected and cultured on the day of birth in DMEM (containing 20% Horse Serum) in 96 well plates. On Day 2, the mitotic inhibitor, Ara-C (10nM), was added and ~75% of the media was exchanged with fresh media 2 days later. Media was again changed every 3-4 days until cells were established in culture for 2 weeks. A? (.03 - 3 μM) was then added to each culture and cellular viability was assessed 48 hr later using the MTT assay.

**Results:** In cultures from each strain, A? was neurotoxic in a concentration dependent fashion; however, there were significant strain differences in the concentration dependency of this toxicity. C57BL/6J cultures were the most susceptible to A?-induced neurotoxicity and C58/J cultures were the least susceptible. The susceptibility of cultures from DBA/2J mice was intermediate between the two other strains.

**Conclusions:** These data represent the first ever demonstration of strain differences in A?-induced neurotoxicity and suggest that genetically mediated differences in susceptibility to the toxic effects of this peptide may influence whether an individual develops Alzheimer's disease.

**Sponsor:** *AG022550*

# AGING/ALZHEIMER'S DISEASE

**104** **Presentation Type:** Poster

**Author:** Nathalie Sumien **Presentor:** Nathalie Sumien
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*N. Sumien, K. Heinrich, and M.J. Forster. Dept of Pharmacology and Neuroscience, UNTHSC, Fort Worth, Texas 76107.*

**LIFE LONG COENZYME Q10 INTAKE FAILED TO ALTER LONGEVITY AND HAD MINIMAL EFFECT ON BEHAVIORAL BIOMARKERS OF AGING IN MICE**

**Purpose:** This study was designed to determine whether life-long coenzyme Q10 (CoQ10) supplementation had a beneficial effect on the longevity of mice and whether this long-term intake provided protection against age-related decline in performance of psychomotor and cognitive functions.

**Methods:** Beginning at four months of age, separate groups of mice were assigned to one of three diets: control or supplemented with low or high concentrations of CoQ10 (yielding daily CoQ10 intakes of 148- or 654mg/kg, respectively). One squad was set aside to assess survivorship of the mice on the different diets. Another squad was utilized to behaviorally assess performance of the mice after 3, 11 or 21 months on their respective diets, when they were 7, 15 or 25 months of age.
**Results:** The longevity study revealed (i) early deaths in the high CoQ groups, (ii) no effect of either CoQ concentration on maximum and median life span. The behavior study illustrated (i) no significant effect on psychomotor performance, even though a possible trend for better performance on the coordinated running test was seen with the high CoQ group at 15 months, (ii) no effects of diets were found on the spatial learning and memory task, (iii) delay of age-associated decline in horizontal distance and vertical activity with both diets, however more pronounced with the high CoQ group.
**Conclusions:** Overall, these results suggested that life long CoQ10 intake failed to alter the life span of these mice and failed to delay or prevent most age-related declines of psychomotor and cognitive functions studied.
**Sponsor:** *NIH/NIA, RO1 AG 13563*

**105** **Presentation Type:** Oral

**Author:** Amit Vashist **Presentor:** Amit Vashist
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**Classification:** GSBS Student
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**DIFFERENTIAL EFFECTS OF SHORT-TERM PHYTOESTROGEN SUPPLEMENTATION ON COGNITIVE AND PSYCHOMOTOR PERFORMANCE OF MALE AND FEMALE MICE**

**Purpose:** Plant-derived, non-steroidal compounds called phytoestrogens have been widely used as substitutes for estrogen in anticipation of estrogen-like therapeutic effects without producing the side effects associated with estrogen therapy. Little is known about the effects of phytoestrogens on brain structure and functions. The goal of this 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 ug/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 cooordination, balance and fatigue), swim maze test (measuring spatial memory of mice by making them use distal cues to locate a platform hidden below the surface of an opaque pool of water), 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 when compared with the age-matched controls. 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 preliminary data suggests 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:** *None*

**106** **Presentation Type:** Poster

**Author:** Paramjit Kaur **Presentor:** Paramjit Kaur
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**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 Alzheimer's 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. In addition, we determined if the synthetic progestin, medroxyprogesterone acetate (MPA), used in most hormone therapy formulations, is equally effective as a protective agent.
**Methods:** Using organotypic explants (slice culture) of the cerebral cortex, we evaluated if progesterone and MPA protect 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 assessed by measuring the amount of Lactate Dehydrogenase (LDH) was 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. Medroxyprogesterone acetate (100 nM, however, did not. Pharmacological inhibition of both the MAPK pathway, using the MEK1/2 inhibitor (UO126, 10 ?M), or the PI-3K pathway, using LY294002 (15 ?M, 30 min), prevented progesterone's 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 levels, suggesting that progesterone's 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) as well as by increasing the expression of the neurotrophic factor, BDNF. The latter may be mediated by the classical mechanism of hormone action, where activation of the intracellular progesterone receptor leads to transcriptional regulation of the BDNF gene.
**Sponsor:** *The National Institutes of Health (NIA) -AG022550 & AG023330, and a NARSAD Young Investigator Award*

**108** **Presentation Type:** Poster

**Author:** Sara Taylor **Presentor:** Sara Taylor
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**THE EFFECT OF EXERCISE ON BEHAVIOR IN AGING MICE**

**Purpose:** The purpose of this study was to study the relationship between exercise and cognitive function in aging C57Bl/6 mice by subjecting young and aged mice first to an exercise regimen followed by age sensitive behavioral tests designed to elucidate neurocognitive status.
**Methods:** C57Bl/6J mice (3 months and 20 months) were exercised daily on a treadmill for a period of 8 weeks. The exercise regimen consisted of running at 14 meters/minute for 60 minutes. Control mice were placed on a stationary treadmill for a similar duration. This design resulted in groups of young sedentary, young exercised, aged sedentary, and aged exercised mice. At the end of 8 weeks, the cognitive performance of the mice was measured by administering behavioral tests including Locomotor Activity, Motor Skills (including Walk Initiation, Alley Turn, Negative Geotaxis, Wire Suspension and Bridge Walking), Morris Water Maze and Startle. The Locomotor Activity test examines exploratory behavior. Walk Initiation, Alley Turn, and Negative Geotaxis are tasks of motor competence and reflexive behavior. The Wire Suspension test assesses motor coordination, muscular strength and balance. The Elevated Path (Bridge) test is used to determine the animal's muscular coordination and balance. Performance on the Elevated Bridge test is an index of cerebellar function. During the Morris Water Maze test, spatial (room) cues are used by mice to locate a hidden platform, this test examines hippocampal dependent learning and memory. Startle tests the animal's reflexive response to electric stimulation.
**Results:** The results of the behavioral testing show that there are significant age-related differences in the ability of young and aged mice to perform the battery of tests chosen for this study. The exercise regimen that the mice completed for this project appeared not to produce significant increases in performance by either young or aged groups with the exception of Bridge Walking. Exercised mice in both the young and aged groups demonstrated a significant improvement in their performance on this behavioral test. Aged exercised mice improved to nearly the performance levels of young sedentary mice.
**Conclusions:** The exercise protocol of this project does not appear to produce significant improvements in cognitive ability in C57Bl/6 mice. The positive results observed during the Bridge Walking test suggest that exercise could have a modulatory effect on cerebellar degeneration in aging mice.
**Sponsor:** *none*

# AGING/ALZHEIMER'S DISEASE

109 **Presentation Type:** Poster

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**BEHAVIORAL SENSITIZATION AND TOLERANCE TO THE LOCOMOTOR STIMULANT PROPERTIES OF METHAMPHETAMINES ACROSS THE LIFESPAN OF THE MOUSE**

**Purpose:** Adults pre-exposed intermittently to moderate doses of psychostimulants can often show a long-lasting increase in their subsequent behavioral response to the drugs (sensitization). Alternatively, with repeated exposure to larger doses of the drug, a decrease in subsequent response to the drug may occur (tolerance). The current study examines the effect of age on the degree of sensitization or tolerance to stimulant properties of methamphetamine (METH).

**Methods:** Sixty-seven C57BL6/JNia mice were used in this study. Mice were of 3 different ages: 3 month (n=32), 15 month (n=17), and 24 month (n=18). Approximately half of the mice (n=33) were injected with 0.5 mg/kg METH s.c. once daily for 5 consecutive days, while remaining subjects (n=34) were injected with body weight-matched volumes of 0.9% saline in an identical injection schedule. Following a 7-day rest period, all mice were injected with vehicle, and then placed in locomotor activity chambers for a METH challenge test. After the initial 10-minute test period and prior to each subsequent 10-minute interval, the mice were injected with METH so as to yield cumulative doses of 0.5, 1.0, 2.0, and 4.0 mg/kg. The last test period lasted for 20 minutes. METH pre-exposed mice were compared to saline pre-exposed mice at each different age.

**Results:** At all ages, horizontal activity increased in a dose-dependent fashion in the METH challenge. Evidence of sensitization was observed in 15 month-old METH pre-exposed mice, while 24 month-old METH pre-exposed mice displayed tolerance to the METH induced locomotor activity. While 3 and 15 month-old METH pre-exposed mice exhibited an increase in the number of repetitive behaviors after the challenge dose of METH, 24 month-old METH pre-exposed mice displayed less repetitive behaviors than their saline pre-exposed cohorts. 15 month-old METH pre-exposed mice responded to the increasing challenge dose of METH by engaging in more circling behavior than saline pre-exposed mice. Conversely, 24 month-old METH pre-exposed mice tended to display less circling behavior than saline pre-exposed mice, and this effect was greatest at the highest doses of METH.

**Conclusions:** The results of the present study suggest that there is a marked shift from sensitization to tolerance that occurs with age. These results may reflect changes in the neuronal processes responsible for sensitization and tolerance, or may be indicative of age differences in the body's functional ability to dispose of methamphetamine.

**Sponsor:** *none*

110 **Presentation Type:** Poster

**Author:** Swati Varshney **Presentor:** Swati Varshney
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*Swati Varshney, M.A.,James R Hall, Ph.D,Michelle Harvey, Ph.D University of North Texas Health Science Center*

**PRELIMINARY SUPPORT FOR BRAIN AT RISK HYPOTHESIS AS A RISK FACTOR FOR DEMENTIA**

**Purpose:** The link between surgery in the elderly and persistent postoperative cognitive dysfunction has been the subject of considerable debate. The frequency of persistent impairment and the degree of deficit vary greatly and are related to several factors The study explored and further identified these risk factors by generating a model of the brain-at-risk hypothesis as a risk factor for dementia.

**Methods:** The sample consisted of 218 participants who were assessed or admitted to the GAP clinic at the University of North Texas-Health Science Center. This included 143 patients with a diagnosis of dementia and 75 patients who had not received a diagnosis of dementia. Statistical analyses included stepwise linear regression and multinomial logistic regression.

**Results:** The logistic regression analyses indicated that a history of surgery was a significant risk factor for dementia. Patients with higher frequency of surgeries were found to be at a higher risk for developing dementia than those with a history of tobacco use, history of hypocholesterolemia or a history of hypertension.

**Conclusions:** This study is a preliminary analysis revealing the influence of undergoing surgical procedure as an important risk factor for cognitive decline and dementia. More investigation is needed regarding the type of surgical procedure associated with dementia type.

**Sponsor:** *none*

111 **Presentation Type:** Poster

**Author:** Nopporn Thangthaeng **Presentor:** Nopporn Thangthaeng
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**SHORT-TERM GALACTOSE SUPPLEMENTATION MAY IMPAIR CEREBELLAR FUNCTIONS**

**Purpose:** Previous studies have suggested that short-term injections with a low dose of galactose, a milk sugar, promotes the formation of advance glycation end products (AGEs) via Maillard reaction in vivo. Accumulation of AGEs is hypothesized to contribute to an acceleration of certain aspects of brain aging. The purpose of the current study was to determine if dietary galactose supplementation affects the cognitive or motor performance of young and old mice.

**Methods:** Young (6 months) and 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 behavior 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. Locomotor activity measures exploratory and rearing behaviors. The wire suspension test was used to assess motor coordination and muscle strength. The elevated path (bridge) test was used to assess balance and fine muscle control. The rotorod test measured fine motor coordination, balance and stamina. Performance on elevated path and rotorod tests are dependent on cerebellar function. Performance on the swim maze test, where mice must use spatial cues to locate a platform hidden below the surface of a pool of opaque water, is dependent on cortical and hippocampal functions. The startle response test was used to measure reaction time to auditory or shock stimuli.

**Results:** Galactose supplemented groups showed a significant increase in water intake when compared to the control groups. Preliminary results suggest that galactose supplementation impaired rotorod performance in both young and old mice. Additionally, galactose supplementation impaired bridge-walking performance in old, but not young mice. The swim maze test did not reveal any observable difference between the treatment groups.

**Conclusions:** The pattern of preliminary results suggests that galactose supplementation may impair cerebellar functions, especially in the old mice.

**Sponsor:** *None*

112 **Presentation Type:** Poster

**Author:** Ritu Shetty **Presentor:** Ritu Shetty
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** GSBS Student
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*2)Michael J. Forster, PhD*
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*4)Margaret Rutledge, PhD*
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*6)Shaohua Yang, MD/PhD*
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**TRANSIENT CEREBRAL ISCHEMIA CAUSES A PROGRESSIVE DECLINE IN BRAIN FUNCTION**

**Purpose:** Stroke is one of the leading causes of death and disability in United States. The disablity associated with stroke may be sensorimotor or cognitive or both, however the underlying mechanisms leading to this functional decline are not fully understood. Previous data suggest that pathology after transient ischemia is similar to that of Alzheimer's disease. The goal of this study was to determine whether or not a progressive functional decline was associated with transient middle cerebral artery occlusion (tMCAO).

**Methods:** Female sprague-dawley rats were obtained from Charles River and maintained on an ad libitum diet. They were ovariectmized at 3 months of age and received ischemia at 4 months of age. The rats were divided in the following groups 30-days post stroke, 7-days post stroke, sham and control. Following stroke the rats were subjected to a battery of behavioral tests for cognitive and psychomotor performance. These tests included locomotor activity, coordinated running performance, swim maze and startle response

**Results:** Transient middle cerebral artery occlusion resulted in a poorer learning of the swim maze task as compared to their age-matched shams and controls. Further, the 30- day post stroke rats tended to perform worse than the 7-day post stroke in learning to locate the platform in swim maze task. In spontaneous locomotor activity there was an increase in activity following stroke and the 30-day post stroke group showed higher activity as compared to the 7-day post stroke group. In acoustic startle response all rats habituated to the 120-dB sound after the first few trials. Interestingly, both stroke groups habituated more slowly than did controls, with the 30-day post stroke group tending to sustain a high level of response for longer than the 7-day post stroke group. In the test for coordinated motor ability there was no difference in performance in both stroke and control groups.

**Conclusions:** The results indicate that the battery of behavioral test can be used to assess transient middle cerebral artery occlusion associated cognitive and motor decline in function. The data also suggest that there is progressive decline in brain function following ischemic events produced by tMCAO.

**Sponsor:** *none*

# AGING/ALZHEIMER'S DISEASE

113 **Presentation Type:** Poster

**Author:** Mark Sanders **Presentor:** Mark Sanders
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**Classification:** Faculty (Not for Competition)
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*Anada I. Gunn-Sanders, JD, UNTHSC-School of Public Health*

**TEXAS PROBATE DELIMA: DEMENTIA AND INPATIENT PSYCHIATRIC CARE**

**Purpose:** Dementia is a costly disease and incidences increase with age. Demographics reveal an aging population. Therefore, an assumption as to increases in the diagnosis of dementia should be addressed. Many issues will arise which our policy makers need be aware of for proper preparations. One area for review is Texas laws which promulgate rules for over-seeing persons that are incapacitated. Persons with dementia may become incapacitated and require inpatient psychiatric care. This issue will only grow as our population with dementia grows.

**Methods:** A review of the Texas Probate Code Chapter 12-Guardianship, Texas Health and Safety Code Section 574.034-Order for Temporary Mental Health Services, several United States Supreme Court Cases, American Psychiatric Association Recommendations on Voluntary Inpatient Mental Health Services were analyzed as they apply to persons with incapacities related to dementia.

**Results:** If an incapacitated person already with a guardian needed inpatient psychiatric services they would have to go before the probate court. Current guardianship laws do not grant guardians the power to admit the incapacitated person for inpatient psychiatric services. The person needs to go before the court prior to admission, unless by clear and convincing evidence they are an imminent danger to themselves or others. The APA recommends allowing a court appointed guardian to temporarily admit a person for inpatient psychiatric care.

This helps to avoid the cost and indignity of court proceedings for those with dementia and ensures that court supervision continues. Some states have successfully adopted the APA version but Texas still requires that incapacitated persons, even those requesting inpatient psychiatric admission, must go before the probate court prior to admission, unless clear and convincing evidence reveals they are an imminent danger to self or others.

**Conclusions:** In instances of persons with advanced dementia, that may require inpatient psychiatric services, there needs to be a way of expediting the judicial process to ensure proper oversight and preserve individual rights of these persons. The system is currently inadequate. As the population ages, policy makers need to adjust the guardianship laws to allow more latitude to court appointed guardians to act in the best interest of the incapacitated person with dementia. Policymakers should adopt reforms closer to those of the APA.

**Sponsor:** *none*

114 **Presentation Type:** Poster

**Author:** Xiaofei Wang **Presentor:** Xiaofei Wang
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**PROTECTIVE EFFECTS OF SODIUM PYRUVATE AGAINST H2O2 TOXICITY IN HUMAN NEUROBLASTOMA SK-N-SH CELLS**

**Purpose:** As an intermediary metabolite and antioxidant, pyruvate has been shown protection in models of ischemia. Here, we tested the effects of pyruvate against H2O2-induced toxicities in human neuroblastoma SK-N-SH cells.

**Methods:** Exposure of neuroblastoma SK-N-SH cells to H2O2 served as in vitro model. Cell viability was measured using calcein AM assay. Effects of pyruvate on reactive oxygen species were assessed using submitochondrial particle superoxide production assay and fluorescence dyes such as dichlorofluorescin diacetate (DCFH-DA) and dihydrorhodamine (DHR). Cellular ATP levels were quantified utilizing a luciferin and luciferase-based assay.

**Results:** : H2O2 (150 ?M) exposure resulted in about 60% cell death in SK-N-SH cells within 20h, and sodium pyruvate at concentrations ranging from 10 ?M to 2 mM significantly and dose-dependently attenuated cell death. At concentrations of 1 mM and above, pyruvate significantly decreased H2O2-induced increase in intracellular reactive oxygen species (ROS) levels, blocked H2O2-induced ATP depletion. Furthermore, in a cell-free system, pyruvate effectively reduced superoxide production by submitochondrial particles.

**Conclusions:** Pyruvate protected neuroblastoma SK-N-SH cells against oxidative stress by scavenging ROS and increasing ATP levels.

**Sponsor:** *AG 10485 and AG 22550*

# CANCER

200 **Presentation Type:** Poster

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**Classification:** GSBS Student
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**EPIGALLOCATECHIN GALLATE UPREGULATES VEGF EXPRESSION IN PROSTATE CANCER CELLS**

**Purpose:** Epigallocatechin gallate (EGCG), a major polyphenol in green tea, has been shown to possess anticarcinogenic and antiangiogenic properties. Vascular endothelial growth factor (VEGF), a pro-angiogenic growth factor, plays a very important role in promoting angiogenesis in the normal as well as diseased states. HIF-1alpha is a key transcription factor in hypoxia-induced upregulation of VEGF. In this study, we investigated the effect of EGCG on normoxic HIF-1a and VEGF expression in PC-3ML prostate cancer cells.

**Methods:** Luciferase assays were used to test the regulatory effect of EGCG on HRE-mediated transcription and VEGF promoter activity. Immunoblot analyses were used to determine the effect of EGCG on HIF-1alpha protein expression in PC-3ML cells. VEGF expression was analyzed with ELISAs. Protein-protein interactions were studied using co-immunoprecipitation and pull-down assays.

**Results:** EGCG treatment increased VEGF promoter activity by about 2.5-fold in PC-3 ML cells compared to that of control cells. EGCG treatment increased VEGF protein secretion up to 3-fold from PC-3ML cells in a dose-dependent manner. Moreover, EGCG increased HRE-mediated transcription up to 7-fold, and HIF-1alpha protein levels upto 3-fold in a dose-dependent manner. Although EGCG has been shown to inhibit proteasome activity, we did not observe any significant accumulation of ubiquitinated HIF-1? after EGCG treatment. On the other hand, addition of exogenous ferrous ions together with EGCG restored levels of ubiquitinated HIF-1? protein to that of the control cells. In addition, EGCG-mediated increase in HRE-promoter activity and VEGF protein secretion was abolished by the addition of exogenous FeSO4.EGCG treatment inhibited interaction between 35S pVHL and HIF-1alpha Oxygen-dependent degradation domain (ODD) in a dose-dependent manner, with 40μg/ml EGCG lowering the 35S pVHL capture by almost 70%.

**Conclusions:** This study provides evidence of EGCG, a major green tea polyphenol, upregulating VEGF expression in prostate cancer cells (PC-3ML) by inhibiting HIF-1alpha degradation under normoxia.

**Sponsor:** *NIH grant # 1R21CA102382*

201 **Presentation Type:** Poster

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*Matthew P. Thompson, Jonathan R. Brody, Kathleen M. Murphy, Michael S. Torbenson, and Gary R. Pasternack. Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, Maryland.*

**MUTATION AND LOSS OF HETEROZYGOSITY OF PP32R1 AND THE PATHOGENESIS OF HEPATOCELLULAR CARCINOMA**

**Purpose:** We have recently shown that pp32r1 is expressed in most neoplastic cell lines and described a mutation in pp32r1 at position 4870 that increases the growth rate of ACHN cells. In the present study, we explored the prevalence and function of the pp32r1?4870 mutation in hepatocellular carcinoma (HCC).

**Methods:** PCR and DNA sequencing were used to screen for pp32r1?4870 in HCC and corresponding normal tissue DNA. HepG2 and Hep3B cell lines were stably transfected with an expression plasmid encoding pp32r1?4870 or with one encoding wild-type pp32r1. pp32r1 expression was confirmed at the mRNA level by hybridization with pp32r1 sequence specific DNA probes. Further confirmation of pp32r1 protein expression was performed by immunoblot. Growth rates of HCC cell lines were measured by staining with SYBR Green and monitoring. IHC was performed on HCC tissue arrays with a specific anti-pp32r1 antibody.

**Results:** Utilizing PCR and DNA sequencing, we detected the pp32r1 mutation in one HCC out of nineteen HCC tumor samples screened. Importantly, this mutation occurred in a patient without cirrhosis, antecedent viral hepatitis, or parasitic liver disease. Analysis of normal tissue DNA from the pp32r1?4870 positive individual indicated that the individual displayed a loss of heterozygosity in the HCC. To analyze the effect of this mutation on the growth potential of HCC, HepG2 and Hep3B cell lines were transfected with an expression plasmid encoding pp32r1?4870 or with one encoding wild-type pp32r1. Both HepG2 and Hep3b cells expressing pp32r1?4870 displayed a markedly increased growth rate compared to cells expressing wild-type pp32r1. Finally, we analyzed expression of pp32r1 immunohistochemically in HCC tissue arrays. Virtually all liver samples analyzed expressed pp32r1, suggesting that pp32r1?4870 would be expressed in vivo.

**Conclusions:** Our data indicate that one of nineteen HCC's was homozygous for pp32r1?4870 and that the patient had none of the usual risk factors for HCC. Furthermore, corresponding normal tissue from this patient was heterozygous for the mutation. Transfection of pp32r1?4870 caused increased growth in two HCC cell lines. The role of pp32r1 in hepatocellular carcinogenesis is not known, recent reports that the overexpression of pp32r1 potentiates transformation and tumorigenesis, coupled with the data we report here suggest that pp32r1, and in particular pp32r1?4870, could play a causal role in HCC.

**Sponsor:** *none*

202 **Presentation Type:** Poster

**Author:** Linda Mooberry **Presentor:** Linda Mooberry
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**THE SMART BOMB AGAINST TUMOR CELLS**

**Purpose:** The optimal formulation and chemical and physical similarity to native HDL was determined for the rHDL/PTX delivery vehicle was determined.

**Methods:** The rHDL delivery vehicle was formed by either sonication or a modified cholate dialysis procedure. The sonication method also requires an emulsifier, either Cremophor or tocopherol polyethylene glycol succinate, a Vitamin E derivative. The incorporation of paclitaxel is monitored by radiolabeled (14C) paclitaxel. The chemical composition of our rHDL/PTX vehicle is determined by various colorimetric assays. The physical characterization of the rHDL/PTX was accomplished by negative staining electron microscopy.

**Results:** The rHDL particle formed by cholate dialysis incorporates an amount of paclitaxel that approaches the concentration of the current commercial formulations. Furthermore, the drug-carrying capacity of this particle is 20-fold higher than our first published particle, which contained Cremophor. Its chemical composition and molecular weight are also similar to native HDL. By electron microscopy, the particles appear to be spherical in shape. The particle diameter varies from 13 ± 3.5 nm, which is in the range for native HDL.

**Conclusions:** Based on the paclitaxel incorporated, the optimal formulation for our drug delivery vehicle uses the modified cholate dialysis procedure. Furthermore, from compositional analysis and electron microscopy, the rHDL/PTX particle is chemically and physically similar to native HDL.

**Sponsor:** *None*

203 **Presentation Type:** Poster

**Author:** Maya Nair **Presentor:** Maya Nair
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**A NOVEL DRUG DELIVERY VEHICLE FOR BREAST CANCER CHEMOTHERAPY.**

**Purpose:** Preparation and in vitro anti cancer evaluation of reconstituted high density lipoprotein (rHDL) delivery vehicle using rHDL/paclitaxel against cultured breast cancer cell lines.

**Methods:** The studies were carried out by preparing rHDL/drug complexes and measuring their cytotoxicity toward breast cancer cells. Immuno blotting and competition studies were carried out to probe the receptor mediated uptake of the anti-tumor agents, transported by rHDL, to evaluate their potential for the selective delivery of anti-cancer agents to breast cancer cells, without concomitant damage to normal cells.

**Results:** rHDL particles containing paclitaxel had a consistent composition, molecular weight and exceptional stability upon ultracentrifugation, gel chromatography and incubation with human plasma. Data on the uptake of paclitaxel (PTX) vs. that of cholesteryl esters showed a strong correlation ($r2=0.89$; $p<0.04$) suggesting that the uptake of CE and paclitaxel were facilitated by the same receptor-mediated mechanism. Additional studies via immunoblotting with an SR-BI antibody showed that the expression of the SR-B1 type receptors in breast cancer cells was consistent with such a hypothesis. Recent studies show that the uptake of PTX, encapsulated in an rHDL/PTX preparation, was inhibited by HDL3 supporting the concept of receptor mediated uptake and the selective targeted delivery of chemotherapeutic agents to beast cancer cells via the rHDL formulation

**Conclusions:** 1) The rHDL/PTX formulation showed markedly higher cytotoxicity against breast cancer cells compared to the free drug. 2) The stability of the rHDL/PTX formulation provides increased confidence for the development of a dramatically effective novel chemotherapeutic strategy for the treatment of breast cancer patients

**Sponsor:** *NONE*

# CANCER

204 **Presentation Type:** Poster

**Author:** Eswar Shankar **Presentor:** Eswar Shankar
**Department:** MOLECULAR BIOLOGY & IMMUNOLOGY
**Classification:** Postdoctoral Fellow/Resident
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**PKC EPSILON OVER EXPRESSION IN BREAST CANCER CELLS CONFERS RESISTANCE TO TUMOR NECROSIS FACTOR RELATED APOPTOSIS INDUCING LIGAND (TRAIL) INDUCED APOPTOSIS BY INDUCING BCL2**

**Purpose:** Tumor Necrosis Factor Related Apoptosis Inducing Ligand (TRAIL) is a member of the TNF family that induces cell death primarily in cancer cells, without any detectable toxicity to normal cells. Although TRAIL induces cell death through the extrinsic pathway, it also cooperates with the intrinsic, mitochondrial events to kill cancer cells. Bcl2 is an anti-apoptotic protein that inhibits mitochondrial cell death pathway. PKC delta has been shown to influence the events occurring in the mitochondria during cell death. Furthermore, our lab has previously shown that PKC epsilon is an anti-apoptotic protein that inhibits TNF-induced apoptosis. The role played by PKCs in TRAIL mediated apoptosis in cancer is not fully understood. Therefore, the objective of this study was to elucidate the role of PKC epsilon in TRAIL mediated cell death and the mechanism(s)involved.
**Methods:** MCF-7 and HCC1806 human breast cancer cells were stably transfected with PKC epsilon in order to determine the role played by PKC epsilon in TRAIL-induced apoptosis. The cells transfected either with vector alone or with a PKC epsilon construct, were treated with different concentrations of TRAIL and protein expression of Bcl-2, BclXL, Bax, PARP and caspase-3 analyzed by immunoblotting.
**Results:** MCF-7 and HCC1806 cells overexpressing PKC epsilon showed an increased expression of Bcl-2 compared to the vector transfected cells. In addition, there was a decrease in the expression of the pro-apoptotic protein Bax in the cells overexpressing PKC epsilon. The levels of anti-apoptotic protein BclxL were not altered in either MCF-7 or HCC1806 cells overexpressing PKCepsilon when compared to controls. We also observed that in the HCC1806 cells, PKC epsilon overexpression abrogated the activation of caspase 3 and cleavage of PARP, which is one of the key substrates of executioner caspases.
**Conclusions:** The results of our study demonstrate that PKC epsilon overexpression in human breast cancer cells causes resistance to TRAIL induced cell death by inducing Bcl2.
**Sponsor:** *NCI/NIH Grant: CA 71727*

205 **Presentation Type:** Poster

**Author:** Matthew Thompson **Presentor:** Matthew Thompson
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**Classification:** TCOM DO Student
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**PP32 IS REQUIRED FOR ESTROGEN RECEPTOR ALPHA-MEDIATED TRANSCRIPTION**

**Purpose:** Although 70% of patients with estrogen receptor (ER)-positive breast cancer initially respond to anti-estrogen therapy, many patients develop resistance. Here we report a relationship between pp32 and ER-alpha that mediates transcription in breast cancer cell lines. Given the data that we report here, pp32 may be a target for inhibition in breast cancer and may be able to overcome resistance or synergize with anti-estrogen therapy.
**Methods:** Estrogen (E2) dependent growth of the ER-alpha positive breast cancer cell lines MCF-7 and T47D and the ER-alpha negative cell line MDA-MB.231 was performed with increasing concentrations of E2 and monitored by trypan blue and SYBR Green fluorescence. pp32 depletion was performed by pp32 RNAi and by a scrambled nonspecific RNAi control. The presence of p53 and PS2 and the phosphorylation status of Rb was determined by immunoblot. E2 stimulated gene expression was assessed with an estrogen response element(ERE)-GFP construct that was transfected into the breast cancer cell lines.
**Results:** E2 signaling through ER-alpha has been shown to increase cell growth, increase p53 and PS2, and increase the hyperphosphorylation of the Rb protein. In addition, ER-alpha has been shown to interact with pp32 in breast cancer cell lines. Depletion of pp32 by RNAi correlated with a decrease in growth compared to controls upon exposure to increasing concentration of E2 in the MCF-7 and T47D cell lines but not in the ER-alpha negative cell line MDA-MB.231. pp32 depletion decreased the expression of the estrogen responsive genes p53 and PS2 when compared to controls in MCF-7 and T47D being exposed to increasing concentrations of E2. pp32 depletion caused no significant change of p53 or PS2 expression compared to controls in MDA-MB.231 being exposed to increasing concentrations of E2. pp32 depletion inhibited Rb hyperphosphorylation compared to controls upon exposure to increasing concentrations of E2 in MCF-7 and T47D, but there was no significant change in RB phosphorylation in MDA-MB.231. Finally, pp32 depletion inhibited ER-alpha signaling through an ERE-GFP reporter construct transfected into the MCF-7, T47D, and MDA-MB.231.
**Conclusions:** Our data indicate that pp32 is required for ER-alpha mediated transcription in breast cancer cell lines. The effects of pp32 depletion mimic the effects of tamoxifen in the breast cancer models and therefore may be an attractive drug target and an alternative for patients with anti-estrogen therapy resistant tumors.
**Sponsor:** *none*

206 **Presentation Type:** Poster

**Author:** Jiyoung Lee **Presentor:** Jiyoung Lee
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**ROLE OF TYROSINE PHOSPHORYLATION OF PKC DELTA IN CISPLATIN-INDUCED APOPTOSIS**

**Purpose:** Cisplatin is one of anticancer agents to treat solid tumors like human cervical 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 apoptotic events caused by DNA damaging agent such as cisplatin. In addition, we have examined if tyrosine phosphorylation influences resistance to cisplatin.
**Methods:** Cells were treated with several tyrosine kinase inhibitors including PP2 that inhibits Src kinase as well as AG1478, inhibitor of EGFR (epithermal growth factor receptor) in presence or absence of cisplatin. Tyrosine phosphorylation of PKC delta was detected by western blot. Cell death was measured by a biocolorimetric cell survival assay, activation of caspases, and Flow Cytometric DNA analysis using Propidium Iodide.
**Results:** PP2 alone had moderate effect on cell death and it increased cisplatin-induced apoptosis. AG1478, EGFR inhibitor, did not cause any cell death either in presence or absence of cisplatin.
**Conclusions:** Tyrosine phosphorylation of PKC delta precedes cisplatin-induced apoptosis, and inhibition of Src-dependent phosphorylation on PKC delta moderately increases effect of cisplatin.
**Sponsor:** *none*

207 **Presentation Type:** Poster

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**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 1gene=1protein 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 celluar function.
Cisplatin is one of the most important anticancer drugs to treat solid tumors including cervical cancer. However, the development of resistance by tissues 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 invitro selection. We have isolated proteins from Hela (cisplatin sensitive) and Hela/cp cells and subjected to two-dimensional gel electrophoresis. This method involves separating the proteins based on their isoelectric pH (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 are currently trying to standardize the protocol and make the results reproducible.
**Conclusions:** none
**Sponsor:** *NCI/NIH Ca85682*

# CANCER

208 **Presentation Type:** Poster

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**UV-INDUCIBILITY OF THE POLYMERASE ETA TRANSCRIPT OF SACCHAROMYCES CEREVISIAE: A MEANINGFUL REGULATION?**

**Purpose:** Saccharomyces cerevisiae RAD30 encodes DNA polymerase eta , carrying out mostly error-free translesion synthesis past UV induced cyclobutane pyrimidine dimers (CPDs). Pol eta accurately inserts two "A" bases in the daughter strand opposite TT (thymine) dimers present in the parent strand during replication. Regulation of this protein is very important as it has very low fidelity for an undamaged DNA. We have observed an increase in the message of RAD30 after UV radiation treatment (254nm) in logarithmic phase. At protein level, Rad30 is constitutively expressed to a significant extent and steady-state level of Rad30 protein remains unchanged even after UV treatment. Using cycloheximide, we determined that the level of Rad30 remains stable for several hours without de novo synthesis. We have observed that the half-life of the Rad30 protein is reduced following UV treatment in stationary phase. Our hypothesis is that increase in RAD30 message after UV exposure is due to induction of the gene i.e promoter regulated.
**Methods:** Transcript expression was observed by Northern blot analysis. Western blot analysis was used to observe protein expression. Primary antibody was used against myc tag (no reliable commercial Ab available against Polymerase eta). Cycloheximide, protein synthesis inhibitor, was used to study the stability of the protein in the logarithmic phase. We have constructed a diploid strain with a truncated promoter by inserting ~1.4 kb His marker region at –120 bp (from translation initiation site).

**Results:** An increase in the message of RAD30 gene was observed post UV treatment in log phase. The corresponding increase in protein level was not seen though. Two RAD30 specific transcripts were observed in stationary phase irrespective of UV treatment. Half-life of the protein changed after UV in stationary phase. By disrupting the promoter, we expect to knock down the inducibility of the transcript but the basal transcription may not be affected. In the absence of induction, we expect to see a significant decrease in protein level after UV treatment in stationary phase. This effect may be less pronounced in log phase where protein is stable.
**Conclusions:** Both transcriptional (promoter dependent) and posttranslational mechanisms may be involved in regulating RAD30 encoded Polymerase eta following UV exposure in S.cerevisiae.
**Sponsor:** *NIH*

209 **Presentation Type:** Poster

**Author:** Shalini Persaud **Presentor:** Shalini Persaud
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**REGULATION OF PKC ETA BY PHOSPHORYLATION**

**Purpose:** The protein kinase C (PKC) family of isozymes plays an important role in signal transduction and cell regulation. PKCeta is a member of the novel group of PKCs which plays a major role in cell proliferation and differentiation, especially in epithelial cells. In many cancers, such as breast tumors, PKCeta protein and mRNA levels are upregulated, possibly as a survival mechanism. Our laboratory has shown that PKCeta
as an anti-apoptotic protein. Therefore, targeting PKCeta downregulation in breast cancer is an important strategy in cancer therapy. The overall objective of my study is to provide insights on the regulation of PKCeta, which may serve as a potential target for the development of improved cancer therapies. Phorbol esters are compounds which activate and subsequently downregulate many PKC isozymes. We have shown that treatment with PKC activator, such as PDBu ( phorbol 12,13-dibutyrate) upregulated PKCeta and treatment with BIM (bisindolymalemide), a PKC inhibitor, downregulated PKCeta. We hypothesize that the stability of PKCeta is regulated by phosphorylation. PKCeta is phosphorylated at three specific serine/threonine sites: threonine 513 in the autophosphorylation domain, threonine 655 in the activation loop and serine 675 in the hydrophobic domain. The objective of this study is to examine how mutations of specific phosphorylation sites affect the stability of PKCeta.
**Methods:** Site-directed mutagenesis was utilized to mutate PKCeta phosphorylation sites to a phosphorylation-deficient form by substituting the Ser/Thr residues to alanine and also to a phosphorylation mimicking form by mutating the Ser/Thr residues to glutamate. Wild-type or mutant PKCeta was transfected transiently into human embryonic kidney cells (HEK-t) by lipofection. The protein expression of PKCeta was detected following treatment with PDBu and BIM by Western blotting using antibodies against PKCeta and phosphorylation of PKCeta was determined using phospho-specific antibody.
**Results:** Preliminary results indicate that the triple mutants were not expressed at the protein level in the HEK-t. No significant change was observed with the double mutants compared to the wild-type control. Mutation at the 513 site appears to allow PDBu to downregulate PKCeta.
**Conclusions:** The phosphorylation status of PKCeta plays a role in regulating the stability and therefore the function of PKCeta.
**Sponsor:** *NCI/NIH Grant CA71727*

210 **Presentation Type:** Poster

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**AUTOCRINE LYMPHOTOXIN PRODUCTION IN EPSTEIN-BERR VIRUS-IMMORTALIZED B CELLS: INDUCTION VIA NF-KAPPAB ACTIVATION MEDIATED BY EBV-DERIVED LATENT MEMBRANE PROTEIN 1**

**Purpose:** We recently reported that LT was used by lymphoblastoid cell lines as an autocrine growth factor. Here, we report the mechanism of LT production and the association with EBV derived LMP1. The discovery of the mechanism of the main growth factor for the leukemia/lymphoma cell lines may hold promise in the development of drugs and treatments designed to abrogate the signaling pathway.
**Methods:** The Z-43 (EBV positive, LMP1 positive), Daudi (EBV positive, LMP1 negative), and 3A4 BJAB (EBV negative, tetracycline inducible LMP1) were used as model systems. LMP1 expression was measured with immunoblot. LT production was measured by enzyme-linked immunosorbent assay (ELISA). NF-kappaB was inhibited by Bay 11-7082. Cell growth was measured by MTS assay. NF-kappaB activation was determined by electromobility shift assay (EMSA).
**Results:** The EBV positive/LMP1 positive Z-43 cell line was shown to have high levels of both LMP1 expression and LT production. The EBV positive/LMP1 negative Daudi cell line expressed neither LMP1 nor LT. Induction of LMP1 expression in the EBV negative/LMP1 inducible 3A4 cell line was accompanied by a 13-fold increase in LT production as compared to uninduced LMP1 negative 3A4 cells. EMSA demonstrated high levels of NF-kappaB activation in Z-43 and LMP1 induced 3A4 cells, but much lower levels in the uninduced 3A4 cells. Exposure of these cells to Bay 11-7082, and inhibitor of NF-kappaB activation, abrogated LT production in a dose-dependent manner in Z-43 and both LMP1 induced and uninduced 3A4 cells.
**Conclusions:** Based on the data we report here, LT production and subsequently, cell growth, in our lymphoblastoid cell line models are driven by the EBV protein LMP1. Furthermore, LMP1 induces LT production by signaling through NF-kappaB. Discovery of the mechanism of autocrine growth regulation in these cancer cell lines may hold promise as a target in the development of drugs and treatments.
**Sponsor:** *none*

211 **Presentation Type:** Poster

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**PROTEIN KINASE CE REGULATES P70S6KINASE IN BREAST CANCER CELLS**

**Purpose:** Tumor necrosis factor (TNF-a), a cytokine that regulates inflammatory responses, can combat tumor growth by inducing apoptosis in tumor cells. TNF-a induces apoptosis via receptor mediated signal transduction pathways. Novel protein kinase Ce (PKCe) is known to inhibit TNF-a-stimulated apoptosis in breast cancer cells, though the exact mechanism of this inhibition is unknown. p70S6K is a serine/threonine kinase that regulates the progression of cells from the G0 to G1 phase of cell cycle by translational up regulation of a family of mRNA transcripts. Furthermore, p70S6K has been implicated in cell survival and has been shown to be constitutively phosphorylated and activated in certain cancer cells. The objective of this study was to determine whether PKCe regulates p70S6k activation in response to TNF-a in MCF-7 breast cancer cells.
**Methods:** To analyze the potential role of PKCe in p70S6K activation, we used MCF-7 cells stably transfected with wild type PKCe. Cells transfected with empty vector served as control. Cells were treated with different concentrations of TNF-a for varying periods of time and cell lysates were harvested. Phosphorylation of p70S6k at the threonine 389 site was detected by Western blotting using a phospho-specific antibody.
**Results:** To analyze the effect of PKCe on p70S6k, MCF-7 cells over expressing PKCe were compared to vector transfected controls. TNF-a treatment caused a concentration-dependent activation of p70S6K in vector-transfected MCF-7 cells, with maximal activation seen with 1 nM TNF-a. Time-course analysis of p70S6K activation revealed peak responses at 30 min. Interestingly, both basal and TNF-a-stimulated p70S6K phosphorylation were enhanced in MCF-7 cells over expressing PKCe when compared to vector-transfected controls.
**Conclusions:** Our results suggest that PKCe regulates the activation of p70S6k in MCF-7 breast cancer cells.
**Sponsor:** *nine*

# CANCER

212 **Presentation Type:** Poster

**Author:** Susobhan Das **Presentor:** Susobhan Das
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*(1)-Postdoctoral Research Associate*
*(2)-Graduate Student*
*(3)- Professor*
**- Associate Dean, Graduate School of Biomedial Sciences*
*Department of Molecular Biology & Immunology*
*UNT Health Science Centre at FortWorth*

**ANNEXIN II- STAT6 INTERACTION STIMULATES STAT6 TRANSCRIPTIONAL ACTIVITY IN PROSTATE CANCER CELL LINES**

**Purpose:** Our hypothesis is that Annexin II-STAT6 mediated signal transduction and gene expression regulates prostate cancer cell proliferation. This hypothesis is based on identification of STAT6 as an interactor protein with annexin II in a yeast two-hybrid interaction analysis. Our rationale is based on 1) the variation in expression profiles of annexin II and STAT6 in primary and metastatic prostate cancer cell lines, 2) the observation that STAT6 is selectively activated during prostate cancer progression and 3) significant stimulation of STAT6 transactivation function in presence of annexin II in prostate cancer cells.
**Methods:** Yeast two hybrid analysis were done by cloning full length annexin II cDNA into pGBKT7 (Clontech, USA) and used as a bait to screen human placental cDNA library (Clontech, USA). Positive clones were selected by prototrophy for histidine or expression of -galactosidase, and then subjected to sequence analysis to search for novel annexin II binding proteins. Association between annexin II and new protein was reconfirmed. Further analysis of this interaction was performed using immunoprecipitation and colocalization experiments in prostate cancer cell lines. Transcriptional activation by STAT6 was measured using a luciferase reporter activation assay. Stable clones of LNCaP cells expressing annexin II were developed using full length annexin II cDNA cloned into pBig2i vector. EMSA were also performed in these stable clones to study DNA binding activity of STAT6.
**Results:** 1. STAT6 interacts with annexin II in prostate cancer cells.
2. Immunoprecipitaion and colocalization experiments confirmed this interaction.
3. STAT6 expression in clinical tissue specimen of prostate cancer was observed to be localized in fibro muscular stromal regions.
4. Luciferase assay confirms that STAT6 transcriptional activity is stimulated by annexin II.
5. STAT6 expression levels were same in both annexin II negative and positive cell lines although greater transcriptional activity were observed only in presence of annexin II.
6. Enhanced STAT6 DNA binding activity was observed in stable clones of LNCaP expressing annexin II.

**Conclusions:** 1. Annexin II is a novel interactor of STAT6.
2. Annexin II might function as a coactivator molecule for STAT6 transcriptional function.
3. STAT6 signaling is a major contributing factor that favors tumor metastasis. Annexin II-STAT6 mediated signaling may play a role as a regulator of prostate cell proliferation.

**Sponsor:** *None*

214 **Presentation Type:** Poster

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**A SYSTEMATIC SCREEN OF THE HAPLOIDS OF YEAST DELETION COLLECTION FOR UNKNOWN MUTAGENESIS-RELATED GENES**

**Purpose:** In our life, UV and other chemicals around us can damage the genetic material---DNA and lead to cancer in our body. So far, lots of genes are known to be related to DNA mutation or repair, but it is far from enough. Yeast is an ideal model to the eucaryotic cells. We do a systematic screen of the haploids of yeast deletion collection for unknown mutagenesis-related genes
**Methods:** Use the toxic arginine analog canavanine to inhibit the growth of the drop-out strains and expose these strains to UV or other DNA-damaging agents such as 4-NQO to induce DNA damage, then observe the mutation rate of each strain by analyzing the canavanine resistance colony number in each strain.
**Results:** We get a list of genes selected from this systematic screen and classify them into several groups in which functions of some of the genes are known such as REV3 which can be trancribed and translated into a protein which is subunit of DNA polymerase zeta and is involved in DNA repair; required for mutagenesis induced by DNA damage, some are unknown, some are uncharacterized so far.
**Conclusions:** After this screen, we can get a list of genes whose functions are unknown ao far and may correlate to the mutagenesis of DNA directly or indirectly, we hope to go further from there and get more details about the cancer-forming mechanism.
**Sponsor:** *NIH*

213 **Presentation Type:** Poster

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**INFLUENCE OF PROMPT VERSUS DELAYED TREATMENT ON SURVIVAL IN PATIENTS WITH NON-SMALL CELL LUNG CANCER**

**Purpose:** The literature suggests that the relation of the time from diagnosis to initiation of definitive treatment and survival in lung cancer is uncertain. It is believed that timely management of non-small lung cancer (NSCLC) can influence prognosis and survival. This study was undertaken to examine if a delay in starting definitive NSCLC treatment affects survival rate, after factoring out the effects of other variables such as age, sex, insurance, treating physicians, performance status, therapy, and enrollment of patients in clinical trials.
**Methods:** Between 2001 and 2002, 250 patients were diagnosed and treated for NSCLC at a multisite community oncology practice in North Texas. Additional clinical and demographic data were extracted from the medical records. A delay in initiating definitive treatment was arbitrarily established as greater than 28 days from the date of diagnosis. The effects of delay and other factors on survival were analyzed by the Kaplin_Meier Method. Multivariate analysis was performed with Cox's proportion hazards.
**Results:** Early treatment significantly altered the survival rate of patients in advanced stages (IIIB and IV) of NSCLC. The median survival time for the patients who received timely treatment was 410 days and for the patients whose treatment was delayed was 178 days. The other factors that could be associated with the survival rate include treating physicians
($p = 0.045$), performance status ($p=0.002$), therapy ($p=0.0001$), gender ($p=0.02$) and enrollment in clinical trials (0.041). Age and insurance did not appear to influence the survival outcomes. Among patients in early stages of NSCLC, only treating physicians and enrollment of patients in clinical trials significantly influenced the survival rate.

**Conclusions:** Having a delay from the date of diagnosis to the time of starting a definitive treatment for advanced stages (IIIB/IV) of NSCLC significantly worsened overall survival. This was not observed in early stages of lung cancer. Good performance status, treating physicians, therapy, and enrollment in clinical trials were also associated with a favorable survival rate. This could be secondary to newer innovative therapies or better performance status of patients eligible for clinical trials.
**Sponsor:** *None*

215 **Presentation Type:** Poster

**Author:** Tiffany Sanderson **Presentor:** Tiffany Sanderson
**Department:** PHYSICIAN ASSISTANT STUDIES (PA Program)
**Classification:** TCOM MPAS Student
*Tiffany A. Sanderson, PA-S; Olive Chen PhD; Laurie Hill, PA-C; Univeristy of North Texas Health and Science Center, Fort Worth, Texas 76107-2699*

**THE PUBLIC AWARENESS REGARDING MALE BREAST CANCER**

**Purpose:** The purpose of this research was to investigate the level of public awareness regarding male breast cancer.
**Methods:** This study used survey and convenience sampling methods to collect data. The included participants were English speaking individuals 18 years of age and older. The survey consists of 10 questions which assessed awareness of male breast cancer, the diagnostic testing utilized and the disease clinical presentation. The survey was distributed during June, July and August 2004 at three different locations in Texas. On completion of the survey, participants were given an educational pamphlet containing statistics, risk factors, signs/symptoms, detection and prevention of male breast cancer. SPSS version 11.5 was utilized to perform Chi-square for the statistical analysis.
**Results:** A total of 355 surveys were distributed and completed. The results showed that 316(89.0%) participants expressed an awareness of male breast cancer. Nearly half of the participants, 164(46.3%), reported awareness of mammography's diagnostic role in male breast cancer. While less than a quarter of the participants (23.2%), acknowledged an awareness of the associated signs and symptoms of male breast cancer. The 3 key questions were also compared by gender, age, ethnicity and educational level. Female participants had a better understanding compared to the male participants regarding the first 2 questions ($X2=4.63$, $X2=10.64$; $p<0.05$). Participants 46 years of age and older were more knowledgeable than participants 18-45 years of age on all 3 questions ($X2=15.69$, $X2=17.32$, $X2=6.039$; all $p<0.001$). There were no statistical significance noted among the different ethnicities on the 2 questions regarding male mammography as well as the disease signs and symptoms. There were no statistical significant differences noted among the different educational levels on all 3 key questions (all $p>0.05$). The most common informational source of male breast cancer was media (56.3%).
**Conclusions:** The study results showed that the public has a general awareness of male breast cancer; however, the results also indicated a superficial depth of understanding. Future public education specifically focused on the clinical signs and symptoms of male breast cancer is necessary. The goal of public education is to increase the depth of public understanding of this nondiscriminatory gender disease and to prevent patients from disregarding a potentially lethal disease.
**Sponsor:** *None*

# CARDIOVASCULAR

**300** **Presentation Type:** Poster

**Author:** Amanda McConnell **Presentor:** Amanda McConnell
**Department:** OCCTIC
**Classification:** OCCTIC Student/Resident
*Amanda McConnell*
*Ohio University of Osteopathic Medicine*

**THE EFFECTS OF CORTISOL AND BLOOD PRESSURE ON KENYAN ELDERS**

**Purpose:** The serum concentration of corticosteroids has been shown to affect blood pressure. Previous studies have shown that aging, as well as disease states, tends to cause increases in glucocorticoid concentrations. In general, an increase in serum cortisol positively correlates with an increase in blood pressure. Although it is apparent that large increases or decreases of cortisol affects blood pressure, there is little data comparing the effects of small fluctuations of cortisol on blood pressure, especially among the geriatric population.

**Methods:** This project focuses on the effect of cortisol on blood pressure amongst the Kenyan Luo elder caregivers (CG) and non-caregivers. This project included 100 participants from the Nyanza Providence all of whom are over 60 years of age and are grandparents (half CG, half not). Saliva samples were collected from each participant three times a day (awakening, mid-morning and evening) on two separate occasions. Likewise, a series of three blood pressure measurements were collected in mid-morning with the patient sitting.

**Results:** The results from the cortisol measurements were compared to the participants' blood pressure and an inverse relationship was seen.

**Conclusions:** Although this result is unusual, an analogous pattern was recorded in a similar research study conducted on the same population last year. In future studies, it would be beneficial to collect blood pressure measurements congruently with the salvia sample collection in order to correlate specific cortisol levels with the individual's blood pressure at the time.

**Sponsor:** *None*

**301** **Presentation Type:** Poster

**Author:** Quinton Barnes **Presentor:** Quinton Barnes
**Department:** INTEGRATIVE PHYSIOLOGY
**Classification:** GSBS Student
*Quinton Barnes1, Shigehiko Ogoh1, James P. Fisher2, Ellen A. Dawson3, Michael J. White2, Niels H. Secher3, Peter B. Raven, FACSM1. 1University of North Texas Health Science Center, Fort Worth, TX. 2University of Birmingham, Birmingham, United Kingdom. 3Copenhagen Muscle Research Center, Copenhagen, Denmark. (Sponsor: Peter B. Raven, FACSM)*

**THE CONTRIBUTION OF THE SYMPATHETIC AND PARASYMPATHETIC SYSTEMS TO CARDIAL-ARTERIAL BAROREFLEX SENSITIVITY DURING DYNAMIC EXERCISE**

**Purpose:** The purpose of this study was to examine the effects of sympathetic and parasympathetic activity to the heart at rest and during exercise on the cardiac-arterial baroreflex sensitivity.

**Methods:** METHODS: Eight subjects performed 20 min bouts of exercise at a steady-state heart rate (HR) of 90 (EX90), 120 (EX120), and 150 (EX150) beats/min with and without metoprolol (0.2 mg/kg) or glycopyrrolate (0.04 mg/kg). Systolic blood pressure (SBP), mean arterial pressure (MAP) and pulse interval (RRI) were continuously measured. Arterial baroreflex sensitivity (BRS) was evaluated by analyzing the slopes of spontaneously occurring sequences of three or more consecutive beats in which systolic blood pressure and pulse interval of the following beat either increased or decreased, in the same direction, in a linear fashion.

**Results:** RESULTS: ?-1 adrenagic blockade decreased ($P<0.05$) and vagal cardiac blockade increased HR ($P<0.05$) at rest and during the three exercise workloads. Without blockade, BRS gradually decreased with increasing exercise workload. While there was no significant difference in BRS with and without ?-1 adrenagic blockade at rest and during exercise, vagal cardiac blockade decreased BRS from $26.0 \pm 4.8$ to $3.2 \pm 0.4$ ms/mmHg at rest ($P<0.05$). However, during EX150 there was no difference in BRS with and without cardiac vagal blockade ($1.8 \pm 0.4$ vs. $1.4 \pm 0.3$ ms/mmHg, $P>0.05$).

**Conclusions:** CONCLUSION: This finding suggests that during exercise the reduction of cardiac-arterial baroreflex sensitivity occurs by vagal withdrawal and this reduction is not influenced by the exercise induced increase in sympathetic activity.

**Sponsor:** *NIH*

**302** **Presentation Type:** Poster

**Author:** Marty Knott **Presentor:** Marty Knott
**Department:** INTEGRATIVE PHYSIOLOGY
**Classification:** Dual Degree Student DO/PhD
*E. Marty Knott, BA*, Myoung-Gwi Ryou, MS*, Jie Sun, BS*, Abraham Heymann*, Arti B. Sharma, MBBS*, Yu Lei*, Mirza Baig,RPh, PharmD†, Robert T. Mallet, PhD*, Albert H. O-Yurvati, DO‡*

*Departments of Integrative Physiology* and Surgery†, University of North Texas Health Science Center 3500 Camp Bowie Blvd. Fort Worth, TX 76107-2699*

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**PYRUVATE CARDIOPLEGIA SUPPRESSES OXIDATIVE STRESS AND BOLSTERS PHOSPHORYLATION POTENTIAL OF CARDIOPLEGICALLY ARRESTED MYOCARDIUM**

**Purpose:** Cardioplegic arrest for bypass surgery imposes global ischemia on the myocardium which has been shown to generate oxyradicals and deplete myocardial energy reserves. The glycolytic metabolite pyruvate, but not its reduced congener lactate, increases energy reserves and lessens oxyradical burden in ischemic and post-ischemic myocardium. Hypothesis: Pyruvate, more substantially than lactate, ameliorates oxidative stress associated with cardioplegic arrest and preserves myocardial energy state.

**Methods:** : In situ swine hearts were arrested with a 4:1 mixture of blood and crystalloid cardioplegia solution containing 188 mM glucose alone (control) or with additional 23.8 mM lactate or 23.8 mM pyruvate. 8-Isoprostane, an indicator of oxidative stress, was measured in coronary sinus plasma before (baseline: BL), at 20 min intervals during, and at 1 and 3 min after cardioplegic arrest. Glutathione (GSH), glutathione disulfide (GSSG), and energy metabolites (phosphocreatine (PCr), creatine (Cr), inorganic phosphate (Pi)) were measured in myocardium snap frozen at 45 min arrest and 3 min reperfusion to determine antioxidant GSH redox state (GSH/GSSG) and phosphocreatine phosphorylation potential ([PCr]/([Cr][Pi])).

**Results:** Pyruvate minimized 8-isoprostane release during arrest (means ± SEM, % baseline: pyruvate: 188 ± 29; lactate: 348 ± 71; control: 302 ± 26). Lactate and pyruvate cardioplegia reduced 8-isoprostane vs control following reperfusion (% baseline: pyruvate: 279 ± 66; lactate: 282 ± 57; control: 636 +118; $P < 0.05$). GSH/GSSG was preserved during arrest but fell in all groups following reperfusion. Phosphorylation potential was maintained during arrest; at 3 min reperfusion pyruvate cardioplegia doubled myocardial [PCr]/([Cr][Pi]) vs. control and lactate cardioplegia (M-1; pyruvate: 275 ± 38; control: 148 ± 32; lactate: 116 ± 16; $P < 0.05$).

**Conclusions:** Pyruvate cardioplegia mitigates oxidative stress during cardioplegic arrest and increases myocardial energy state upon reperfusion.

**Sponsor:** *Osteopathic Heritage Foundation*

**303** **Presentation Type:** Poster

**Author:** Michael Clearfield **Presentor:** Michael Clearfield
**Department:** INTERNAL MEDICINE
**Classification:** Faculty (Not for Competition)
*Michael Clearfield, D.O., Craig Spellman, Ph.D., D.O., Paul Garcia, D.O., Adam Smith, D.O., Karan Singh, Ph.D. and Walter McConathy, Ph.D.*
*University of North Texas Health Science Center at Fort Worth, Fort Worth, Texas, 76107*

**TRADITIONAL AND EMERGING RISK FACTORS FOR INDIVIDUALS DEVELOPING DIABETES, METABOLIC SYNDROME, AND CORONARY HEART DISEASE.**

**Purpose:** The goal of this project is to determine the prevalence of traditional and emerging coronary heart disease (CHD) risk factors for individuals developing diabetes, metabolic syndrome and CHD as part of the Diabetes, Research, Education and Metabolic Studies (DREAMS) Center. Our study objective is to examine the frequency of these emerging risk factors (ERF) in those at risk for developing CHD, and in individuals with CHD who fell out of the conventional treatment guidelines.

**Methods:** To explore the role of emerging risk factors in CHD, we plan to study one group with established CHD at their stated National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) goals and four groups of subjects free of evidence of cardiovascular disease who are at ATP III goals (each group consists of 80 subjects: Hispanic diabetic/metabolic syndrome, non Hispanic diabetic/metabolic syndrome (MS), controls, and bariatric surgery participants). ERF to be assessed include: LDL and HDL particle size; apolipoproteins B and A-I; lipoprotein (a) ; hsCRP; homocysteine ; PAI-1; phytosterol levels; myeloperoxidase; resistin, IL-6, leptin; lipoprotein associated phospholipase A2 (LP-PLA2). The electron beam computed tomography (EBCT) for coronary calcium quantification will be used as an assessment of CHD risk.

**Results:** Primary expectation is ERF will identify the majority of individuals at risk for CHD (via EBCT), who are currently at their stated LDL-C level by ATP III guidelines. Secondary expectations include: Identify subjects requiring intervention to reduce CHD risk; Hispanic vs Caucasian MS patients will have a different pattern of ERF and distribution of calcification in the periphery; Hispanic vs Caucasian diabetic patients will also have a different pattern; weight loss due to bariatric surgery will alter the pattern of ERF and calcification; pattern of ERF between controls and those at risk will be different; and EBCT score will correlate with some ERF scores.

**Conclusions:** These studies should provide new knowledge regarding nontraditional CHD risk factors especially in ethnic minorities. If new markers for CHD risk are identified, this will assist in identifying individuals without currently recognized risk factors still experiencing CHD events. Identification of these factors will serve as a basis for the application of primary prevention strategies in populations previously not considered at risk relative to their LDL-C.

**Sponsor:** *CDC*

# CARDIOVASCULAR

**304** **Presentation Type:** Poster

**Author:** R Brothers **Presentor:** 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.*
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**METABOLIC INHIBITION OF PHENYLEPHERINE AND ANGIOTENSIN-II INDUCED VASOCONSTRICTION DURING LOW AND MILD EXERCISE WORKLOADS**

**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 ?g / kg) and Ang?? (4 ?g / 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 ?g / kg) and Ang?? (32.0 ?g / 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 ?g / kg) and Ang?? (32.0 ?g / 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.
Supported in part by Danish Grant Research Award and NIH grant HL 045547

**Sponsor:** *Danish Research Grant and NIH*

**305** **Presentation Type:** Poster

**Author:** Wendy Eubank **Presentor:** Wendy Eubank
**Department:** Select a Department
**Classification:** GSBS Student
*W.L. Eubank1, R.M. Brothers1, M.L. Haslund2, D.W. Wray1, M.L. Smith1, FACSM, P.B. Raven1, FACSM, M. Sander2, FACSM.*
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**METABOLIC INHIBITION OF PHENYLEPINEPHERINE AND TYRAMINE INDUCED VASOCONSTRICTION DURING LOW AND MILD EXERCISE WORKLOADS**

**Purpose:** In exercising human thigh muscle ?2-adrenergic vasoconstriction is very sensitive to metabolic inhibition. In contrast, exogenous ?1-vasoconstrictors produce some vasoconstriction in the exercising thigh. Whereas activation of ?1-receptors proximate to sympathetic boutons are thought to be involved, it is unknown whether ?1-receptors dislocated from the sympathetic boutons play a functionally significant role. PURPOSE: This study tested whether ?1-vasoconstriction observed in exercising thigh muscles could be partly related to activation of ?1-receptors distal from the sympathetic boutons.
**Methods:** We compared the dose-dependent vasoconstriction induced by intraarterial phenylephrine (PE, selective ?1 agonist) and tyramine (TYR, indirect sympathomimetic releasing endogenous norepinephrine, NE) in 8 healthy subjects at rest and during dynamic knee-extensor exercise at 7 and 27W. Ultrasound Doppler and thermodilution provided direct measurements of femoral blood flow (FBF) and intra-arterial pressures were used to calculate vascular conductance (FVC). All values are responses taken from the plateau of the dose-response-curves (i.e. maximal responses).
**Results:** : At rest, PE (0.2 ?g ? kg ?1) and TYR (8 ?g ? kg ?1) reduced FBF and FVC similarly (dFVC -49 ± 4 and -52 ± 8 %, respectively). Vasoconstriction elicited by higher doses of PE (1.6 ?g ? kg ?1) was reduced during exercise at 7W (-28 ± 5 % FBF, -37 ± 7 % FVC) and further attenuated at 27W (-17 ± 5% FBF, -31 ± 3% FVC). Vasoconstriction by higher doses of TYR (64 ?g ? kg ?1) was reduced even more at 7W (-17 ± 6 % FBF, -16 ± 7 % FVC), and 27W (-11 ± 3 % FBF, -11 ± 4 % FVC).
**Conclusions:** There are two new findings in this study: 1) The dose-response to TYR shows that this indirect sympathomimetic is markedly inhibited in the exercising human thigh. However, the response to the larger doses does cause a small, but significant decrease in FBF and FVC. 2) The inhibition of PE induced vasoconstriction was reduced when compared to inhibition of TYR. This provides the first indication in intact humans that "scattered" alpha-receptors may still activate functionally intact signal transduction pathways and cause vasoconstriction.

**Sponsor:** *Danish research grant and NIH*

**306** **Presentation Type:** Poster

**Author:** Disha Dumka **Presentor:** Disha Dumka
**Department:** MOLECULAR BIOLOGY & IMMUNOLOGY
**Classification:** GSBS Student
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*1University of North Texas HSC, Fort Worth, TX 76107 & 2University of Miami School of Medicine, Miami, FL 33136*

**MUTATIONS IN THE REGULATORY LIGHT CHAIN ALTER THE MYOSIN CROSS-BRIDGE CYCLING IN FAMILIAL HYPERTROPHIC CARDIOMYOPATHY MUSCLE FIBER**

**Purpose:** Familial hypertrophic cardiomyopathy (FHC) is an autosomal dominant disease characterized by left ventricular and/or septal hypertrophy, myofibrillar disarray and sudden cardiac death. Mutations have been found in some of the sarcomeric proteins, one of which is the ventricular isoform of myosin regulatory light chain (RLC). The E22K mutation located in the RLC Ca2+ binding site was shown to cause septal hypertrophy in humans with a benign phenotype. In this study, we measured rotational motion of the lever-arm domain of myosin – the part that is believed to rotate upon hydrolysis of ATP to cause muscle contraction.
**Methods:** Recombinant essential light chains (ELC) of myosin were labeled with red fluorescent probe and exchanged with native ELC in cardiac myofibrils from transgenic (Tg) mice overexpressing the E22K mutation of RLC. Thus the lever arm of myosin contained both the RLC with hypertrophy-causing mutation and the fluorescent ELC. A modified confocal microscope was used to observe orientation (anisotropy) of lever-arms of a small population of myosin molecules (~400) in vivo. The cross-bridges were activated by a precise delivery of ATP from a caged precursor.
**Results:** Our results indicate that on release of ATP from the cage anisoTropy drops rapidly, indicating dissociation of cross bridges from the filaments. The rate of this change was too rapid to be measured. Following dissociation, cross-bridges rebind to thin filaments as indicated by the slow exponential rise. Following rapid change anisotropy recovered slowly. Our preliminary results indicate that the rate of recovery for E22K-RLC mutant was slowest, although it was statistically insignificant. (to DSC).
**Conclusions:** These results suggest that the mutation in RLC situated in the C-terminus of the myosin lever arm does not significantly interfere with rotation of its N-terminal region as monitored by labeled ELC.
**Sponsor:** *Supported by NIH grants R01 R21CA9732 and R01AR048622 (to JB) and AHA0355384 and NIH-HL071778*

**307** **Presentation Type:** Poster

**Author:** Robert Mallet **Presentor:** Robert Mallet
**Department:** INTEGRATIVE PHYSIOLOGY
**Classification:** Faculty (Not for Competition)
*Robert T. Mallet, Pu Zong, Wei Sun, Myoung-Gwi Ryou, E. Marty Knott, Linda Howard, Arthur G. Williams Jr., H. Fred Downey*
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**BETA-ADRENERGIC RECEPTOR BLOCKADE DURING INTERMITTENT HYPOXIA ABROGATES HYPOXIA-INDUCED CARDIOPROTECTION**

**Purpose:** Background: Intermittent, normobaric hypoxia conditioning (IHC) strikingly ameliorates myocardial infarction and minimizes the incidence of lethal ventricular arrhythmias, 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. Purpose: To determine whether beta-1-adrenergic blockade would abrogate IHC-induced cardioprotection.
**Methods:** Mongrel dogs were conditioned by a 20 day program of 5-8 cycles (5-10 min) of normobaric hypoxia (FIO2 9.5-10%), with intervening 4 min periods of normoxia, or sham conditioned with room air (FIO2 20.5-21%). To interrogate the role of beta-1 adrenoceptor-activated mechanisms in IHC cardioprotection, beta-1-adrenergic receptors were blocked with metoprolol throughout the IHC program. 24 h after the last IHC session, the left anterior descending coronary artery (LAD) was occluded with a snare for 60 min, then the LAD was reperfused for 5 h by releasing the snare. Ventricular arrhythmias were monitored by electrocardiography. Area at risk (AAR) was demarcated by Evans blue dye; infarct size (IS) was determined by 2,3,5-triphenyl tetrazolium staining. Collateral blood flow (CBF) to the central ischemic region was measured with radioactive microspheres.
**Results:** Table: means +/- SEM. LV: left ventricular mass. VT, VF: incidences of ventricular tachycardia and fibrillation. *P < 0.05 v sham; †P < 0.05 v IHC. Results: IHC prevented infarction and ventricular arrhythmias. Metoprolol abrogated this IHC-induced protection, but did not exacerbate injury in sham-conditioned hearts.

| Group | *n* | IS/AAR | AAR/LV | CBF | VT | VF |
|---|---|---|---|---|---|---|
| | | % | % | ml/min/g | | |
| Sham | 6 | 37 ± 6 | 27 ± 3 | 0.05 ± 0.01 | 3 | 2 |
| Sham + metoprolol | 4 | 37 ± 1 | 29 ± 4 | 0.04 ± 0.02 | 4 | 0 |
| IHC | 6 | 0.5 ± 0.3* | 32 ± 3 | 0.08 ± 0.02 | 0 | 0 |
| IHC + metoprolol | 4 | 28 ± 3† | 27 ± 3 | 0.05 ± 0.02 | 3 | 1 |

**Conclusions:** Conclusion: Beta-1-adrenergic activation during IHC is required for IHC-induced prevention of myocardial infarction and ventricular arrhythmias. NIH support: HL-64785, HL-76184
**Sponsor:** *NIH-NHLBI*

# CARDIOVASCULAR

308 **Presentation Type:** Poster

**Author:** woineshet Zenebe **Presentor:** Woineshet Zenebe
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**Classification:** Postdoctoral Fellow/Resident (Not for Competition)
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*University of North Texas Health Science Center, Fort Worth, TX 76107*

**ENDOTHELIUM DEPENDENT VASCULAR REACTIVITY IN DIET-INDUCED OBESE EXERCISE-TRAINED RABBITS**

**Purpose:** To determine whether endothelium-derived relaxing factor (NO) plays a major role in the maintenance of vascular tone in lean and obese exercise trained rabbits.

**Methods:** Rabbits were assigned to lean control (LC), lean exercise-trained (LX,), obese control (OC) and obese exercise trained (OX) groups. Isometric tension of isolated arterial rings was recorded after preconstriction with phenylephrine (PHE), followed by relaxation to acetylcholine (ACh, 10-10-10-4 M), ACh + NO synthase inhibitor NG-nitro-L-arginine methyl ester (L-NAME, 10-5 M). For ACh, data were analyzed using four-parameter nonlinear regression and compared using one-way ANOVA. ACh+L-NAME data were compared using two-way repeated measures MANOVA.
**Results:** Responses to ACh were not significantly different between LC and LX or between OC and OX. Responses to ACh after L-NAME administration did not differ between OX and OC in femoral arteries and aortae. However, L-NAME blockade of ACh-induced relaxation was attenuated in renal arteries of OX compared to OC ($p=0.05$; relaxation at 10-5M was 66.8±9.5% and 47.7±7.8%, respectively). In lean rabbits, L-NAME blockade of ACh-induced relaxation was attenuated in both femoral and renal arteries from LX compared to LC ($p=0.05$; relaxation at 10-5 M was 24.8±3.9% vs 0.2±4.8% in femoral arteries, and 68.5±5.2% vs 6.5±9.3% in renal arteries, respectively).
**Conclusions:** These results suggest that exercise training impacts endothelial function differently in lean and obese rabbits. The data further suggest that NO-independent mechanisms may play a more important role for ACh-induced relaxation of renal arteries in obese trained rabbits, and in renal and femoral arteries of lean trained rabbits.
"Supported by NIH Grant R01 HL64913"

**Sponsor:** *Supported by NIH Grant R01 HL64913*

309 **Presentation Type:** Poster

**Author:** Shekhar Deo **Presentor:** Shekhar Deo
**Department:** INTEGRATIVE PHYSIOLOGY
**Classification:** GSBS Student
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*Department of Integrative Physiology & Cardiovascular Research Institute, University of North Texas Health Science Center, Fort Worth, TX 76107, USA*

**REPEATED ARTERIAL OCCLUSIONS IMPROVE VAGAL TRANSMISSION IN THE SINOATRIAL NODE WITHOUT ELIMINATING THE VAGOLYTIC RESPONSE TO OPIOIDS**

**Purpose:** Higher doses of met-enkephalin-arg-phe (MEAP) acting on delta-2-opioid receptors (OR) interrupt vagal transmission (vagolytic). Ultra-low doses of MEAP improve vagal transmission (vagotonic) via delta-1-OR within the SA node. Repeated occlusion (preconditioning) of the SA node artery produced a similar vagotonic response that was reversed by the delta-1-antagonist, BNTX. A protocol was designed to test whether the vagotonic effect develops gradually and whether preconditioning improves vagal transmission directly or unmasks a more efficient vagal transmission by abolishing opposing vagolytic effects.
**Methods:** Mongrel dogs were anesthetized, intubated and right thoracotomies performed. A microdialysis probe was introduced in to the substance of the SA node to facilitate direct nodal infusion of various agents. The SA node artery was briefly occluded and released. Vagally-mediated bradycardia was tested at intervals.
**Results:** The data obtained thus far suggests that vagal transmission improves gradually during subsequent occlusions. When MEAP was added into the SA node by microdialysis during occlusion, its vagolytic effects were easily demonstrated.

**Conclusions:** These observations suggest that the vagotonic result observed during arterial occlusion requires preconditioning for expression. Furthermore, the vagotonic effect is not the result of abolishing competing vagolytic effects though it may reflect a decrease in their potency.
**Sponsor:** *Texas ARP program and AHA Texas Affiliate*

310 **Presentation Type:** Poster

**Author:** Dongdong Zhou **Presentor:** Dongdong Zhou
**Department:** INTEGRATIVE PHYSIOLOGY
**Classification:** GSBS Student
*Dongdong Zhou, Rebecca Deaton, Chang Su, Joel Ellis, Tom Valencia and Stephen R. Grant Molecular Genetics, Cardiovascular Research Institute, University of North Texas Health Science Center at Fort Worth, 3500 Camp Bowie Boulevard, Fort Worth, Texas, 76107*

**ANALYSIS OF THE ROLES OF PKN AND RHO IN SMOOTH MUSCLE CELL PROLIFERATION AND DIFFERENTIATION: AN INDUCIBLE TRANSGENIC MOUSE MODEL**

**Purpose:** A novel serine/threonine protein kinase, designated PKN, has a catalytic domain homologous to the PKC family and unique amino-terminal sequences. PKN plays a significant role in the control of mitotic timing by inhibition of Cdc25C and functions as a cell-cycle regulator. Rho, a small GTP-binding protein, binds to PKN in a GTP-dependent fashion leading to the activation of PKN. Rho regulates actin-based cytoskeletal structures, including focal adhesions, stress fibers, the contractile ring, and also works as a switch in stimulus-evoked cell adhesion and cytokinesis. In this study, we seek to identify in vivo functions of PKN and Rho GTPAse in smooth muscle cells.
**Methods:** We will utilize the benefits of an optimized tet-off system and a specific smooth muscle gene (SM22) promoter to generate a smooth muscle-specific, doxycycline (Dox) controlled over-expression system in transgenic mice. A DNA construct will be generated in which the codon optimized reverse tetracycline transactivator (rtTA) is placed under control of a smooth muscle-specific SM22 promoter. Transgenic mice containing this construct will expresse rtTA exclusively in smooth muscle cells. These mice will be crossed to a second transgenic line containing a bi-directional promoter centered on a tet responsive element driving either tagged PKN gene or tagged Rho gene. Dox dependent smooth muscle-specific induction of the tagged PKN and Rho proteins will be demonstrated by western blot and immunocytochemical analysis.
**Results:** We hypothesize that the generation of this inducible transgenic mouse model will provide a tightly regulated over expression system in adult smooth muscle. This will allow us to study the function of PKN and Rho GTPase in regulation of smooth muscle cell proliferation and differentiation.
**Conclusions:** The application of this type of system will proven invaluable to giving insights into the function and regulation of PKN and Rho under physiological and pathological conditions.
**Sponsor:** *Stephen R. Grant*

311 **Presentation Type:** Poster

**Author:** Shavsha Davis **Presentor:** Shavsha Davis
**Department:** GRADUATE SCHOOL OF BIOMEDICAL SCIENCES
**Classification:** GSBS Student
*Shavsha Davis, Shekhar Deo, Matthew Barlow, Darice Yoshishige, and James L. Caffrey Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, Texas 76107*
**DELTA-2 RECEPTOR PLASTICITY AND GM-1**

**Purpose:** Methionine-enkephalin-arginine-phenylalanine (MEAP) alters vagally induced bradycardia when introduced into the sinoatrial (SA) node by microdialysis. The responses to MEAP are bimodal in character with lower doses (10-15 moles/min) enhancing bradycardia (vagotonic) while higher doses (10-12 moles/min) suppress bradycardia (vagolytic). The two opposing effects appear to be mediated by subtypes, delta-1 and delta-2 respectively, of the same delta opioid receptor. Each of the responses is blocked by sub-type a specific antagonist. Chronic delta- receptor stimulation appears to reduce delta-2 receptor responses by increasing the monosialosyl ganglioside, GM-1. This study tested the hypothesis that adding GM-1 into the SA node reduces delta-2 opioid receptor responses.

**Methods:** Deltorphin was introduced into the SA node by microdialysis at a dose of 0.7 nmol/min. The right vagus nerve was stimulated and deltorphin was administered to evaluate the delta-2-mediated vagolytic response.

**Results:** GM-1 was then perfused for one hour without any apparent effect on baseline vagal transmission. Following GM-1, deltorphin was reintroduced and a clear attrition of the previous vagolytic response was observed. The delta-1 selective antagonist 7-benzylidenaltrexone (BNTX) added afterward failed to restore the delta-2 mediated vagolytic response. Deltorphin produces a similar attrition in the delta-2 response which was blocked by pretreatment with BNTX.

**Conclusions:** These data suggests that deltorphin combined with GM-1 suppressed the delta-2 opioid receptor response per se and that the loss in delta-2 activity was not the consequence of a coincident increase in delta-1 mediated vagotonic activity. It would also appear that deltorphin may have intrinsic delta-1 activity. Alternatively, deltorphin may provoke the release of or facilitate the activity of an endogenous delta-1 agonist.

**Sponsor:** *none*

# CARDIOVASCULAR

312 **Presentation Type:** Oral

**Author:** Arti Sharma **Presentor:** Arti Sharma
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**Classification:** GSBS Student
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**ANTIOXIDANT PRETREATMENT PROTECTS MYOCARDIAL ENZYMES DURING CARDIAC ARREST**

**Purpose:** Cardiac arrest elicits oxidative stress that may inactivate myocardial enzymes and, thus, compromise post-arrest recovery of cardiac metabolism and function. This study tested whether antioxidant therapy prevents inactivation of the key metabolic enzymes creatine kinase (CK), phosphofructokinase (PFK) and glucose 6-phosphate dehydrogenase (G6PDH) in arrested myocardium of open-chest beagles

**Methods:** Pharmacological (N-acetylcysteine: NAC) or metabolic (pyruvate) antioxidants were infused iv to respective arterial plasma concentrations of 0.44 ± 0.05 mM and 4.1 ± 0.5 mM for 30 min before cardiac arrest. Left ventricular myocardium was sampled at 5 min arrest for measurement of glutathione redox state (GSH/GSSG) and enzyme activities (U/mg protein). Table: means ± SEM, n = 6-7; *P < 0.05 v pre-arrest; †P < 0.05 v untreated arrest.

**Results:**

| | GSH/GSSG | CK | PFK | G6PDH |
|---|---|---|---|---|
| **Prearrest** | 14.9 ± 1.7 | 40 ± 5.2 | 0.66 ± 0.13 | 0.0075 ± 0.0014 |
| **Untreated** | 9.3 ± 0.9* | 25 ± 1.3* | 0.37 ± 0.04* | 0.0030 ± 0.0005* |
| **NAC** | 14.5 ± 0.8† | 57 ± 3.1*† | 0.66 ± 0.09† | 0.0066 ± 0.0003† |
| **Pyruvate** | 15.9 ± 1.0† | 44 ± 2.5† | 0.95 ± 0.09*† | 0.0048 ± 0.0008 |

GSH/GSSG and CK, PFK and G6PDH activities fell during arrest. Pretreatment with N-acetylcysteine or pyruvate prevented GSH oxidation and protected CK, PFK and G6PDH during arrest.

**Conclusions:** Cardiac arrest depletes myocardial glutathione redox state and inactivates key enzymes. Intravenous antioxidant therapy can mitigate these metabolic impairments, thereby implicating oxidative stress as mediator of enzyme inactivation in arrested myocardium.

**Sponsor:** *NIH support: HL 71684*

313 **Presentation Type:** Poster

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**Classification:** Postdoctoral Fellow/Resident
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**ENHANCED CARDIAC RESPONSE TO LOWER BODY NEGATIVE PRESSURE (LBNP) IN PHYISCALLY FIT ELDER**

**Purpose:** The study aimed at testing the hypothesis that physically active life style would alleviate the age-related diminution of cardiac response in elderly.

**Methods:** Twelve sedentary healthy (Sed, 65±2 yr., 85±5 kg, 1.67±.02 m, 20.8±1.0 ml kg-1 min-1) and 12 high-fit seniors (Fit, 68±6 yr., 73±4 kg, 1.70±.03 m, 31.2±7.3 ml kg-1 min-1) were voluntarily exposed to graded LBNP up to -50 Torr, which was approved by IRB of UNTHSC.

**Results:** At rest heart rate (HR, electrocardiograph) was lower while stroke volume (SV, thoracic impedance) was greater in Fit than Sed (Fit vs. Sed: 50±2 vs. 68±3 bpm, 53.8±3.5 vs. 39.9±4.2 ml). However, neither cardiac output (Q, 2.66±0.11 vs. 2.68±0.29 L/min) nor arterial blood pressure (ABP, using Tonimetry, 122±6/71±4 vs. 132±6/73±7 mmHg) was statistically different between the groups. LBNP significantly decreased SV and Q, which activated a tachycardiac response in both groups. This cardiac response appeared to be more significantly augmented in Fit than Sed (+25±4 vs. +12±5% or +12±2 vs. +7±3 bpm). As a result of this tachycardiac compensation, in terms of unit decrease in SV, decrease in Q was less affected (P<0.01) by LBNP (slope of Q/SV in Fit vs. Sed: 0.57±0.03 vs. 0.79±0.03).

**Conclusions:** We concluded that the reflex cardiac compensation was significantly enhanced in Fit, which improved the cardiovascular stability under orthostatic stress.

**Sponsor:** *NIH HL65613*

314 **Presentation Type:** Poster

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**Classification:** Staff (Not for Competition)
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**ACTIVE LIFESTILE IMPROVES CAROTID-HEART RATE REFLEX FUNCTION IN ELDERLY MEN.**

**Purpose:** There is scant data regarding the effect of physical fitness on arterial baroreflex function in elderly adults. The study sought to test the hypothesis that active lifestyle could alleviate an age-related diminution of carotid baroreflex (CBR) function.

**Methods:** Seven healthy sedentary men(SED: 66.0±1.6 yr, 86.0±7.7kg, 173±3cm, 25.5±1.3ml/min/kg, 63±4bpm, 130±6/72±5mmHg)and seven physically-active elderly men (ACT: 68.6±1.4 yr,78.9±3.6kg, 176±2cm, 34.9±3.6ml/min/kg, 57±4bpm, 117±4/59±7mmHg)gave written consent to participate in the study approved by IRB. Physical fitness level was determined by peak O2 consumption (VO2peak) tested on a stationary bicycle. CBR function was assessed using 5-sec neck suction (NS: -80, -60, -40 and -20 Torr) and pressure (+20 and +40 Torr) randomly delivered through a custom-made flexible collar that encompassed the anterior two-thirds of the subject's neck at rest and during lower body negative pressure (LBNP) -15 and -40 Torr. During the test heart rate (HR) and arterial blood pressure (ABP) were continuously monitored by electrocardiogram and tonometry (Colin). Carotid sinus pressure (CSP) was estimated from the difference between mean ABP (MAP) and neck collar pressure (NCP) delivered. CBR-HR and CBR-MAP gains (G) were calculated from the ratio of the changes in HR and MAP to CSP, respectively.

**Results:** Both GCBR-HR and GCBR-MAP peaked around NS -20 Torr in both groups. GCBR-HR was significantly greater in ACT than SED (-0.31±0.09 vs -0.19±0.03 bpm/mmHg) while GCBR-MAP was not different between the groups (-0.30±0.08 vs -0.26±0.06 mmHg/mmHg) across all LBNP levels. LBNP -40 Torr significantly decreased pulse pressure (-7.4±2.9 mmHg) in SED, not in ACT group (-4.2±1.8 mmHg). On the other hand, Tachycardiac response at -40 Torr LBNP was only significant in ACT (+5.8±1.6 bpm), not SED (2.3±2.1 bpm) group.

**Conclusions:** Our data indicate that active lifestyle improves CBR-HR reflex function in elderly and helps prevent cardiac events associated with aging.

**Sponsor:** *NIH HL65613*

315 **Presentation Type:** Poster

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**VAGOTONIC EFFECTS OF ENKEPHALIN ARE NOT MEDIATED BY SYMPATHOLYTIC MECHANISMS**

**Purpose:** This study examined the hypothesis that the vagotonic and sympatholytic effects of cardiac enkephalins are independently mediated by different opioid receptors.

**Methods:** In study one, the heart rate response to increasing doses of the ?-receptor opioid, MEAP was determined during autonomic nerve stimulation. MEAP was administered by microdialysis into the interstitium of the canine sinoatrial node during sympathetic (right ansa subclavia) and parasympathetic (right cervical vagus) stimulation. Dose response relationships were constructed by recording the change in heart rate during nerve stimulation as the dose of MEAP was increased in 5-min steps from 0.05 pmoles/min to 1500 pmoles/min. In study two, a similar dose response relationship was constructed with the kappa-opioid receptor agonist, U-50488H to illustrate an independent sympatholytic effect and to verify its kappa-receptor character. Study three was conducted to determine whether the sympatholytic effect to U-50488H could be prevented by co-administration of the kappa-antagonist norBNI.

**Results:** In study one a significant increase in vagal transmission was observed during the administration of the delta-agonist, MEAP at 0.5 pmoles/min as evident by a greater decline in heart rate. The sympathetically mediated tachycardia was unaltered at this or any other dose of MEAP. In study two, U-50488H gradually suppressed the sympathetic tachycardia with a significant effect obtained at the highest dose (1500 pmoles/min). The sympatholytic effect was not reversed by norBNI when added afterward. U-50488H had no effect on vagally mediated decreases in heart rate. In study three, norBNI blocked the sympatholytic effect of the U-50488H throughout 90 min of exposure. When norBNI was discontinued after 90 min and U-50488H was continued alone, its sympatholytic effect reappeared within 30 min.

**Conclusions:** Collectively these observations support the hypothesis that the vagotonic influence of MEAP was independent of sympathetic transmission and sympathetic transmission was unaltered by MEAP. Furthermore the observed sympatholytic effect of U-50488H was mediated independently by kappa-receptors. The sympatholytic effect of sustained kappa-receptor stimulation appears to evolve gradually into a functional state not easily reversed.

**Sponsor:** *AHA*

# CARDIOVASCULAR

316 **Presentation Type:** Poster

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**14-3-3 DIMERIZATION IS A NOVEL REGULATORY POINT FOR THE PROGRESSION CARDIAC HYPERTROPHY**

**Purpose:** The myocyte enhancer factor-2 (MEF2) family of transcription factors regulates transcription of muscle-dependent genes in skeletal, smooth and cardiac muscle types. MEF2 is activated by calcium/calmodulin (CaM)-dependent protein kinases I and IV and silenced by CaM kinase II delta C. MEF2 is held inactive in the nucleus by the class II histone deacetylaces (HDAC4 & 5) until phosphorylated by either CaM kinase I or IV. This phosphorylation results in HDAC transport out of the nucleus via a 14-3-3-dependent mechanism thereby freeing MEF2 to drive transcription. 14-3-3 proteins exists as homodimers, which are modulated by the phosphorylation of serines 60 and 65 in the dimerization region. We propose that 14-3-3 dimerization is a key regulatory point in the cell signaling of cardiac hypertrophy and represents a novel therapeutic taget in which we can reduce hypertrophy's adverse effects.
**Methods:** We are generating 14-3-3 peptide inhibitors that are designed to prevent the dimerizaton of 14-3-3 proteins. These peptides will be delivered by the HIV TAT protein transmembrane domain which will result in peptide entry into the cardiomyocytes without the aid of any additional chemical or porative processes.
**Results:** We generated conervative amino acid point mutations of 14-3-3 at serines 60 and 65 (S60/65D) which were changed to aspartates. In MEF2 enhancer/reporter assays in cardiomyocytes, expresstion of 14-3-3 S60/65D attenuated MEF2 enhancer activity driven by CaM kinase I or IV. A mammalian two-hybrid assay showed that the serine to aspartate mutation was unable to dimerize with the wild type 14-3-3 monomer. We show that it is possible to control the expression of 14-3-3 S60/65D in a tetracycline-dependent manner in primary cardiomyocytes.
**Conclusions:** These data suggest that the dimerizaztion of 14-3-3 is a key regulatory point in the signaling of cardiac hypertrophy, and privides a promising point of therapeutic intervention.
**Sponsor:** *NIH, AHA*

317 **Presentation Type:** Poster

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**HYPERBARIC OXYGEN ATTENUATES AORTIC VASOCONSTRICTION FOLLOWING SIMULATED MICROGRAVITY IN RATS**

**Purpose:** The hindlimb suspended (HLS) rat model has been used extensively in land-based research evaluating effects of simulated microgravity. Previous research demonstrated that 2-4 wks of HLS in rats reduced vasoconstrictive responses of aortic, mesenteric, and femoral arterial rings to phenylephrine (PHE). On the other hand, acute exposure to high oxygen levels amplified constrictive response to PHE. Therefore, the purpose of this study was to determine if hyperbaric oxygen treatment (HBO) during HLS would reverse effects of HLS on PHE-induced vasoconstriction.
**Methods:** Five month old male Sprague-Dawley rats were randomly divided into aging controls (AC), AC-HBO, HLS, and HLS-HBO groups for 4 wks. Groups receiving HBO (AC-HBO; HLS-HBO) were placed in a cage that was fitted for the animal hyperbaric chamber; HLS was maintained during HBO treatments. HBO groups were treated 6 d/wk (1X/d) for a total of 24 treatments, using a standard clinical protocol for treating chronic wounds in humans. The chamber was flushed with 100% oxygen and then compressed over 10 min to a pressure equivalent to 45 feet of sea water (22.5 psig). Treatment lasted for 90 min followed by a 10 min decompression time. After 28 d of HLS, animals were sacrificed under isoflurane anesthesia and thoracic aorta segments isolated. Relaxation of aortic rings were measured in response to acetylcholine (ACh) and sodium nitroprusside (SNP) after preconstriction with PHE (3X10-7). Constriction of aortic rings was also determined in response to increasing concentrations of PHE. All drugs were administered cumulatively in vessel baths at 10-10-10-4M. Data were analyzed using four-parameter (i.e., minimum, maximum, EC50, slope) nonlinear regression, and groups compared using 2X2 ANOVA with HBO and HLS as main effects.
**Results:** Responses to ACh and SNP were not affected by HLS or HBO. However, in response to PHE, there was a decrease in maximum vasoconstriction in HLS compared to controls (44.7±7.3% vs 82.4±6.0%, respectively, p?0.05) and in HBO compared to controls (48.5±6.5% vs 78.6±6.8%, p?0.05).

**Conclusions:** These results indicate that PHE-induced constriction of thoracic aorta is decreased after HLS. HBO did not reverse HLS-induced reductions in contractile responses; instead HBO independently reduced PHE-stimulated constriction of aortic segments. This suggests that HBO may be useful in models where constriction is enhanced, such as hypertension or diabetes.
"Intramural Funding from the University of Texas in Arlington"
**Sponsor:** *Intramural Funding from the University of Texas in Arlington*

318 **Presentation Type:** Poster

**Author:** T.J. Bartosh **Presentor:** T.J. Bartosh
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**DEVELOPMENT OF A NOVEL CARDIAC STEM CELL 3D-MODEL**

**Purpose:** The regenerative inadequacy of the myocardium following pathological processes leads to adverse remodeling, cardiac dysfunction, and ultimately heart disease. Stem cell-replacement of damaged myocardium appears to be a promising treatment strategy, but faces major challenges including undesirable differentiation, cellular uncoupling, and accelerated stem cell-death rates following transplantation. These challenges could be met by engineering novel systems for delivery of stem cells to the injury site. This study, therefore, was designed to establish a cardiac stem cell model capable of differentiating into three-dimensional (3D) cellular aggregates with phenotypic characteristics of adult myocardial tissue. Furthermore, the response of the 3D-model to ischemic conditions and oxidative stress will be evaluated.
**Methods:** Adult cardiac stem cells isolated from canine left ventricular (transmural) tissue were expanded in vitro and induced to form 3D-cellular aggregates called cardiospheres. Sphere-generating cells were characterized using immunocytochemistry, Western blotting, and RT-PCR; and subjected to ischemia or oxidative stress using serum-free/glucose-free medium or hydrogen peroxide, respectively. Cell survival was determined using MTS assay and staining with fluorescent dyes (calcein AM and ethidium homodimer).
**Results:** Adult cardiac stem cells were capable of long-term self renewal and assimilated into cardiospheres with characteristics of adult myocardial tissue. Sphere formation and cardiac structural gene induction were enhanced by culturing on a poly-L-ornithine substratum in the presence of bFGF and EGF. The formation of cardiospheres from stem cells attenuated the rapid cell-death response observed in monolayer cultures following conditions of oxidative stress.
**Conclusions:** Our study verifies the existence of stem cells in adult mammalian hearts. Adult cardiac stem cells are capable of differentiating in vitro into 3D-cardiospheres expressing phenotypes characteristic of adult myocardial tissue. This 3D-model system would facilitate investigations of the molecular mechanisms of neo-myocardial formation and identification of micro-environmental cues that regulate stem cell fate. Furthermore, the increased resistance to oxidative stress exhibited by cardiospheres provides a novel stem cell delivery system in the treatment of heart disease.
**Sponsor:** *None*

319 **Presentation Type:** Poster

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**OSMOTIC CELL VOLUME CHANGES REGULATE ENOS OF VASA RECTA**

**Purpose:** Vasa recta (VR) of kidney medulla are exposed to osmotic stresses. We hypothesize that osmotic cell volume changes affect endothelial nitric oxide synthase (eNOS)of VR endothelial cells. Studies were focus on VR in outer medulla of mouse kidney.
**Methods:** We used microelectrode to detect [NO] for eNOS activity, confocal imaging endothelial expressed GFP for VR cell volume changes, imaging fura-2/AM loaded renal sections (150μm) for [Ca++]i, immunofluorescence for eNOS localization and western blotting for eNOS, Akt and their phosphorylation.
**Results:** VR endothelial cells showed eNOS expression, releasing 732±68 nM NO (mean±sem, n=5) in isotonic HBSS which was inhibited by L-NAME (500μM). Cell shrinking (in HBSS+200mM mannitol) decreased NO releasing to 335±69 nM (n=5) that was recoverable by returning to isotonic HBSS. At normal condition, random [Ca++]i oscillation was common in VR endothelial cells. Hyperosmotic treatments by 200 mM mannitol or 100 mM NaCl, but not 200 mM urea, inhibited the [Ca++]i oscillation. Cell swelling was followed by immediate [Ca++]i increase. Buffering [Ca++]i by BAPTA/AM decreased NO releasing to 370±88nM (n=5) under normal condition, also decreased eNOS dimer/monomer ratio. Cell swelling caused higher eNOS dimer/monomer ratio, more phosphorylated Akt (ser473) and eNOS (ser1177) than in shrinking cells. Inhibition of Akt signaling with 400nM wortmannin decreased NO releasing to 400±21nM (n=5).
**Conclusions:** In conclusion, osmotic cell volume changes regulate eNOS activity of vasa recta; cell shrinking inhibits eNOS that can be reactivated by cell swelling. Both Ca++ and PI3K/Akt signaling are involved in eNOS regulation of VR endothelium. (Supported by American Heart Association and Faculty research grant of UNTHSC to S.Chu)
**Sponsor:** *AHA*

# CARDIOVASCULAR

320 **Presentation Type:** Poster

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**INTERMITTENT HYPOXIC CONDITIONING SUPPRESSES NITRIC OXIDE SYNTHASE ACTIVITY IN CANINE MYOCARDIUM**

**Purpose:** During oxidative stress, as with reperfusion of ischemic myocardium, excess generation of nitric oxide (NO) leads to the formation of cytotoxic peroxynitrite, modification of iron-sulfur centers of respiratory chain components, and inactivation of metabolic and antioxidant enzymes. This study tested the hypothesis that intermittent hypoxic conditioning (IHC) progressively lowers myocardial nitric oxide synthase (NOS) activity and blunts the lethal NO burst upon release of coronary occlusion.
**Methods:** Mongrel dogs were conditioned by a 20-day program of 5-8 cycles (5-10 min) of normobaric hypoxia (FIO2 9.5-10%), with intervening 4 min periods of normoxia, or sham conditioned with room air. Myocardium was harvested for biochemical analyses on the day following completion of the hypoxia or sham conditioning programs. NOS activity and eNOS content were measured by spectrophotometry and Western blot, respectively, in left and right ventricular myocardium.
**Results:** NOS activity was considerably lower in IHC myocardium (left ventricle: IHC: 34 ± 2 nmoles/min/g protein vs. sham: 82 ± 2 nmoles/min/g protein; right ventricle: IHC: 33 ± 3 nmoles/min/g protein vs. sham: 83 ± 14 nmoles/min/g protein), in parallel with sharply lower eNOS content as revealed by Western blot.
**Conclusions:** These results suggest that IHC suppresses eNOS expression as a mechanism to lower formation of cardiotoxic NO derivatives upon reperfusion. Also iNOS expression did not increase to compensate for decreased eNOS content.
**Sponsor:** *NIH support: HL71684, HL64785*

321 **Presentation Type:** Poster

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**DETERMINANTS OF PAIN-MEDIATED SYMPATHOEXCITATION**

**Purpose:** We investigated the quantitative relationship between acute cold pressor pain stimuli, cardiovascular responses, and muscle sympathetic nerve activity (MSNA) in healthy individuals, addressing the hypotheses that: (1) repeat stimulus does not change the baseline characteristics of the cold pressor response, (2) increased pain perception provokes graded increases in SNA, and (3) cold-induced sympathoexcitation occurs only above a pain threshold for SNA activation.
**Methods:** A total of 15 healthy normotensive volunteers, 18-60 years of age were recruited for this study. Subjects were studied at the same time of day and instrumented to record MSNA, arterial pressure (MAP), heart rate (HR), respiration, and calf blood flow followed by a 20-minute rest period. Subjects in the adaptive response group submersed one hand for 2 minutes in a 2C cold water bath. Pre, CP, and post data were collected. Randomized recovery periods of 10, 20, and 30 minutes separated each stimulus over the course of 6 repeat CP tests. Subject in the graded response group submersed one hand for 2 minutes in water baths set at 1 of 5 randomly-ordered temperatures (2, 6, 10, 14, 18C) with a standard 20-minute rest period between stimuli. All subjects reported their pain perception using Borg's 15-point Rating of Perceived Pain (RPP) Scale prior to each stimulus and every 15 seconds until no pain was reported.
**Results:** Repeat 2C cold pressor stimuli did not significantly alter response characteristics (HR, MAP, RPP) pre-, during, or post-stimulus. Varying recovery time between stimuli did not significantly alter sympathetic neural and cardiovascular response characteristics ($p>0.05$). In addition, sympathoexcitatory responses correlated significantly with pain perception ($r = 0.$ ) and demonstrated a graded response to the graded temperatures.
**Conclusions:** CP responses do not adapt significantly during repeat stimuli with at least a 10 min recovery period. Sympathoexcitatory and pressor responses are a function of pain perception.

**Sponsor:** *NIH*

322 **Presentation Type:** Poster

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**Classification:** GSBS Student
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**AGING DIMINISHES DYNAMIC REFLEX CONTROL OF HEART RATE: A COMPARISON OF TRANSFER FUNCTION ANALYSIS**

**Purpose:** Transfer function analysis between systolic blood pressure (SBP) and heart rate (HR) signals has been commonly applied for assessment of dynamic reflex control of HR. It is known that aging diminishes the arterial baroreflex control of HR as a result of cardiac vagal dysfunction. The purpose of this study was to test the hypothesis that the statistical outcome was not altered using mean arterial pressure (MAP) or SBP signals in transfer function analyses to assess dynamic reflex control of HR.
**Methods:** Nine healthy young (27.3±1.2 yr, 84.9±3.4 kg, 178±4 cm, 64±2 beats/min, and 117±3/63±2 mmHg) and fourteen elderly (66.9±1.2 yr, 82.5±4.2 kg, 75±2 cm, 59±4 beats/min and 132±4/73±4 mmHg) men gave written consent to participate in the study approved by IRB. A section of 5-min steady-state HR, MAP and SBP data was selected for fast Fourier transform and transfer function analysis between MAP-HR signals and SBP-HR signals using Welch Spectral estimator. Magnitude, coherence, and phase of transfer function of low-frequency (LF, 0.04 – 0.15 Hz) and high-frequency (HF, 0.15 – 0.40 Hz) were compared.
**Results:** Transfer function gain was smaller in elderly than young adults in terms of the transfer function gains using both MAP-HR signals (elderly vs young: 0.68±0.09 vs 1.06±0.11 bpm/mmHg, $P = 0.012$) and SBP signals (0.49±0.07 vs 0.85±0.10 bpm/mmHg, $P = 0.007$) in LF. Though the gains in both groups were higher assessed using MAP-HR signals than SBP-HR signals, the correlations in LF transfer function gain, coherence, and phase between MAP-HR signals and SBP-HR signals were highly related, $r = 0.91$, slope = 1.03±0.17, $P = 0.0005$ for gain, $r = 0.94$, slope = 0.97±0.13, $P = 0.0001$ for coherence, and $r = 0.95$, slope = 1.00±0.12, $P = 0.0001$ for phase in the young group, $r = 0.88$, slope = 1.07±0.17, $P = 0.0001$ for gain, $r = 0.93$, slope = 0.92±0.10, $P = 0.0001$ for coherence, and $r = 0.91$, slope = 0.74±0.10, $P = 0.0001$ for phase in the elderly group. However, HF transfer function gains had variation between MAP-HR signals and SBP-HR signal in both the age groups.
**Conclusions:** Our data indicate that aging diminishes dynamic reflex gain in terms of transfer function analysis using MAP-HR signals and SBP-HR signals.
**Sponsor:** *NIH HL65613*

# CELLULAR & MOLECULAR SCIENCE

400 **Presentation Type:** Oral

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**PHOSPHORYLATION PLAYS A ROLE IN REGULATING INTRACELLULAR LOCALIZATION OF HUMAN ANNEXIN II**

**Purpose:** This study is focused on the role of phosphorylation on the intracellular distribution of annexin II.

Annexin is a family of proteins that bind to phospholipid in calcium dependent manner. Members in this family share considerable homology in their c-termini, and a specific N-terminus defines the physiological role of each annexin molecule. Annexin II has been studied as tyrosine kinase substrate. It has also been suggested that annexin II has many biological functions, such as being a component of primer recognition protein complex and regulating exocytotic and endocytotic pathways in chromaffin cells. Several studies revealed that annexin II could be phosphorylated by protein kinase C (PKC) on Serine 11 and Serine 25 (Ser11 and Ser 25) and by protein tyrosine kinase pp60src on Tyrosine 23 (Tyr 23), but the role of phosphorylation on the these residues is yet unknown. Recently, a nuclear export signal (NES) was found in the N-terminus of annexin II. Given the approxicimity between the NES and phosphorylation sites and an observation showing that nuclear annexin II is phosphorylated, we hypothesized that phosphorylation plays a role in regulating the in intracellular distribution of annexin II.

**Methods:** Western blotting and Northern blotting were used to screen for a cell line that do not express annexin II so that we could study the distribution of annexin II without the effects of the background endogenous annexin II.

pEGFP-C1 was used as vector for the expression of wild-type and mutant annexin II.

We used site-directed mutagenesis to generate mutants at different phosphorylation sites.

Confocal microscopy was used to observe the intracellular localization of annexin II.

The plasmids that express GFP fused N-terminus of wild type or mutant annexin II were constructed using PCR-based truncation mutation and traditional cloning methods.

**Results:** Annexin II-null LNCaP cell line is a good model to study the intracellular distribution of annexin II.

Mutating of both Ser11 and 25 to glutamate (Glu), which mimicking the phosphorylation of these two sites, cause inhibition of nuclear entry of annexin II.

Expressing GFP fused N-terminus of annexin II containing Ser11 to Glu and Ser25 to Glu mutation did not result in nuclear entry inhibition.

**Conclusions:** Phosphorylation of annexin II in Ser11 and Ser25 results in nuclear entry inhibition of annexin II, and it is suggested that C-terminus of annexin II also plays a role in this process.

**Sponsor:** *none*

401 **Presentation Type:** Poster

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**PROTEIN KINASE C EPSILON ACTS UPSTREAM OF AKT/PROTEIN KINASE B TO INFLUENCE TUMOR NECROSIS FACTOR INDUCED CELL DEATH IN BREAST CANCER CELLS**

**Purpose:** Tumor necrosis factor-alpha (TNF), a multifunctional cytokine, was originally identified by its anti-tumor activity. The mechanism(s) by which cancer cells evade TNF-induced cell death is incompletely understood. Novel protein kinase C epsilon (nPKC-epsilon) has been shown to regulate TNF induced apoptosis in breast cancer cells. However, the level of PKC-epsilon was not sufficient to explain cellular sensitivity to TNF. Since Akt/protein kinase B (PKB), another serine/threonine kinase closely related to PKC, plays a critical role in regulating cell survival and apoptosis, we examined if the level/activation status of PKB influences anti-apoptotic signaling by nPKC-epsilon in breast cancer cells.

**Methods:** Akt/PKB level/activity was manipulated in MCF-7 and BT-20 cells using constitutively-active PKB, dominant-negative PKB or specific siRNA against PKB. The effect of changes in PKB activity on TNF-mediated cell death was determined using Flow cytometric analysis. TNF-induced PKB phosphorylation was detected in BT-20 cells using Western blot. Effect of PKC-epsilon overexpression on PKB phosphorylation/activity was tested in MCF-7 cells transfected with empty vector and PKC-epsilon construct by Western blot as well as non-radioactive kinase assay. PKC-epsilon specific siRNA was transfected into MCF-7 cells to determine the effect on PKB phosphorylation.

**Results:** Overexpression of constitutively-active PKB in MCF-7 cells, which overexpress PKB but not constitutively active PKB, protected MCF-7 cells from TNF-mediated cell death. Introduction of dominant-negative PKB into BT-20 cells, which express constitutively active PKB, enhanced sensitivity of BT-20 cells to TNF. In addition, knockdown of PKB expression by specific siRNA targeted to PKB, sensitized BT-20 cells to TNF. TNF caused a transient increase in PKB phosphorylation in BT-20 cells; the maximum increase was evident at 30 min and then returned to the basal level by 6 h. Overexpression of nPKC-epsilon into MCF-7 cells increased PKB phosphorylation as well as PKB activation as determined by a non-radioactive kinase assay. Knock down of nPKC-epsilon using specific siRNA decreased TNF induced PKB phosphorylation.

**Conclusions:** These results suggest that the status of PKB in breast cancer cells influences antiapoptotic signaling by nPKC-epsilon. Furthermore, nPKC-epsilon may act upstream of PKB to regulate its anti-apoptotic function.

**Sponsor:** *CA/NCI/NIH 71727*

402 **Presentation Type:** Poster

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**MEASURING FLUORESCENCE FROM ATTOLITER VOLUME OF MUSCLE BY A NOVEL METHOD OF CONFOCAL TOTAL INTERNAL REFLECTION MICROSCOPY**

**Purpose:** Proteins in cells are present in micromolar concentrations. Observing kinetics of single protein molecules in vivo requires therefore that signal be collected from attoliter (10-18L) volume. Confocal Total Internal Reflection provides a way to obtain such data with high Signal-to-Noise.

**Methods:** In this method, the observational volume is made shallow by illuminating sample with an evanescent field produced by total internal reflection of the incident laser beam. A confocal aperture inserted in the conjugate image plane of the objective guarantees the small lateral dimensions of the observational volume.

**Results:** It is shown, by measuring diffusion of fluorescent microspheres, that in our experimental setup the evanescent field is ~114 nm deep. The technique was applied to glycerinated fibers of skeletal muscle using a 10 mm diameter confocal aperture, which defined the observational volume of ~3 attoL (170 nm x 170 nm x 114 nm). Actin filaments in a single muscle fiber were labeled with rhodamine-phalloidin. Fluorescence was contributed by ~18 molecules of actin-phalloidin.

**Conclusions:** Photobleaching caused fluorescence decay to occur in a series of discrete steps, which we think correspond to bleaching of single molecules of rhodamine-phalloidin.

(NIH RO1 AR048622 & R21 CA97321)
**Sponsor:** *NIH RO1 AR048622 & R21 CA97321*

404 **Presentation Type:** Poster

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**Classification:** Staff (Not for Competition)
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**TOPICAL OXYGEN ALTERS ANGIOGENESIS-RELATED GROWTH FACTOR EXPRESSION IN CHRONIC DIABETIC FOOT ULCERS**

**Purpose:** Following tissue vascular and oxygen delivery disruption, normal wound healing is a complex process requiring restoration of supplies of oxygen and other nutrients through blood vessel regeneration, or angiogenesis. Angiogenesis is stimulated by synergistic interactions of growth factors and cytokines secreted by damaged cells in wound tissues exhibiting hypoxia, high lactate levels and inflammation. Chronic wounds, often complications of diabetes, are characterized by chronic hypoxia, inflammation and insufficient growth factor secretion. To test growth factor sensitivity to reversed wound hypoxia, we administered pure oxygen topically and used molecular probes to measure growth factors previously found to regulate angiogenesis and improve delayed healing, i.e. VEGF, FGF2, PDGF, HGF, KGF, etc.

**Methods:** By multiplex ELISA assays of growth factor cytokines, we quantified pg/ug levels of total proteins detectable in fluids collected from wounds after exposure to topical oxygen delivered in 0-50 mm Hg pulses at to above normal atmospheric pressure (760-810 mm Hg) during 90 minute treatments four days per week over a five week protocol.

**Results:** Our initial data show increased expression in angiogenesis-related growth factors (bFGF, PDGF, HGF, KGF, VEGF) in wound fluid from chronic diabetic foot ulcers using the Topical Hyperbaric Oxygen Chamber (Advanced Hyperbaric Technologies, Inc., Farmingdale, NJ). The most crucial angiogenic factor, VEGF, was altered by 8-fold to 20-fold increases using the described protocol.

**Conclusions:** These data show evidence of a molecular mechanism for the scientific basis of topical hyperbaric oxygen-modulated growth factor expression in chronic diabetic wounds, previously unresponsive to standard wound care. We conclude that topically applied hyperbaric oxygen alters angiogenesis-related growth factor expression in wound fluids from chronic diabetic foot ulcers in a manner consistent with renewed healing.

**Sponsor:** *none*

# CELLULAR & MOLECULAR SCIENCE

**405** **Presentation Type:** Poster

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*Hriday K. Das, University of North Texas Health Science Center, Department of Pharmacology and Neuroscience*

**ZNF237 INTERACTS WITH THE TRANSCRIPTION FACTOR ERM AND INHIBITS THE TRANSCRIPTION OF THE HUMAN PRESENILIN 1 GENE**

**Purpose:** We have mapped a presenilin 1 promoter region in SK-N-SH cells from -118 to +178 flanking the major initiation site (+1). It includes several Ets motifs both upstream and downstream from the +1 site. We have identified several Ets factors targeting the PS1 promoter including Ets2, ER81, ERM and Elk1 by yeast one-hybrid selection in a human brain cDNA library using as a bait the -10 Ets motif. We chose to analyze further the role of ERM because little is known about its interactions with cellular proteins, and we have searched for ERM interacting proteins by yeast two-hybrid selection

**Methods:** We have searched for ERM interacting proteins by yeast two-hybrid selection in a human brain cDNA library where cDNAs were inserted into pACT2. The bait was the C-terminal 984 amino acid of ERM inserted into pGBKT7. It included protein sequence that are specific to ERM as well as the Ets domain, but excludes the N-terminal acidic domain which is highly conserved between Ets factors

**Results:** One of the interacting proteins identified in 2 independent clones is ZNF237. It has recently been described as a member of the MYM gene family since it contains a copy of a novel putative zinc-binding motif (or MYM motif). ZNF237 is widely expressed in eukaryotes and found under several forms derived by alternative splicing. A major transcript encodes a large 387 amino acid (aa) protein containing the MYM motif, and 2 shorter forms of 208 and 213 aa respectively are also generally expressed. The sequences present in the 2 library clones included the entire cDNA from the larger 387 aa specie (excluding the first 22 aa). We tested the effects of both the large 387 aa as well as the shorter 208 aa form on PS1 expression. Both ZNF237 forms appear to repress PS1 transcription in transfection assays in SH-SY5Y neuronal cells where we have not detected any endogenous ZNF237 RNA by PCR analysis. Comparing the repressor activity of a set of 3' deletions of ZNF237indicates that crucial sequences are located in the fragment N-terminal portion between amino acid 162 and 120

**Conclusions:** We have identified an interaction between ZNF237 and the Ets transcription factor ERM. ERM recognizes several sites on the presenilin 1 promoter and activates the transcription of PS1 in transfection assays in neuronal cell lines. Cotransfection with ZNF237 inhibits PS1 expression likely in part by counteracting the activating effect of endogenous ERM

**Sponsor:** *NIH*

**406** **Presentation Type:** Poster

**Author:** Sherry Hannon **Presentor:** Sherry Hannon
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**TRPC PROTEINS IN HUMAN GLOMERULAR MESANGIAL CELLS**

**Purpose:** Store-operated Ca2+ channels (SOC) in glomerular mesangial cells mediate Ca2+ entry in response to circulating or locally produced vasoactive peptides. However, the molecular entity of SOC is still unknown. Recently, the members of the canonical transient receptor potential (TRPC) protein family have been suggested to be potential candidates of SOC. The present study was performed to identify the subtypes of endogenous TRPC proteins in human mesangial cells (HMCs) and the role of TRPC1 protein in store-operated Ca2+ entry.

**Methods:** Western blots as well as immunofluorescent confocal microscopy were used to study the expression of various TRPC subtypes in HMCs, including TRPC1, TRPC3, TRPC4, TRPC5, TRPC6, and TRPC7. TRPC 5, TRPC6 and TRPC7 expression were also examined at the mRNA level via RT-PCR. Whole-cell patch clamp experiments were used to demonstrate the role of TRPC1 in thapsigargin-induced Ca2+ currents. Ca2+ entry was also measured by fluorescent ratiometry in cells over-expressing TRPC1 as well cells with RNA interference (RNAi) inhibition of TRPC1 expression.

**Results:** Western Blot showed that TRPC1, TRPC3 and TRPC4 were expressed in cultured HMCs. Consistently, immunofluorescent confocal microscopy revealed specific staining for TRPC1, TRPC3 and TRPC4 with predominant.expression in cytoplasm. However, TRPC5, TRPC6 and TRPC7 were not detectable at protein level by either Western blotting or immunofluorescent staining, although RT-PCR studies confirmed the expression of each transcript. In whole-cell patch clamp experiments, inhibition of TRPC1 function via inclusion of mouse monoclonal anti-TRPC1 antibody (200 ng/ml) into the patch pipette significantly depressed thapsigargin-induced Ca2+ currents. Furthermore, knocking down TRPC1 using RNAi technique dramatically reduced store-operated Ca2+ entry measured by fluorescent ratiometry. In agreement with the results from the loss-of-function experiments, the thapsigargin-stimulated Ca2+ entry was significantly augmented in TRPC1-overexpressing HMCs.

**Conclusions:** These results suggest that HMCs express subtypes of TRPC1, TRPC3 and TRPC4 proteins. TRPC1 might be a functional component of SOC in this type of cells.

**Sponsor:** *American Heart Association*

**407** **Presentation Type:** Poster

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**FRACTION OF MYOSIN HEADS INTERACTING WITH THIN FILAMENTS DURING MUSCLE CONTRACTION**

**Purpose:** Myosin consists of the N-terminal globular part (myosin head), middle a-helical part (lever-arm) and the C-terminal coiled-coil (myosin rod). It is the cyclic interactions of heads with actin that cause muscle contraction. The purpose of this experiment is to find out what fraction of myosin is attached to thin filaments at any given time during contraction. This number is important because it provides information about duty cycle of acto-myosin, i.e. the fraction of time that myosin interacts strongly with actin during one ATPase cycle. Estimates vary from low 5% [1] to high 80% [2].

**Methods:** Methods: Preparation of muscle fibers; labeling with fluorescent dyes; cross-linking; SDS PAGE; Western blotting; microscopic and fluorescent analysis.

**Results:** The number can be measured if myosin head is labeled with a probe that is sensitive to acto-myosin binding. One such probe is CFDA [3], but labeling is not highly specific [4]. A more direct approach is to exploit our earlier finding that the N-terminus of the essential light chain 1 (LC1) residing on the lever-arm binds to actin whenever myosin head binds to it [5]. Cross-linking of LC1 to actin with water soluble reagent EDC yields 66KD adduct, which is formed only when heads are tightly bound to actin. Further, if LC1 is fluorescently labeled at the N-terminus, the orientation of the probe is an indication of fraction of heads bound, because the N-terminus is oriented only when it is bound to highly oriented actin filaments. Thus when the cross-linking or probe orientation is measured in relaxation and the heads are dissociated from actin, the production of 66KD adduct and polarization of fluorescence must be 0%. In contrast, rigor condition when the heads are fully bound to actin leads to the production of adduct and polarization of fluorescence must be maximal.
We exchanged native LC1 of myosin in skeletal muscle fibers with genetically engineered LC1 containing Cys residue at position 2. This residue was specifically reacted with fluorescent reagent 5'-iodo-acetamido-tetramethyl-rhodamine (5'-IATR).

**Conclusions:** The measurements done during contraction revealed that the fraction of heads bound to actin during contraction was ~30%.

1. Uyeda, et al., 1990, JMB 214: 699-710; 2. Harada et al., 1990, JMB 216: 49-68; 3. Bertrand et al., 1995, Biochemistry 34: 9500-7; 4. Cooper et al., 2000, Biophys J. 78: 1449-57; 5. Andreev et al., 1999, Biochemistry 38: 2480-5.

**Sponsor:** *NIH RO1 AR048622; R21 CA97321*

**408** **Presentation Type:** Poster

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**ALTERATIONS IN MRNA STABILITY OF EXTRACELLULAR SUPEROXIDE DIMUTASE TRANSCRIPT AS A RESULT OF A 10 BASE PAIR DELETION IN THE SHORT ALLELE**

**Purpose:** Our lab has previously observed that 129P3/J mice express a shorter variant of the extracellular superoxide dismutase (ecSOD) mRNA due to the presence of a "short" allele. These mice were shown to have higher activity and mass of circulating and heparin-releasable ecSOD, when compared to C57Pl/J mice, which express the long, wild-type allele. The 10 base pair deletion in the 3' untranslated region, found only in the short allele, may alter mRNA stability and lead to changes in overall enzyme expression. To further understand the molecular mechanisms that control the expression of ecSOD, it would be important to assess the differences, if any, in levels of mRNA degradation as a result of the 10 base pair deletion.

**Methods:** Mice will be injected with 1.5 ml sterile 4% thioglycolate to induce macrophage accumulation. Four days after thioglycolate injection, the macrophages will be collected by intraperitoneal cavity lavage with sterile PBS. Cells will be incubated in the presence of actinomycin D (1ug/ml of media) and harvested after 12 and 24 hours. Control cells will be incubated in DMEM alone. After each incubation, RNA will be isolated and cDNA will be prepared for quantification of mRNA levels by RT-PCR. Using primers designed to amplify a part of the ecSOD open reading frame, a 441 base pair PCR product will be generated. Cycle threshold results will be directly compared to determine fold differences in ecSOD mRNA between the products of the 2 alleles at specific time points.

**Results:** Half-life of mRNA can be determined by graphing % degradation over time. Time-dependent loss of mRNA transcript can be evaluated between the cells from the two strains of mice to determine the significance of the 10 base pair region, absent in the short allele, in terms of mRNA stability.

**Conclusions:** We believe that the 10 base pair deletion in the 3' untranslated region of the short allele leads to a change in the mRNA stability of the shorter transcript, resulting in a shorter half-life as compared to the longer transcript. This may lead to altered mechanisms of post-transcriptional regulation of the ecSOD product. The successful completion of this project will enable us to begin the elucidation of observed differences in the ecSOD phenotype in mice differing in their genotype.

**Sponsor:** *None*

# CELLULAR & MOLECULAR SCIENCE

409 **Presentation Type:** Poster

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## SPONTANEOUS DNA DAMAGE DUE TO MITOCHONDRIAL METABOLISM TRIGGERS CHECKPOINT ACTIVATION IN REPAIR-DEFICIENT SACCHAROMYCES CEREVISIAE

**Purpose:** The purpose of this research was to investigate the mechanisms which are involved in the repair of spontaneous and oxidative DNA damage in Saccharomyces cerevisiae.
**Methods:** In this research work we have used PCR assisted direct gene replacement to delete one or more pathways of DNA repair in Saccharomyces cerevisiae. Phosphorylation of kinase Rad53p has detected by immunoblotting for yeast cell cycle check point activation by DNA damage.rho0 mutants confirmed by mitochondrial staining.
**Results:** We have observed Rad53 phosphorylation in stationary phase S. cerevisiae cultures incubated beyond 4 days if two major pathways of oxidative damage repair, base excision repair and nucleotide excision repair (NER), are inactivated.This effect has not found after inactivation of a single pathway.Also this Rad53p response is absent in rho0 strains (lacking detectable mitochondrial DNA) but also in cor1 deletion mutants (defective in the core subunit of the ubiquinol-cytochrome C reductase complex I).
We have extended the analysis to other repair mutants and mutant combinations. Certain mutants such as rad52 (defective in homologous recombination) show Rad53 modification in logarithmic phase also in stationary phase. Interestingly, a combination of a yku70 deletion (the budding yeast Ku70 homolog) and rad52 or rad4 (NER) elicits the Rad53 phosphorylation response in stationary phase.
The survival of yeast mutants in exponential phase under oxidative stress shows that the percentage survival of double mutant yku70rad4 is less as compared to single mutants yku70 and rad4.
**Conclusions:** Our results conclude that two major pathways of oxidative damage repair, base excision repair and nucleotide excision repair (NER), must be inactivated to get check point activation response by Rad53. Inactivation of a single pathway is insufficient to induce Rad53 modification. This effect is strictly dependent on mitochondrial function and therefore absent in rho0 strains.
Certain mutants such as rad52 (defective in homologous recombination) show some Rad53 modification in logarithmic phase, presumably due to double-strand breaks arising during S phase. Also our findings may indicate an unsuspected role of non-homologous endjoining (NHEJ) and nucleotide excision repair (NER) in oxidative damage repair. We could correlate this effect in stationary phase with sensitivity to externally added oxidative agents.

**Sponsor:** *NIH grants ES11163 and CA87381*

410 **Presentation Type:** Poster

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## IDENTIFICATION OF COMPONENTS OF THE NUCLEAR IMPORT APPARATUS OF GLUCOCORTICOID RECEPTOR BETA: A DISTINCT MECHANISM FOR NUCLEAR TRANSPORT IN TRABECULAR MESHWORK CELLS

**Purpose:** Glucocorticoids (GCs) are associated with increasing the intraocular pressure in some patients, particularly in patients with glaucoma. The altered responsiveness to GC has been attributed to differences in the expression of GC receptor GR beta, which functions as a dominant inhibitor of GC receptor, GR alpha. GR alpha and GR beta differ at their C-terminus and their abilities to bind glucocorticoids. GR alpha undergoes GC-dependent nuclear translocation by associating with heat shock protein (Hsp90) and immunophilin FKBP52 multi-protein complex. The nuclear transport pathway of the non-ligand-binding GR beta is still unknown. Currently we investigate the components involved in nuclear transport of GR beta.
**Methods:** Confocal microscopy was performed to detect the correlation of subcellular expression of Hsp90 with GR beta in TM cells. Hsp90 inhibitor, 17-AAG, was used to study the chaperone function of Hsp90 in nuclear transport of GR beta. Proteasome inhibitor, lactacystin, was applied to identify the degradation pathway of GR beta. Co-immunoprecipitation was used to investigate the protein components, including Hsp90, immunophilins, and dynein, which complex with GR beta.
**Results:** In TM cells, the nuclear concentration of Hsp90 is correlated with the nuclear expression of endogenous or de novo synthesis of GR beta. 17-AAG completely blocks the nuclear accumulation of GR beta in GR beta-transfected TM cells and consequently leads to the degradation of GR beta through a lactacystin inhibited proteasome-mediated pathway. Co-immunoprecipitation verify that GR beta complexes with Hsp90. Furthermore, co-immunoprecipitation identified that GR beta complexes with immunophilin FKBP51, but not FKBP52, a protein which regulates nuclear translocation of ligan-activated GR alpha. FKBP51 also complexes with Hsp90 and the microtubular motor protein dynein. Interestingly, similar to GR beta, non-ligand-binding GR alpha complexes with FKBP51.
**Conclusions:** Hsp90 is identified as an essential molecular chaperone for nuclear import of GR beta. Immunophilin FKBP51, the motor protein, dynein, and microtubules are implicated in this nuclear import of non-ligand-binding GR beta in a parallel track different from that for the ligand-activated GR alpha-FKBP52 complex. This finding also suggests that regulation of the GR beta nuclear transport could influence subsequent GC responses that are often seen clinically, such as GC-resistance in asthma or enhanced GC sensitivity in glaucoma.
**Sponsor:** *NEI EY11979*

# DIABETES

500 **Presentation Type:** Poster

**Author:** Cherice Anderson **Presentor:** Cherice Anderson
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**Classification:** GSBS Student
*Cherice Anderson UNTHSC, Derrick White McNair Scholar, Richard Easom UNTHSC*
**GLUCOSE REGULATION OF PROTEIN PHOSPHATASE 2A AND INSULIN SECRETION IN TYPE II DIABETES**
**Purpose:** Type 2 diabetes is characterized in part by impaired glucose stimulated insulin secretion. The signal transduction mechanism underlying the control of insulin secretion is incompletely understood. It is hypothesized that the serine/threonine protein phosphatase (PP2A) plays a central role in this process. PP2A is regulated by association with regulatory subunits, PP2A/B. Preliminary data hs shown that the inhibition of PP2A with okadaic acid and endothall enhanced glucose-induced insulin secretion. The purpose of this study was to identify which PP2A/B subunits are expressed in the insulin secreting B-cell.
**Methods:** cDNA was generated from total RNA extraction from cultured INS1 cells, mouse islets, and rat forebrain by AMV reverse transcriptase. PCR was done via vendor specification using Taq polymerase (Promega). PP2A was affinity purified by Microcystin-Agarose binding and PP2A/B was then analyzed via B-isoform specific antibodies (ECL, Amersham).
**Results:** By RT-PCR insulinoma and primary rat islets express multiple B & B' genes and select B" at the mRNA levels. By immunoblotting we have found that B cells express PP2A/B alpha, gamma, and delta with minimum expression of PP2A/B beta and multiple of B' isoforms. Interestingly, the exocytotic protein, synapsin I co-purified with PP2A from B-cells. Moreover Okadaic acid (OKA) induced the phosphorylation of synapsin I at Ser603 but only in the presence of higher concentrations of glucose.
**Conclusions:** The pancreatic B-cell expresses several isoform of both the B and B' families are expressed consistent with it's involvement of PP2A in multiple process in the pancreatic B-cell. These data also suggest that synapsin I is a substrate for PP2A and that their association is responsible for maintaining the dephosphorylation of synapsin I in a resting state. The ability of OKA to enhance synapsin I phosphorylation supports an involvement of PP2Ain glucose-induced insulin secretion.
**Sponsor:** *American Heart Association*

501 **Presentation Type:** Poster

**Author:** Susan Franks **Presentor:** Kathryn Kaiser
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**Classification:** Faculty (Not for Competition)
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**DREAMS: DIABETES RESEARCH, EDUCATION AND METABOLIC STUDIES. EFFECT OF BARIATRIC SURGERY ON PSYCHOPHYSIOLOGICAL AND HORMONAL REGULATION OF EATING BEHAVIOR**
**Purpose:** The purpose of this study is to determine cardiovascular, hormonal, and metabolic status of morbidly obese subjects before and after bariatric surgery, and to determine relationships among eating behaviors, responses to stress, and hormonal and autonomic activation as they pertain to the development of type 2 diabetes. Hypotheses to be investigated involve the response of appetite changes and autonomic nervous system (ANS) to stress, changes in neurohormones and sympathetic nervous system (SNS) activity associated with body fat loss after bariatric surgery, and responses of hunger and satiety hormones to a meal.
**Methods:** Participants will include 70 morbidly obese subjects undergoing elective bariatric surgery and 30 age- and gender-matched normal weight controls. Study tests for obese subjects will be performed prior to and at 6- and 12-months post-surgery. Self-report surveys will be used to assess psychological aspects of eating behavior and stress. Stress reactivity will be evaluated by measuring heart rate variability in response an induced stress condition. The response of hunger and satiety hormones to eating will be evaluated by measuring plasma concentrations of leptin, ghrelin, insulin, glucose, glucagon, plasma renin activity, aldosterone, GLP-1, and blood lipids before and after a standardized meal. Participants will also receive a CT scan for analysis of body fat composition and regional fat distribution.
**Results:** It is anticipated that (1) obese persons will differ from normal weight controls in eating behavior profiles and ANS response to stress, (2) bariatric surgery will result in neurohormonal changes, resulting in changes in hunger perception, (3) neurohormonal changes associated with body fat loss will correlate with reductions in abdominal visceral fat and with reductions in SNS activation, and (4) hormonal responses to eating will be normalized as abdominal visceral fat is lost.
**Conclusions:** Results of this study will shed light on the complex interplay between nervous, endocrine, and psychological systems that govern eating behavior and weight control. The extent that cardiovascular, hormonal, metabolic, and psychological variables can be normalized as a result of weight loss will be further established. The interrelationship of biological and psychological systems as related to appetite regulation and obesity will lead to more effective treatment of obesity and metabolic syndrome.
**Sponsor:** *CDC*

502 **Presentation Type:** Poster

**Author:** Nicole Bereolos **Presentor:** Nicole Bereolos
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*UNTHSC, Fort Worth, TX*
**DIABETES RELATED PSYCHOSOCIAL VARIABLES IN NON-HISPANIC AMERICANS AND MEXICAN NATIONALS**
**Purpose:** The health-related psychosocial issues between non-Hispanic Americans and Mexican Nationals with type 2 diabetes were evaluated. It has been estimated that 24% of Mexicans residing in the U.S. have type 2 diabetes and some have reported more than 50%. As diabetes grows with epidemic proportions in the U.S., it becomes more essential to gain knowledge about the psychosocial complexities this population brings to the management of diabetes. The role of self-efficacy and social support as important moderators of health behavior has been emphasized for a number of chronic disease conditions, but is poorly understood as it relates to diabetes management in Mexicans residing in the U.S. Studying a Mexican National sample can provide a foundation to understand the needs of less acculturated Mexican diabetics entering the U.S. health care system.
**Methods:** All subjects had diabetes and included 120 adult non-Hispanic Americans (NHA) from a university based family medicine clinic and 76 Mexican Nationals (MN) from a rural hospital-based outpatient clinic. Subjects completed the following self-report questionnaires: Multidimensional Diabetes Questionnaire, Multidimensional Health Profile, and Diabetes Knowledge Questionnaire. HbA1C levels were also obtained.
**Results:** HbA1C levels were higher in MN than NHA $F(1, 162) = 52.550$, $p < .001$. Data was analyzed via a MANOVA with self-efficacy (SE), social support (SS), and diabetes knowledge (DK) as the DVs and nationality as the IV. Results indicated that MN were significantly different than NHA $F(3, 174) = 36.074$, $p < .001$, having higher levels of SE $F(1,176) = 27.172$, $p < .001$ and SS $F(1,176) = 8.072$, $p = .005$ but lower DK, $F(1,176) = 67.248$, $p < .001$.
**Conclusions:** These results may be contrary to what some health care providers would expect, however Mexican-Nationals have a strong belief concerning their ability to care for themselves and their illness even though their glycemic control is poor. This information emphasizes the importance that culture plays in the management of diabetes.
**Sponsor:** *none*

503 **Presentation Type:** Poster

**Author:** Sherry Biddy **Presentor:** Sherry Biddy
**Department:** CELL BIOLOGY and GENETICS
**Classification:** GSBS Student
*Sherry Biddy, Suzanne Shaffer, and Margaret Garner; Department of Cell Biology and Genetics, University of North Texas Health Science Center, Fort Worth, TX 76107*
**PREPARATION OF PROBES FOR THE 5' AND 3' UTR OF THE HUMAN ATP1A2 GENE**
**Purpose:** The purpose of this experiment is to isolate and clone regions 5' and 3' of the ATP1A2 gene to be used as probes for Southern blot analysis of restriction fragment length polymorphisms (RFLP's) in healthy, type-2 diabetic, and hypertensive individuals.
**Methods:** Genomic DNA was isolated from whole blood and amplified by PCR using five primer sets specific for regions of interest in the ATP1A2 gene and its 5' and 3' UTR's. After confirming the size of each of the five PCR products by agarose gel electrophoresis, each PCR product was purified and sequenced using dRhodamine dye-labeled dideoxynucleotide termination. Each PCR product was then inserted into a pCR2.1 vector and transformed into E. coli (INVaF'). DNA was isolated from the bacteria and digested with EcoR1. Agarose gel electrophoresis was again used to verify successful cloning of each PCR product.
**Results:** DNA was isolated from a whole blood sample at a final concentration of 144.7 ug/mL. Agarose gel electrophoresis indicated a band at the predicted size for each PCR product. The PCR products were isolated from the gel and sequenced. All five PCR products had the correct sequence as verified by BLAST. The insertion of the vector into E. coli was verified by blue/white screening on LB agar plates containing Xgal and ampicillin. The DNA was isolated form the E. coli for all five primer sets at concentrations ranging form 20 ug/mL to 190 ug/mL. Restriction enzyme analysis was done on the isolated DNA using EcoR1, which cuts the DNA on either side of the inserted PCR product. When run on an agarose gel, digestion products showed a band at the appropriate size for each insert.
**Conclusions:** ATP1A2 probes were successfully isolated and cloned. They will now be used to determine the frequencies of 5' and 3' RFLP's in blood samples of normal, diabetic, and hypertensive subjects.
**Sponsor:** *none*

# DIABETES

504 **Presentation Type:** Poster

**Author:** Susan Franks **Presentor:** Nicole Bereolos
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*Susan F. Franks, PhD, Nicole Bereolos, MPH, Sarah Arnquist, BS, James R. Hall, PhD, Clifton Cage, DO, Mark Sanders, DO, Samuel Coleridge, DO, Elizabeth Palmarozzi, DO, Mary Luna Hollen, PhD, and Craig Spellman, DO, University of North Texas Health Science Center, Fort Worth, TX 76107*

**DREAMS: DIABETES RESEARCH, EDUCATION AND METABOLIC STUDIES. ACCULTURATION, HEALTH BELIEFS, AND HEALTH PRACTICES IN MEXICAN AMERICANS WITH DIABETES**

**Purpose:** The purpose of this study is to identify culturally related psychosocial attributes of Mexican Americans living with type 2 diabetes that may contribute to management of the disease. Mexican culture has been found to differ from the Anglo culture on numerous psychological dimensions, and Mexican Americans have demonstrated a wide range of variability in the extent to which individuals assimilate the sociocultural and psychological characteristics of the Anglo society. These differences in acculturation appear to be critical to a number of areas of health-care utilization and health behaviors, but have not been examined as related to diabetes. Because the complex demands of the diabetes regimen typically predict poor adherence, regimen adherence has been of special interest in diabetes research. It is hypothesized that differences in acculturation among Mexican Americans with type 2 diabetes will affect adherence to a physician prescribed diabetes regimen via key psychosocial variables and health behaviors.

**Methods:** Subjects will include 100 Mexican Americans with type 2 diabetes who are being treated at a Family Medicine clinic. Self-report inventories will be completed to obtain information regarding acculturation, health status, diabetes knowledge, health behaviors, and psychosocial variables related to management of diabetes. Hemoglobin A1c values will be obtained as an index of adherence to a diabetes regimen.

**Results:** It is anticipated that the results will demonstrate that high, moderate, and low acculturation groups who have either good or poor glycemic control will display signficant differences in key psychosocial variables and health behaviors related to successful diabetes management.

**Conclusions:** The clear identification of cultural issues involved in successful management of diabetes will be used to improve patient-physician collaboration in the primary care setting. Educational programs will be developed to expand the cultural competency of health care providers and improve the quality of medical care for Mexican Americans with type 2 diabetes.

**Sponsor:** *CDC*

505 **Presentation Type:** Poster

**Author:** Ximena Urrutia-Rojas **Presentor:** Ximena Urrutia-Rojas
**Department:** Social & Behavioral Sciences
**Classification:** Faculty (Not for Competition)
*Ximena Urrutia-Rojas, Dr.PH., Mary Luna Hollen, Ph.D., Martha Montiel, MS, Dr.PH Candidate, and Jennifer Castillo, MA, Dept Social & Behavioral Sciences UNTHSC School of Public Health, Fort Worth TX, 76107; Sejong Bae, Ph.D., Godavari Patil, Ph.D., Department of Biostatistics UNTHSC School of Public Health, Fort Worth TX, 76107; Andras Lacko, Ph.D. UNTHSC Department of Molecular Biology and Immunology, Fort Worth TX, 76107; Paula Bower, BSN, City of Fort Worth Public Health Department Outreach Division, Fort Worth TX, 76104; John Menchaca MD, Cook Children's Network, Fort Worth TX, 76104; Paul Garcia, D.O., Sulabha Paranjape, MS., Walter McConathy, Ph.D. and Craig Spellman, D.O., Ph.D. UNTHSC Department of Internal Medicine, Fort Worth TX, 76107.*

**T2DM AND CVD PRIMARY PREVENTION FOR HISPANIC FAMILIES. D.R.E.A.M.S. PROJECT 1**

**Purpose:** The purpose of this study is to decrease the risk factors for T2DM and CVD related to lifestyle such as low level of physical activity and diet in Hispanic families with overweight or obese children, previously identified as "at risk" for Type 2 diabetes mellitus (T2DM), using trained Hispanic community health workers.

**Methods:** Previously identified overweight Hispanic children (~240), at risk of diabetes and cardiovascular disease, and their family members are being invited for an assessment of risk factors for type 2 diabetes (based American Diabetic Association [ADA] guidelines), metabolic syndrome, and cardiovascular disease. The study includes: a) an in-depth assessment of clinical parameters (health history, physical assessment, and laboratory studies to determine risk for diabetes and heart disease); and b) it provides referral to a preventive educational intervention program utilizing Hispanic community health workers ("Promotores de Salud"). The primary prevention program is designed to improve lifestyle patterns and reduce risk for T2DM and related metabolic disorders using trained community health workers "Promotores de Salud". Enrolled families are randomely assigned to an intervention and to a control group.

**Results:** Update of research activities: The project organizational activities started on October 2004. As of January, 2005, 140 families were contacted and confirmed interested and committed to participate in the study. Enrollment of participants started on February 1st, 2005. As of March 2, 2005, thirty nine families were enrolled, which yielded a total of 120 participants (~50 adults and 70 children).

**Conclusions:** This is an ongoing study that started enrollment on February 2005. Assessment preliminary results are expected to be available in May 2005. [CDC/The UNTHSC Center for Diabetes, Research, Education and Metabolic Studies (DREAMS.)]

**Sponsor:** *CDC*

506 **Presentation Type:** Poster

**Author:** Mary Luna Hollen **Presentor:** Mary Luna Hollen
**Department:** SCHOOL OF PUBLIC HEALTH (SPH)
**Classification:** Faculty (Not for Competition)
*Mary Luna Hollen, PhD/RD/LD, Dept Social & Behavioral Sciences, UNTHSC School of Public Health; Ximena Urrutia-Rojas, DrPH, Dept Social & Behavioral Sciences, UNTHSC School of Public Health, Walter McConathy, PhD, Dept Internal Medicine, UNTHSC; Craig Spellman, DO/PhD, Dept Internal Medicine, UNTHSC; Sejong Bae, PhD, Dept Biostatistics, UNTHSC School of Public Health; Isabel Vecino, MD, Dept Social & Behavioral Sciences, UNTHSC School of Public Health; Martha Montiel, DrPH Candidate, Dept Social & Behavioral Sciences, UNTHSC School of Public Health; Mateo Stahl, BS, Dept Social & Behavioral Sciences, UNTHSC School of Public Health; Enisa Arslanagic, MD, Dept Internal Medicine, UNTHSC; Paula Bower, BSN, City of Fort Worth Public Health Department Outreach Division.*

**DIABETES PREVENTION PROMOTOR/A COMMUNITY OUTREACH MODEL**

**Purpose:** The purpose of this study is to provide bilingual culturally competent healthy lifestyle behavior education through the utilization of lay health educators (promotores de salud) and culturally sensitive bilingual print materials targeting Hispanic families with overweight or obese children previously identified as "at risk" for Type 2 Diabetes Mellitus (T2DM).

**Methods:** Previously identified overweight Hispanic children at risk of diabetes and cardiovascular disease, and their family members are enrolled and randomly assigned to an intervention utilizing promotores de salud in family sessions and blingual culturally competent print material, or to a control group receiving blingual culturally competent print material only. The intervention family groups will receive culturally and youth/family-oriented health promotion activities through family sessions for six weeks conducted by promotores de salud. During the six-month intervention period, families will continue to engage in healthy behavior within their extended family and within the community as promoted by the promotores de salud community outreach model. Control families receive monthly educational print material by mail for six months. Self-reported pre/post lifestyle behavior questionnaires are among the series of evaluation instruments called cuentamelo (tell me the story) that quantitatively and qualitatively measure the program.

**Results:** Twenty-five promotores de salud from the promotor/a network alliance received a four-day Salud para su Corazon and Diabetes training. Eight promotores de salud from the alliance were selected to work in the DREAMS Diabetes program following the December 2004 training and have received more than 30 hours of training and in-service in preparation for the project. Families from the DREAMS Diabetes Study Project 1 Phase 1 initiated enrollment on February 1st, 2005. As of March 2, 2005, the first of eight groups of 15 Hispanic families, in each the intervention and the control family groups (to total 120 intervention and 120 controls) have been confirmed. The first of four teams of promotores are currently calling the families for the first family intervention group to decide as a group, the family class day. Family sessions are scheduled to begin mid March 2005.

**Conclusions:** This is an ongoing study that initiated promotor/a recruitment and training in December 2004. Preliminary results are expected in mid September 2005 with complete results available by the end of November 2005.

**Sponsor:** *USDHHS*

# EDUCATION

**600** **Presentation Type:** Poster

**Author:** Catherine Rhodes **Presentor:** Catherine Rhodes
**Department:** LIBRARY
**Classification:** Faculty (Not for Competition)
*Catherine Rhodes, M.L.I.S., Jay Shores, Ph.D., Daniel E. Burgard, M.S.L.I.S., A.H.I.P., Jerry Alexander, Ph.D., Don Peska, D.O. University of North Texas Health Science Center, Fort Worth, Texas 76107*

**PERCEPTION VS. REALITY: EFFECTIVENESS OF PROBLEM-BASED INFORMATICS TRAINING AS MEASURED BY STUDENTS' PERCEIVED VS. ACTUAL SKILLS IN SEARCHING MEDLINE**

**Purpose:** (1)To compare third-year medical students' perceived levels of MEDLINE search competence with their actual performance;(2)to determine the effectiveness of problem-based learning (PBL) in teaching students to search MEDLINE;(3)To determine the efficacy of using self-reports (S-R) and indirect computerized observations (ICO) to measure MEDLINE searching skills of MS3s.
**Methods:** The target population was 123 medical students in a required three-week clinical skills course at the beginning of their third year. Students completed a patient interaction scenario based on a problem-based learning model, which required them to locate literature pertinent to the case. Case Scenarios were posted sequentially on the Clerkship web page. Students emailed their search histories and selected citations to librarian facilitators in sequenced segments. After the case segments, students attended a review session where they viewed MEDLINE search demonstrations. Students completed online pre- and post-surveys and conducted the same sample search, videorecorded by screen-capturing software, at the beginning and end of the course.
**Results:** Ten skills from the survey were matched to observed performance in recorded searches, scored as either positive or negative. Analysis reveals:
1.Students believed that they possessed a greater amount of MEDLINE searching knowledge after the intervention than they did before it was given (p?.001)
2.Students performed significantly better following the intervention than they did before (p?.001)
3.Students' perceptions of their searching skills were significantly inflated when compared to their actual performance levels (p?.001)
4.The gap between perceived and observed skill levels was significantly greater after the intervention than it was before (p?.001)
**Conclusions:** Students' ability to judge their own MEDLINE searching skills is limited. Although students believe that they are aware of and can employ good search techniques, they do not use the concepts and tools required to return comprehensive and precise results. Also, while the students' abilities significantly increased on both the S-R and ICO (p ?.001) measures, the ICO provided more precise estimates of a student's MEDLINE searching skills than the S-R did. However, the PBL approach effectively raised both perceived and actual searching skill levels. Librarians should continue to instruct students in MEDLINE search skills and to refine teaching methods to help close the gap between perceived and actual skill levels.
**Sponsor:** *none*

**602** **Presentation Type:** Poster

**Author:** Barbara Adams **Presentor:** Barbara Adams
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*Barbara D. Adams, MSA, UNT Health Science Center, Fort Worth TX, 76107*
*Patti Pagels, MPAS, PA-C,UNT Health Science Center, Fort Worth TX, 76107*
*Karen Wood, MPH, UNT Health Science Center, Fort Worth TX, 76107*

**A BORDER HEALTH EXPERIENCE INCREASES CULTURAL SENSITIVITY**

**Purpose:** To determine the impact of a Spring Break trip to the west Texas border area on health profession students' (1) future practice plans and (2) knowledge about border health issues.
**Methods:** A total of 29 health professions students completed a pre- and post-experience survey instrument before and after the designated field trip. The quantitative portions of the pre- and post-survey data were analyzed to determine if there were any significant differences in how students responded to going on the trip compared to after returning from the trip. Wilcoxon matched-pairs signed rank tests quantified the magnitude of difference between pre- and post- responses and determined if those differences were statistically significant at the ? = 0.05 level. Two-tailed p-values are reported.
**Results:** There were significant results relating to career plans, knowledge of border area culture and border health issues. Pre-trip, 88% of students were unsaure about practicing medicine in the border area. Post-trip, shifts to "no" increased by 17% and "yes" by 14%. Pre-trip and post-trip comparisons showed that the number of students deciding against practicing in a rural area increased by 18%. Statistically significant increases were seen in the number of students who believed that border health issues are more of an international problem than a Texas problem and that a person's cultural beliefs are important to medical outcomes.The awareness of the significant impact that lack of basic sanitation and potable water has on border community health increased by almost 30 percent.Students also ranked the importance of specific issues that affect border community health in Texas. Results showed that there were statistically significant differences in the rankings of four out of six issues and that there was a shift in rankings. Lack of immunizations and lack of potable water/clean air were ranked as less important, while poverty/economics and cultural issues were ranked as more important than before the trip.

**Conclusions:** The field trip increased students' knowledge of border culture as it relates to population health and the delivery of healthcare. It also effected change in early career plans related to location.
(Financial support provided by the HETCAT, Texas Tech Office of Border Health,Grant number 1D39 PE00006-12, from Health Resources and Services Administration, DHHS.)
**Sponsor:** *HETCAT*

**601** **Presentation Type:** Poster

**Author:** Roberto Cardarelli **Presentor:** Roberto Cardarelli
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*Roberto Cardarelli, DO, MPH*
*Mark Sanders, DO, JD*
*Department of Family Medicine*
*Division of Education and Research*
*Center for Evidence-based Medicine*

**AMBULATORY TEACHING AND EVIDENCE-BASED MEDICINE: APPLYING CLASSROOM KNOWLEDGE TO CLINICAL PRACTICE**

**Purpose:** The hurdling block of getting students interested in evidence-based medicine (EBM) is the lack of applicability and practical experience in most medical school curriculums.Our purpose is to not re-iterate the steps of practicing EBM, but to provide realistic goals by presenting rational approaches on how to teach EBM in an ambulatory care setting. We came to the realization that certain steps of EBM can be accomplished during clinic, while other steps need to be performed when free time is available.
**Methods:** Suggestions were provided for each of the principles for practicing evidence-based medicine during the family medicine clerkship.
**Results:** Asking an answerable question:
For inquisitive students, we focus on helping the student to be less vague and more systematic using the PICO (Population, Intervention, +/- Comparison, and Outcome) format. Since each student's knowledge base differs, we need to probe on what they already know.
Searching for the evidence:
We do not need to "create" a clinical question for every patient we see. Students will mainly search for the evidence on their own free time. We have a list of web sites that are bookmarked on the computers. We teach students, as time permits, how to use the sites using the best search terms.
Appraising the Evidence:
We assume students have completed their EBM didactic course prior to starting clerkships. If not, more time is expected on your part. If needed, we recommend reading the Users' Guides to the Medical Literature that can be found at the Centres for Health Evidence web site. Consider looking through pre-appraised evidence from web sites like the American College of Physicians or the Journal of Family Practice POEMS.
Applying the evidence to the patient:
This last step is easily applied at the point-of-care. It helps to re-emphasize that we need to keep the entire context of the patient in mind prior to making and offering medical decisions.
**Conclusions:** Actively practicing EBM on every patient is not realistic. We are clinical experts and already have the inherent knowledge about the majority of the issues we face daily. We need to find a means to initiate EBM practice in the family medicine clerkship.
**Sponsor:** *None*

**604** **Presentation Type:** Poster

**Author:** Lisa Smith **Presentor:** Linda King
**Department:** LIBRARY
**Classification:** Faculty (Not for Competition)
*Lisa Smith, MLS*
*Linda King, MLS, AHIP*
*Gibson D. Lewis Health Science Library, UNT Health Science Center Fort Worth*

**ENHANCING INTERNAL MEDICINE RESIDENTS' INFORMATION ACCESS--USING PUBMED'S CLINICAL QUERIES, SYSTEMATIC REVIEWS, AND CUSTOMIZED SEARCH STRATEGIES**

**Purpose:** To provide Internal Medicine residents online access to citations of relevant topics in the medical literature to assist in their clinical decision making and enhance the education process.
**Methods:** The Lewis Library of the University of North Texas Health Science Center (UNTHSC) implemented a Clinical Librarianship Program in the summer of 2003. The goal of this program is to provide physicians with timely, evidenced-based information to improve patient care. To ensure residents continued access to current research information, a web site was developed to provide distributed access to relevant literature.

A web page was constructed which provides direct links to search results on frequently requested topics. Results of these MEDLINE searches allow residents to utilize current medical literature to complement their vertical file. Searches were developed utilizing the PubMed filters for clinical queries (therapy, diagnosis, etiology, and prognosis) and systematic reviews. Searches are limited to human studies, in English, entered into the MEDLINE database in the last 2 years.
**Results:** A demonstration of the web page and explanation of search strategies was conducted for morning report attendees in May 2004. The web page contains a link to PubMed for end-user searching, and selected Internal Medicine sites. The Reference phone number is displayed to encourage users to contact librarians to request searches or other assistance.
**Conclusions:** As the Clinical Librarianship Program is expanded, tailored web pages and resources will be developed for each participating residency program. Internet links to topical clinical research literature will provide residents an additional decision-making and educational tool.
**Sponsor:** *none*

# EDUCATION

**605** **Presentation Type:** Poster

**Author:** Carol Stehly, MS, MED **Presentor:** Carol Stehly, MS, MED
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**DUAL RESIDENCY TRAINING IN PRIMARY CARE/MASTER OF PUBLIC HEALTH**

**Purpose:** The purpose of this project is to train osteopathic family medicine residents in public health by residents completing a Master of Public Health degree program within the three-year family medicine residency program at the University of North Texas Health Science Center at Fort Worth/Texas College of Osteopathic Medicine/Plaza Medical Center. Although osteopathic physicians are well known for their roles as primary care physicians, there are no osteopathic medical schools that have systematically implemented a MPH curriculum as part of their family medicine residency training.

**Methods:** Rotations in a public health department and a research thesis, based on from the Healthy People 2010 objectives with a focus on health disparities and workforce development, will be the theme of the project. Starting in July 2005, four post-doctoral graduates that have been accepted into both the UNTHSC residency program as well as into the UNTHSC School of Public Health will begin public health curricular components. The specific objectives of the proposed project is to accomplish the BHPr objectives through developing a public health residency curriculum focused on health promotion/disease prevention. Forty-five total hours will be required to complete the MPH program.One of the required courses is the South Texas Environmental Education/Research class, in addition to 6 hours of public health clinical rotations. Specific public health medical and social issues will be addressed during core public health classes and a monthly Family Medicine Public Health Grand Rounds series. Additionally, residency MPH residents will conduct a research project under the mentorship of Family Medicine faculty, School of Public Health faculty and Tarrant County Public Health Department personnel. The research thesis will be related to the Healthy People 2010 objectives. The thesis is intended to reinforce and apply concepts of public health principals. Available databases will be used to facilitate the completion of a research project prior to graduation.

**Results:** Project evaluation will use a modified Stufflebeam approach, including context, input, process, and products (outcomes). This data will be analyzed and disseminated to departmental, institutional, and extramural audiences.

**Conclusions:** Presently there are two students enrolled. We project four residents per year will enroll. We anticipate this will enhance the residency training and prepare physicians for research and practice in public health related areas.

**Sponsor:** *HRSA Funding Submitted*

**606** **Presentation Type:** Poster

**Author:** Lisa Ireland **Presentor:** Lisa Ireland
**Department:** PHYSICIAN ASSISTANT STUDIES (PA Program)
**Classification:** TCOM MPAS Student
*Lisa Ireland, PA-S; Patti Pagels, PA-C, MPAS; Olive Chen, PhD; Jay Shores, PhD; University of North Texas Health Science Center, Fort Worth, Texas 76107-2699*

**A PROPOSED CURRICULUM DESIGN FOR A POSTPARTUM DEPRESSION WORKSHOP FOR CLINICIANS**

**Purpose:** Early recognition and treatment for patients with postpartum depression is of great importance. The purpose of this project was to design a workshop that would: 1) provide knowledge and tools to help clinicians determine risk factors, recognize signs and symptoms, and to be able to screen patients for postpartum depression and psychosis; and 2) provide clinicians information about current treatment options and interventions.

**Methods:** This proposed workshop is designed to be a Continuing Medical Education (CME) activity which consists of two one-hour interactive lectures and a one-hour case study workshop. The primary target audience in this workshop is clinicians who have contact with women who may be pregnant or plan to become pregnant, have contact with women of childbearing age, or women with children under the age of two years. The effectiveness of this workshop will be assessed by using pre and post workshop surveys and a follow-up survey six months after the workshop.

**Results:** There are three hours of curriculum included in this workshop. The first hour contains a motivational briefing by providing the prevalence, statistics, and the importance of recognizing postpartum depression. The main lecture consists of 1) Defining postpartum blues, depression, and psychosis; 2) Recognizing risk factors; 3) Recognizing major signs and symptoms; and 4) Developing a differential diagnosis; followed by: 1) Interviewing techniques and communication skills; 2) Screening tools; and 3) Treatment options for the second hour. The goal for the third hour is to apply learned knowledge to two case studies. This section includes practice in: 1) Developing a case-specific list of risk factors and interview questions by using two designed cases; 2) Analyzing results of screening tools for each case; and 3) Formulating an assessment and plan of action for each case.

**Conclusions:** It is anticipated that upon completion of the workshop, the participating clinicians will significantly increase their ability and confidence in assessing postpartum women for depression. Implementation of this workshop would be required to determine whether attending this workshop would result in improved recognition of postpartum women with depression.

**Sponsor:** *none*

# EDUCATION

607 **Presentation Type:** Poster

**Author:** John Bowling, DO **Presentor:** Barbara Adams, MSA
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*John R. Bowling, DO, UNT Health Science Center, Fort Worth, TX*
*Barbara D. Adams, MSA, UNT Health Science Center, Fort Worth, TX*

**PREPARING MEDICAL STUDENTS FOR A RURAL MEDICINE PRACTICE: THE PREDOCTORAL CURRICULUM IN RURAL MEDICINE**

**Purpose:** This presentation describes the proposed predoctoral rural medicine curriculum that is designed to prepare the osteopathic graduate for practice in a rural environment in the 21st century.
**Methods:** In the Spring of 2004 the Rural Medicine Curriculum Task Force was formed to address the need for an expanded curriculum that would focus on preparing Texas College of Osteopathic Medicine graduates for practice in a rural environment. Rural-based adjunct faculty, state and national experts in rural health and rural medical education, and faculty from various departments and schools within the Health Science Center were invited to be members of the Advisory Group or Work Group.

Building on the foundation of a successful community-based curriculum in rural family medicine implemented since 1996, the Task Force has developed an enhanced rural medicine curriculum. Initially a questionnaire was developed and sent to Advisory Group members for their input. The Work Group then met and established the mission and goals for the new curriculum. Subsequently, a workshop was held where members of the advisory group, work group, and other interested TCOM preceptors discussed issues related to rural practice, lifestyle and education. Following this workshop, subcommittees within the Work Group were formed to address didactic content, competencies, Year 3 and 4 clinical experiences, admissions policies and potential funding through grants.

**Results:** A 4-year parallel curriculum for Rural Medicine has been outlined.
**Conclusions:** The curriculum is scheduled for full implementation beginning with the class matriculating August 2006 (Class of 2010).
**Sponsor:** *None*

608 **Presentation Type:** Poster

**Author:** Michael Oglesby **Presentor:** Michael Oglesby
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** Faculty (Not for Competition)
*Michael W. Oglesby, Ph.D.1, Frank Papa, D.O., Ph.D.2, David Aldrich2, Bruce Dubin, D.O.3, Fredrick Schaller, D.O.3, Alvin Mathe, D.O.3, Tahir Tak, M.D.3*
*1Department of Pharmacology & Neuroscience, 2Department of Education, 3Department of Internal Medicine*

**USE OF A COMPUTER-BASED TOOL TO FACILITATE DIAGNOSTIC COMPETENCE**

**Purpose:** Medical educators are calling for objective evidence that students attain some minimal level of competence in knowledge-based tasks including differential diagnosis (DDX).
We recently instituted a program of training second-year medical students to perform DDX to specific competence levels for five problems across two courses (Cardiovascular and Respiratory).
**Methods:** Demonstrated competence in DDX was required of students for the problems of Chest Pain, Leg Pain, Murmur, Dyspnea and Hemoptysis. Between 6-9 diseases served as the differentials in each problem. Training was conducted with the aid of an artificial intelligence tool (KBIT, Knowledge Based Inference Tool), which was programmed to provide training cases that were highly typical of the 6-9 disease differentials represented in each problem. Immediately following training, a series of test cases were randomly presented. In order to achieve objective evidence of 'performance to competence,' students had to diagnose all diseases correctly at least once plus also correctly diagnose 8 of 10 consecutive cases.
**Results:** A total of 121 students attempted the 5 problem spaces (data from 117 are available). Students performed DDX to criterion quickly: approximately two more cases than the minimum possible were all that were necessary to reach criterion (number of cases beyond minimum ranged from 1.4 to 2.3, and averaged 1.9; means did not differ significantly across problems). The time to achieve criterion was rapid, although there was significant variability. Across all problems the mean time (+ S.D.) to achieve competence was 31.5 + 19.3 minutes/problem.
**Conclusions:** These data document that second-year medical students who are tutored by KBIT can become proficient in a short period of time at performing differential diagnosis; in addition, KBIT can be used to provide objective, criterion-based measures of diagnostic competence.
**Sponsor:** *None*

609 **Presentation Type:** Poster

**Author:** Eric Sims **Presentor:** Henry Lemke
**Department:** PHYSICIAN ASSISTANT STUDIES (PA Program)
**Classification:** TCOM MPAS Student
*Eric Sims, PA-S;*
*Henry Lemke, MMS, PA-C;*
*Olive Chen, PhD;*

*Fort Worth, TX 76107*

**THE INFLUENCE OF PRIOR EDUCATION, MENTOR, AND EMPLOYMENT EXPERIENCE AS PRACTICE SETTING DETERMINANTS OF PHYSICIAN ASSISTANTS IN TEXAS**

**Purpose:** This study intended to identify how education, mentor, and employment experiences prior to entry into PA school would effect predicting a PA's choice of practice setting after graduation.
**Methods:** A total of 1,288 practicing PAs who were members of the Texas Academy of Physician Assistants (TAPA) were electronically solicited to participate in an online survey. The survey consisted of 21 questions, 15 items reflecting the potential influences of education, mentors, and/or employment experience prior to entry into PA school on choice of practice setting, and 6 demographic questions. SPSS (11.5) was used to perform descriptive statistics and discriminant analysis. Data was collected from late August to mid-September 2004.
**Results:** A total of 255 PAs responded to the survey for an overall response rate of 21%. Among the 3 potential influences (education, mentor, and employment experience), employment experience can best predict PAs' practice setting choice after PA school (Wilks' ?=0.890, p<0.001). Prior experience in working with patients was a better predictor for choosing primary care practice settings (Wilks' ?=0.709, p<0.001), and prior experience in working with technology was a better predictor for choosing non-primary care practice settings (Wilks' ?=0.822, p<0.001).
**Conclusions:** The results of this survey indicated that employment experience prior to PA school seems to be able to better predict what practice setting a PA will choose after graduation. Questions could be added to PA schools' supplemental applications that focus on applicants' prior employment experience. These prior employment questions could help PA schools whose primary intent is to recruit students interested in primary care practice settings due to the current shortage of practitioners there. The other two factors (prior education or mentor experience) did not show predictive value on PAs' choice of practice setting, most likely due to the timing of the influences and the fact that experiences prior to PA school are overshadowed by those taking place during PA school. Further studies are required to determine the influences of these factors.
**Sponsor:** *None*

610 **Presentation Type:** Poster

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**SOAP ORE© NOTE AS TEACHING TOOL FOR OSTEOPATHIC MEDICAL STUDENTS**

**Purpose:** In 2004, the American Board of Osteopathic Medical Examiners (ABOME) implemented a new addition to step 2 of the Comprehensive Osteopathic Medical Licenses Examination (COMLEX), the Clinical Simulated Examination. This requires student adequately perform a history and physical exam and appropriately document the clinical encounter. A component of this clinical encounter is to perform and adequate osteopathic examination, diagnosis and treatment. Without these components passage of this portion of the COMLEX is unlikely.
**Methods:** To ensure osteopathic medical students remember these components a progress note mnemonic was created called the SOAP ORE© Note. This mnemonic stands for :S (subjective findings), O (objective findings), A (assessment), P (plan), O (osteopathic treatment), R (return to clinic) and E (education). Osteopathic medical students were instructed on the utilization of this format of progress note for their clinical medicine encounters. They were instructed to always formulate an osteopathic treatment, therefore must formulate an osteopathic assessment. This should necessity an osteopathic objective finding to back up their assessment. They were assigned cases and required to complete a SOAP ORE© Note throughout their first year of undergraduate medical education.
**Results:** Students will have completed multiple practice SOAP ORE© Notes during their first year of undergraduate medical education which should lead to application of osteopathic principles in each clinical encounter throughout their career. This should ensure adequate osteopathic findings, assessments and treatments to successfully complete the simulated clinical encounter of their national board examination.
**Conclusions:** Creating means for osteopathic medical students to easily remember to include osteopathic principles in their practice is essential to ensure successful completion of their board examination. This assists them in the completing the goal of becoming a licensed physician. Regardless of specialty all osteopathic students must master this type of progress note.
**Sponsor:** *none*

700 **Presentation Type:** Poster

**Author:** SHAOQING HE **Presentor:** SHAOQING HE
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**INVOLVEMENT OF ERK-MAPK AND PKC IN THE EXPRESSION OF MATRIX METALLOPROTEINASES (MMPS) AND TISSUE INHIBITORS OF METALLOPROTEINASES (TIMPS) 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 & 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. We have previously reported that ERK-MAPK and PKC are involved in endothelin-1-induced signaling in astrocyte proliferation and reactivation. In the present study, the expression of MMPs and TIMPs in ET-1-activated astrocytes and the role of ERK-MAPK and PKC were determined.
**Methods:** 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. Phosphorylation of ERK1/2 was detected by Western blot analysis.
**Results:** ET-1 caused a rapid phosphorylation of ERK1/2, which could be blocked by treatment with U0126 (a MEK1/2 inhibitor), in both U373MG cells and hONA cells. ET-1 increased the expression and activity of MMP2, which could be blocked by U0126. U0126 blocked even basal expression as compared with vehicle-treated control. In hONAs, expression of MMP3 was not detectable in Western Blot, however, activity of MMP3 was seen using casein zymography. Blockade of ERK-MAPK by U0126 and PKC by chelerythrine increased the activity of MMP3. In U373MG cells, there was no detectable MMP3 by both zymography and Western Blot. In both cell types, treatment of ET-1 increased the expression of TIMP-1 and 2. ERK-MAPK blockade by U0126 not only abolished the ET-1 effects, but also lowered the basal level of expression of TIMP-1 and 2. Furthermore, there were no apparent differences in the profile of expression of MMPs and TIMPs in hONA cells form normal human and POAG patients.
**Conclusions:** ET-1 activated phosphorylation of ERK1/2, which plays an important role in proliferation and reactivation for hONAs and U373MG astrocytoma cells. ET-1 also increased the expression of MMP2 and TIMP-1, 2. ERK-MAPK and PKC are involved in the regulation of remodeling of ECM in both cell types. Balance of MMPs/TIMPs may be important relative to ET-1 treatment. In future studies, the temporal and spatial regulation of MMPs and TIMPs induced by ET-1 will be investigated.
**Sponsor:** *non*

701 **Presentation Type:** Poster

**Author:** Kissaou Tchedre **Presentor:** Kissaou Tchedre
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**NEUROPROTECTIVE SIGMA LIGANDS PROTECT RGC-5 CELLS FROM GLUTAMATE-INDUCED NEUROTOXICITY**

**Purpose:** The purpose of these studies was to study the effect of sigma receptors on retinal ganglion cells, which offer a unique and compatible model to study the mechanism of neurodegenerative disease such as glaucoma progression.
**Methods:** Differentiated and undifferentiated retinal ganglion cells (RGC-5) were used to determine first the expression of sigma receptors and second sigma ligands and neursosteroids that have neuroprotective actions. Reverse transcriptase polymerase chain reaction (RT-PCR) was used to verify the presence of the sigma receptor message (mRNA) in RGC-5 cells. A DNA fragmentation technique was used to assess retinal ganglion cell apoptosis after treatment with 1mM glutamate for 24 hours. Cells were treated with either sigma ligands (1,3-Di-o-tolylguanidine (DTG), Haloperidol, (+)-N-Allylnormetazocine hydrochloride [(+) SKF10047]) or endothelin-1 for 1 hour before glutamate treatment.
**Results:** Reverse transcriptase polymerase chain reaction (RT-PCR) have shown the expression of sigma receptors in both differentiated and undifferentiated RGC-5 cells. 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.
**Conclusions:** Sigma ligands (DTG, 10 uM) and (+) SKF10047, 10uM) protected differentiated RGC-5 cells from apoptosis compared to haloperidol (10uM), which fails to protect differentiated RGC-5 cells from apoptosis.
**Sponsor:** *none*

702 **Presentation Type:** Poster

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**TRANSFORMED RAT RETINAL GANGLION (RGC-5) CELLS RESPOND TO GLUTAMATE AFTER CO-CULTURE WITH HUMAN NON-PIGMENTED CILIARY EPITHELIAL (HNPE) CELLS**

**Purpose:** Previously we have shown that transformed rat retinal ganglion (RGC-5) cells undergo a morphological change indicative of a differentiated phenotype, after co-culture with human non-pigmented cilliary epithelial (HNPE) cells. These differentiated RGC-5 cells have exhibited an consistent increase in intracellular calcium ([Ca2+]i) in response to 100 mM NMDA as shown by Fura-2 imaging and whole cell patch clamping. The purpose of this study was to determine if the differentiated RGC-5 cells respond to glutamate treatment and to evaluate the expression of Thy-1 and Brn-3b, which are known markers of retinal ganglion cells.
**Methods:** HNPE cells were seeded on collagen inserts and placed over RGC-5 cells seeded on glass coverslips in 6-well plates. After 3 days of co-culture the wells were observed by light microscopy for morphological changes. Changes in [Ca2+]i were measured in response to 50mM, 250mM, and 500 mM glutamate using Fura-2 imaging in the presence or absence of 10mM MK-801, a NMDA receptor antagonist. Immunocytochemistry was performed using antibodies against Thy-1 and Brn-3b.
**Results:** After co-culture the [Ca2+]i of RGC-5 cells increased in response to 50mM, 250 mM, and 500 mM glutamate. Pretreatment with 10mM MK-801 inhibited the glutamate-induced increase in [Ca2+]i. The morphologically different RGC-5 cells continued to express Thy-1 and Brn-3b.
**Conclusions:** RGC-5 cells upon co-culture with HNPE cells develop a differentiated phenotype which is responsive to glutamate. The glutamate-induced increases in [Ca2+]i was inhibited by MK-801, a NMDA receptor antagonist. Although these cells change morphology, they continue to express Thy-1 and Brn-3b. Further characterization of these cells and the channels involved are currently being conducted using whole cell patch clamping.
**Sponsor:** *EY11979*

703 **Presentation Type:** Poster

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**CELLS ISOLATED FROM THE HUMAN OPTIC NERVE HEAD ARE CAPABLE OF RESPONDING TO EXOGENOUS BMP-4 VIA RECEPTOR SMADS**

**Purpose:** Bone morphogenetic proteins (BMP) are members of the TGF beta family of growth factors and initiate signaling via binding to cell surface type I and type II serine/threonine kinase receptors. The type II BMP receptor is a constitutively active kinase that transphosphorylates the type I BMP receptor upon ligand binding. Receptor regulated
Smads (Smad1, Smad5, and Smad8) transiently associate with the type I BMP receptor and undergoes direct phosphorylation. Subsequently, the phosphorylated receptor Smad associates with a common Co-Smad4 and the heteromeric complex translocates to the nucleus to regulate target genes. We have previously demonstrated that cells isolated from the human optic nerve head (ONH) express mRNA and protein for BMP receptors. The purpose of this study was to determine if ONH cells express both receptor and common Smad(s) and respond to exogenous BMP-4.
**Methods:** Well-characterized human ONH astrocytes (N=5) and lamina cribrosa (LC) cells (N=5) were treated with exogenous BMP-4 (20ng/ml) for various times. Intracellular localization of Smad6, Smad7, Co-Smad4 proteins in ONH astrocytes and LC cells was studied via immunocytochemistry. In addition, Co-localization of phoshorylated Smad 1 (pSmad1) and phosphorylated Smad1, 5, 8 (pSmad1, 5, 8) were studied. Western blot analysis was used
to determine total Smad1, Smad5, Co-Smad4, smad6, phosphorylated Smad1 and phosphorylated Smad1, 5,8.
**Results:** Immunocytochemistry demonstrated increased co-localization of pSmad1 and Smad4 when ONH astrocytes and LC cells were treated with BMP-4. Immunocytochemistry also demonstrated increased cytoplasmic localization of Smad6 when ONH astrocytes and LC cells were treated with BMP-4. Western blot analysis demonstrated the presence of R-Smad1, R-Smad5 and Co-Smad4 proteins in cell lysates of both ONH astrocytes and LC cells. Western blot analysis also demonstrated R-pSmad1 and R-pSmad1, 5 ,8 proteins in cell lysates of both ONH astrocytes and LC cells. Exposure to BMP-4 for 10 minutes, 30 minutes, 60 minutes and 2 hours caused an increase in p-Smad1 and pSmad1, 5. Western blot analysis also demonstrated increased smad4 proteins when ONH astrocytes and LC cells were treated with BMP-4.
**Conclusions:** These studies demonstrate that ONH astrocytes express Smad1, Smad5, Smad6 and Smad4 and are capable of responding to exogenous BMP-4 via receptor Smads. Thus, cells of the ONH may be targets for and respond to locally released BMP.
**Sponsor:** *NIH Grant EY12783 and Alcon Research Ltd., Forth Worth, TX.*

# EYE/VISION

**704** **Presentation Type:** Poster

**Author:** Allison Heath **Presentor:** Allison Heath
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**MICROSCOPIC AND IN VITRO ANALYSES OF RAT AND HUMAN RETINAL PROGENITOR CELLS**

**Purpose:** The principal objective of this research is to characterize virally-transformed rat and human retinal progenitor cells following stimulation by retinal pigment epithelial (RPE) cell secreted proteins and by immunocytochemistry and scanning electron microscopy. To date, therapy for patients suffering from age-related macular degeneration (ARMD) and retinitis pigmentosa (RP) has not been successfull. The ultimate goal of this work is to transplant stimulated progenitor cells into diseased retinas to restore sight.

**Methods:** Progenitor cells were isolated from explants of postnatal day 2 rat and fetal human retinas that were cultured in proteins secreted by neonatal rat RPE cell in vitro. Isolated progenitor cells were cloned, analyzed by microscopy and immunocytochemistry, and following growth factor stimulation.

**Results:** Rat and human progenitor cells grown in serum expressed the PAX6 transcription factor, which is indicative of immature cells. In addition, rat progenitor cells expressed vimentin and nestin, both markers for immature retinal cells. When examined by scanning electron microscopy, rat progenitor cells showed a flat cell body with multiple processes or a small round cell body with few processes. Rat and human progenitor cells grown in RPE secreted proteins or basic fibroblast growth factor (FGF-2) formed small clusters, but did not exhibit processes. However, when these clusters were grown in serum, the progenitor cells proliferated and showed process formation. Progenitor cells were also grown in serum supplemented with RPE secreted proteins. Cells grown under these conditions proliferated and showed processes; however, the cellular response was not as significant as when progenitor cells were grown in serum alone. Furthermore, progenitor cell populations were cloned from single rat progenitor cells. Progenitor cells from these clones expressed PAX6 and the FGF-2 receptor flg and have been grown to passage 7.

**Conclusions:** The rat and human progenitor cells described in this work have an unique, immature character that under the influence of specific growth factors may be useful in transplantation therapy in diseased retinas of ARMD and RP patients.

**Sponsor:** *None*

**705** **Presentation Type:** Oral

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**17BETA-ESTRADIOL ATTENUATES MITOCHONDRIAL DEPOLARIZATION IN POLYOL-STRESSED CULTURED LENS EPITHELIAL CELLS**

**Purpose:** Lens epithelium cultured in high extracellular galactose converts the aldose sugar to its respective sugar alcohol, galactitol (GalOH), via aldose reductase (AR). This study determined the consequence of GalOH accumulation on mitochondrial membrane potential(MMP) and if estrogen (17beta-E2) or the AR inhibitor (ARI), Sorbinil administered prior to and concomitant with galactose exposure might prevent or delay mitochondrial depolarization.

**Methods:** Normal secondary cultures of bovine lens epithelial cells (BLECs) and a virally-transformed human lens epithelial cell line (HLE-B3) were maintained in 40 mM galactose (Gal). Endogenous accumulation of reactive oxygen species (ROS) was assessed by loading cells with DCFH-DA which upon oxidation in the presence of ROS becomes the fluorescent compound DCF. In order to assess MMP, the potentiometric fluorescent dye, JC-1 was used in conjunction with confocal microscopy. Red fluorescence indicates polarization; green fluorescence is typical of mitochondrial depolarization. 17beta-E2 as well as its isomer, 17alpha-E2 (which exhibits marginal binding affinity for estrogen receptor) as well as the ARI, Sorbinil were administered to the cell cultures to determine their comparative protective effects. Eight random confocal images per treatment were evaluated for green/red fluorescence ratio in order to determine the extent of mitochondrial membrane depolarization after 3 days of Gal ± estradiol or ARI.

**Results:** BLECs more so than HLE-B3 cells accumulate high intracellular levels of GalOH with exposure to ambient Gal. BLECs were significantly depolarized while HLE-B3 cells showed little to no depolarization over the same course of Gal exposure. Intracellular accumulation of ROS exhibited marginal increase over control cells in BLECs and was similar to levels seen with estradiol or ARI administration. The addition of either 17alpha-E2 or 17beta-E2 to BLECs over a dose range of 0.01 ?M to 1.0 micromolar completely prevented mitochondrial membrane potential depolarization, as did the addition of Sorbinil.

**Conclusions:** Polyol accumulation promotes mitochondrial depolarization and the decrease in MMP is prevented by prior treatment and co-administration of estradiol or ARI with Gal. Estradiol is not acting as an ARI nor can the Gal-induced depolarization be attributed to intracellular ROS production. Results with 17alpha-E2 suggests that the stabilization of MMP against polyol accumulation is mediated via an estrogen receptor-independent mechanism.

**Sponsor:** *EY05570*

**706** **Presentation Type:** Poster

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**MECHANISM OF ESTROGEN-MEDIATED CYTOPROTECTION AGAINST OXIDATIVE INSULT: INCREASED SEQUESTRATION OF MITOCHONDRIAL CALCIUM**

**Purpose:** Multiple defense mechanisms assemble at a point of regulation of mitochondrial control to provide a mitochondrial defense state which puts forward antioxidative cytoprotection against acute oxidative stress. These diverse systems involve a complex convergence of genomic and non-genomic associations; including, but not limited to, 17?-estradiol (17?-E2)-induced activation of signal transduction survival pathways and regulation of mitochondrial calcium homeostasis so as to prevent opening of the mitochondrial permeability transition pore. Herein we illustrate how 17?-E2 is cytoprotective against oxidative insult which triggers excessive sustained increase in intracellular calcium ([Ca2+]i).

**Methods:** HLE-B3 cells were grown on 25mm cover slips and the cells preincubated with 17?-E2 (1 μM) or vehicle for 24 hrs prior to the bolus addition of 300 ?M H2O2 and intracellular calcium movement monitored by Fura-2 imaging (n=70 cells per treatment).

**Results:** 17?-E2 pretreatment of HLE-B3 cells lessened the peroxide-induced sustained [Ca2+]i in spite of the fact that the hormone initially potentiates the influx of Ca2+ induced by peroxide.17?-E2-induced attenuation of [Ca2+]i is mediated through the increased uptake and accumulation of Ca2+ into mitochondria. Similar results with 17?-E2 indicate that the regulation of mitochondrial Ca2+ transport is an estrogen receptor-independent function. Mitochondrial sequestration of Ca2+ is blocked by the administration of antimycin, which nullifies mitochondrial membrane potential, thus preventing mitochondrial Ca2+ transport.

**Conclusions:** The 17?-E2-induced attenuation of peroxide-induced sustained [Ca2+]i puts forward a novel mechanism which confers cellular protection against oxidative stress through a process of increased mitochondrial sequestration of cytosolic Ca2+. Estradiols exert their protective effects (against oxidative stress), at least in part, by stimulating mitochondrial Ca2+ transport and adjusting, to a higher-level set point, mitochondrial tolerance for Ca2+ load, thereby preventing apoptotic and/or necrotic forms of cell death that are associated with mitochondrial dysfunction otherwise initiated by disproportionate Ca2+ overload. These data establish a new mechanistic role for antioxidants and identifies novel approaches for targeting mitochondrial function to reduce oxidative stress.

**Sponsor:** *EY05570*

**708** **Presentation Type:** Poster

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**INVOLVEMENT OF MITOGEN ACTIVATED PROTEIN KINASE- C-JUN N-TERMINAL KINASE AND P38 MAP KINASE IN ENDOTHELIN-1 MEDIATED APOPTOSIS OF RAT RETINAL GANGLION CELLS**

**Purpose:** Previous Studies from our laboratory have shown ET-1 treatment promotes apoptosis of cultured rat retinal ganglion cells. The purpose of this study was to determine the involvement of C-Jun-N-terminal kinase (JNK1/2) and p38 mitogen activated protein kinase (p38 MAP kinase) in the ET-1 mediated apoptosis of rat retinal ganglion cells

**Methods:** Virally transformed rat retinal ganglion cells (RGC-5) were synchronized by thymidine treatment, which blocks the cells at G0/G1 phase of the cell cycle. The synchronization was confirmed by flow cytometric analysis of the DNA content. The synchronized RGC-5 cells were treated with ET-1 (100nM) a dose selected from previous dose response study, for either 5,10,15 & 30 min or long-term treatments for 12, 18 & 24 hours. The synchronized RGC-5 cells were pre-treated for 30 min with SB203580 (10?M) a specific p38 MAP Kinase inhibitor, BQ788 (1?M), a selective ETB receptor antagonist and BQ 610 (1?M), a selective ETA receptor antagonist and subsequently treated with ET-1 (100nM) for 5 min. Activation of JNK1/2 and p38 MAP kinase were determined by immunoblotting using anti phospho JNK1/2 and anti phospho p38 MAP kinase antibodies. In-vitro p38 MAP kinase activity assays were carried out using ATF-2 as substrate in the presence of ?32P. The kinase assay samples were separated by SDS/PAGE (10%) and radioactivity incorporated into ATF2 was detected by autoradiography.

**Results:** The synchronized cells had a greater number of cells in the G0/G1phase (95%) versus the unsynchronized cells (80%). More consistent results were obtained in the phosphorylation of p38 MAP kinase using the synchronized RGC-5 cells. An increase in the p38 phosphorylation as early as 5 min was observed following ET-1 (100nM). A corresponding increase in ATF-2 phosphorylation at 5 min was observed as determined by the In-vitro kinase activity assay. The activation of p38 MAP kinase by ET-1 was appreciably blocked in the cells pre-treated with SB203580. An increase in JNK1/2 phosphorylation was observed following ET-1 (100nM) treatment for 5, 10 min and a subsequent increase at 24 hrs. The activation of JNK1/2 was reduced in cells pre-treated with BQ788 a selective ETB receptor antagonist.

**Conclusions:** ET-1 mediated apoptosis in RGC-5 cells appears to be mediated through an ETB receptor - activated JNK1/2 and p38 MAP kinases.

**Sponsor:** *EY11979*

# EYE/VISION

709 **Presentation Type:** Poster

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**NEUROPROTECTIVE MECHANISMS OF THE NON-FEMINIZING ESTROGEN ANALOGUE ZYC-3 AGAINST GLUTAMATE INDUCED CYTOTOXICITY OF RGC-5 CELLS**

**Purpose:** To determine the neuroprotective mechanisms of the novel estrogen analogue, ZYC-3, against glutamate induced cytotoxicity of rat retinal ganglion cells (RGC-5 cells).

**Methods:** RGC-5 cells were pretreated with ZYC-3 followed by an insult with L-glutamic acid (5 mM). Cell viability was assessed using the neutral red dye uptake assay. Glutamate/cystine anti-porter levels and function, ?-glutamylcysteinsynthetase levels, buthionine-sulfoxamine cell viability studies, and glutathione levels were used to determine the ability of ZYC-3 to affect the glutathione synthesis pathway. ZYC-3's ability to effect mitochondrial membrane potential against glutamate challenge was determined using live cell confocal microscopy with JC-1mitochondrial dye. Modulation of pro versus anti-apoptotic signaling cascades by ZYC-3, were examined by inhibitor studies and Western blot analysis

**Results:** ZYC-3 treatment enhanced 35S-cysteine uptake, enhanced ?-glutamylcysteinsynthetase levels, and attenuated glutathione loss in glutamate challenged RGC-5 cells. Furthermore, cell viability was comparable to control in these studies, reiterating ZYC-3's neuroprotective capability. ZYC-3 pretreament prevented loss of mitochondrial membrane potential observed with glutamate challenge of RGC-5 cells. ZYC-3 promoted cell survival signals: Bcl-2 levels and activation of the Akt pathway were significantly enhanced in RGC-5 cells pretreated with ZYC-3.

**Conclusions:** The non-feminizing estrogen analogue ZYC-3 protects RGC-5 cells against glutamate induced cytotoxicity by protecting the glutathione synthetic pathway, preventing loss of mitochondrial membrane potential, and activating cell survival signaling cascades. These are the first such reports for a non-feminizing estrogen analogue. The data support the hypothesis that ZYC-3 may be useful in the neuroprotection of retinal ganglion cells in ocular pathologies such as glaucoma.

**Sponsor:** *NIH-NIA*

710 **Presentation Type:** Poster

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**IN VITRO EFFECT OF BMP-4 ON TRABECULAR MESHWORK CELLS**

**Purpose:** The transforming growth factor beta (TGF beta) superfamily consists of bone morphogenetic proteins (BMPS), TGF beta, and activins. Bone morphogenetic protein 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 whole complex translocates from the cytoplasm into the nucleus. The BMPs are regulated at the extracellular and intracellular level. At the extracellular level, BMP assocated proteins act as BMP antagonists. BMP associated proteins include gremlin. BMP antagonists bind directly to BMPs interfering with the ligand-receptor interaction. Another class of BMP regulators is Smurf-1 an ubiqitin ligase. Smurf-1 targets BMP specific Smads for degradation. We have previously demonstrated that trabecular meshwork cells (TM) express mRNA and protein for BMP and their receptors. The purpose of this research is to determine the effects of exogenous BMP-4 on the expression of gremlin, Smurf-1, and TGF beta 2.

**Methods:** Human TM cells were grown until approximately 80% confluent and treated with BMP-4 (20ng/ml) in 0.5% media for various times. Untreated cell lines acted as controls. Western Blot analysis was used to demonstrate the presence of gremlin, Smurf-1, and TGF beta 2.

**Results:** Protein expression for gremlin, Smurf-1, and TGF beta 2 is present in human TM in both normal (N=3) and glaucomatous cells (N=3). There were increased levels of gremlin and Smurf-1 in glaucomatous cell lines compared to normal. In addition cells treated with exogenous BMP 4 demonstrated an increase in TGF beta 2 at various time points compared to controls.

**Conclusions:** These studies demonstrate that human TM express protein for gremlin, Smurf-1, and TGF beta 2. In addition exogenous BMP-4 treatment causes an increase in protein level for TGF beta 2 by TM cells.

**Sponsor:** *Alcon Research Ltd., Forth Worth, TX.*

711 **Presentation Type:** Poster

**Author:** Oloruntoyin Mafe **Presentor:** Oloruntoyin Mafe
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**LOCALIZATION OF INOSITOL 1, 4, 5-TRISPHOSPHATE RECEPTORS IN MOUSE RETINA GANGLION CELLS**

**Purpose:** Inositol-1, 4, 5-triphosphate receptors (IP3Rs) are intracellular Ca2+ channels known to be involved in several intracellular signaling pathways. IP3R mediated changes in cytosolic Ca2+ concentrations control neuronal functions ranging from synaptic transmission to differentiation and apoptosis. Similarly, retinal ganglion cell physiology and pathophysiology is determined by cytosolic Ca2+ transients. Determining the distribution of biophysically distinct IP3Rs in retina ganglion cells provides necessary information on the molecular substrates of IP3R mediated Ca2+ signaling in these interneurons.

**Methods:** Primary cultures were prepared using acute isolation of retinal ganglion cells from adult mouse followed by enzymatic and mechanical dissociation. Cell cultures were maintained for 14 days. Cryosections of adult mouse retina were prepared and immunocytochemical labeling of IP3Rs in cultured retinal ganglion cells and of retinal ganglion cells in vertical sections of the retina was carried out using isoform specific antibodies and was detected with fluorescence microscopy. Retinal ganglion cells were identified by the use of morphological criteria and retinal ganglion cell specific immunocytochemical markers.

**Results:** Retinal ganglion cell morphology and immunoreactivity to neurofilament 68 kDa and Thy1.1 were identified in both retinal ganglion cell primary cultures and tissue cyosections. Retinal ganglion cells showed differential distribution of IP3R isoforms 1, 2, and 3.

**Conclusions:** Expression of all three IP3Rs by retinal ganglion cells indicates that all IP3R types potentially play a role in Ca2+ homeostasis and Ca2+ signaling in these cells. Differential localization of IP3 receptor subtypes may be an important molecular mechanism by which retinal ganglion cells organize their cystosolic Ca2+ signals. These data will help to delineate the potential involvement of IP3R channels in signal processing and neuroprotection of retinal ganglion cells.

**Sponsor:** *NIH grant EY14227*

712 **Presentation Type:** Oral

**Author:** Everett Nixon **Presentor:** Everett Nixon
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**Classification:** GSBS Student
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**DIFFERENTIALLY DISTRIBUTED IP3 RECEPTORS AND A NEW ROLE FOR GROUP I MGLUR IN THE RETINA**

**Purpose:** Inositol (1,4,5)-trisphosphate receptors (IP3R) contribute substantially to cytosolic free calcium ion (Ca2+) concentration transients and thereby modulate neuronal function. The present study was undertaken to determine the contribution of IP3R to the function of rod bipolar cells in the retina.

**Methods:** Immunoreactivity for IP3Rs in rod bipolar cells from mouse retinas was detected using immunocytochemistry. Intracellular Ca2+ concentrations were optically recorded in acutely isolated rod bipolar cells and biophysical properties of IP3Rs were analyzed with single channel electrophysiology.

**Results:** The distribution of IP3R isoforms was correlated with cytosolic Ca2+ transients induced by activation of group I metabotropic glutamate receptors (mGluRs) and with biophysical properties of differentially expressed IP3Rs.

**Conclusions:** The differential distribution of IP3Rs is used by rod bipolar cells to convey Ca2+ signals that are distinct in their duration, amplitude and kinetics at the sub-cellular level, and that serve the functions of individual sub-cellular compartments. Group I mGluR initiated Ca2+ signaling indicates a novel potential mechanism for the adaptation of the ON-pathway of vision and for coincidence and threshold detection in retinal neurons.

**Sponsor:** *UNTHSC Intramural Research Program, and NIH/NEI Grant EY014227*

715 **Presentation Type:** Poster

**Author:** Erin Roney **Presentor:** Erin Roney
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**KINASE DEPENDENT DIFFERENTIATION OF A TRANSFORMED RAT RETINAL GANGLION CELL LINE, RGC-5**

**Purpose:** Recently, RGC-5 cells were identified as a useful in vitro model of retinal ganglion cells (RGCs). These cells have certain characteristics of native RGCs as they are positive for several RGC specific markers such as thy-1 antigen, Brn3-C, neuritin, NMDA-R and negative for GFAP (Muller cell marker); 8A1 (retinal horizontal cells marker), and HPC-1 (amacrine cell marker). In spite of these markers, the RGC-5 cells morphologically do not look like neuronal cells and lack characteristic electric currents. Therefore, the purpose of this study was to determine if staurosporine, a broad range kinase inhibitor would result in differentiation of RGC-5 cells.

**Methods:** RGC- 5 cells were cultured in 24 well tissue culture dishes and treated with various concentrations (50 nM to 1 uM) of staurosporine for 24 hrs. The cells were then observed under the microscope for morphological changes. To establish the specificity of the kinase dependent differentiation of RGC-5 cells, several kinase inhibitors were used. Immunocytochemistry was used to establish if differentiation of RGC-5 cells resulted in increased levels of thy-1 antigen. Furthermore, to determine the extent of glutamate cytotoxicity, staurosporine treated and untreated control RGC-5 cells were incubated with various concentrations of glutamate and the cell viability following glutamate treatment was determined by using a neutral red dye uptake assay.

**Results:** Treating the cells with staurosporine caused the RGC-5 cells to differentiate with characteristic long neurite processes. The differentiated cells had higher levels of thy-1 antigen. The rho kinase and protein kinase inhibitors did not differentiate these cells. Staurosporine induced differentiation resulted in enhanced glutamate sensitivity as compared with the control untreated RGC-5 cells.

**Conclusions:** Staurosporine differentiated RGC-5 cells offer an useful alternative to primary RGCs.

**Sponsor:** *none*

716 **Presentation Type:** Poster

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**ADULT RETINAL STEM CELLS RESCUE RPE CELLS FROM PHOTO-OXIDATIVE DAMAGE VIA SECRETED MOLECULES**

**Purpose:** Age-related macular degeneration (AMD), the most common cause of irreversible vision loss in the elderly, results mainly from photo-oxidative damage to the retinal pigment epithelium (RPE) and concomitant photoreceptor cell apoptosis due to loss of RPE trophic support. Inspite of several therapeutic modalities proposed for AMD, including transplantation of embryonic stem (ES) cells into the retina, the treatment of AMD remains unsatisfactory. Stem cell transplantation mostly requires driving the uncommitted ES cells to differentiate and replace specific degenerating neurons. However, recent studies suggesting stem cells as a source of trophic factors in damaged murine hearts led us to investigate the potential of retinal stem cell-derived factors in protecting RPE cells from photo-oxidative damage.

**Methods:** Adult stem cells isolated from human donor retinas (hRPCs) were expanded in vitro and characterized for stemness by immunoblotting and RT-PCR analysis. The effects of photo-oxidative damage on a human RPE cell line (BHR cells) were investigated in the presence or absence of 48h-conditioned media from hRPCs using intense light exposure and a hydrogen peroxide-generating system utilizing glucose oxidase/glucose. Cell survival was determined by MTS assay and fluorescent dyes (calcein AM and ethidium homodimer). JC-1 labeling was employed to determine mitochondrial membrane permeability changes during hRPE cell death.

**Results:** Cultured hRPCs rapidly proliferated and formed ball-like clusters (neurospheres) in the presence of growth factors such as basic fibroblast growth factor and epidermal growth factor. Immunoblotting and RT-PCR analysis showed expression of nestin (marker for neuronal stem cells), pax6 (marker for retinal progenitor cells), and neurofilament 68 (marker for immature neurons) in hRPCs. However, consistent with their undifferentiated phenotype, hRPCs expressed low levels of mature retinal cell markers using antibodies such as Rho4D2 (rod photoreceptors), 7G6 (cone photoreceptors), GFAP (Müller glia), or glutamine synthetase (astrocytes). Conditioned medium of hRPCs distinctly inhibited RPE cell death and collapse of mitochondrial membrane potential due to oxidative damage.

**Conclusions:** Our study showed that hRPCs secrete pro-survival molecules that could protect the RPE from photo-oxidative damage in vitro. Adult human retinal stem cell-derived trophic factors might prove useful in the treatment of AMD.

**Sponsor:** *None*

717 **Presentation Type:** Oral

**Author:** John Fuller **Presentor:** John Fuller
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**Classification:** GSBS Student
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**EXPRESSION OF P75NTR AND NERVE GROWTH FACTOR IN HUMAN OPTIC NERVE HEAD AND RETINA**

**Purpose:** The mechanism for retinal ganglion cell (RGC) death in glaucoma is unknown. Recent studies have demonstrated that proneurotrophins are capable of elucidating 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 astrocyte and lamina cribrosa (LC) cell cultures from the human optic nerve head. We have also demonstrated that astrocytes and LC cells are positive for the Trk A neurotrophin receptor, but are negative for p75NTR. The purpose of this study is to determine the expression patterns for p75NTR and NGF in the human retina and optic nerve.

**Methods:** Posterior chambers from postmortem human donors were stained for p75 and NGF, as well as counterstained using neurofilament, glial fibrillary acidic protein (GFAP), as well as wheat germ agglutinin (WGA). Sections were deparaffnized, stained, and analyzed using confocal microscopy. Conditioned media was analyzed for the presence of proNGF via Western blot analysis using an antibody made against the pro segment of NGF.

**Results:** p75NTR stains predominantly in the RGC layer of the retina, and is found in the optic nerve head, but decreases posteriorly. NGF staining is predominant in the RGC layer, and is colocalized with GFAP positive astrocytes. In addition, the 32 kDa and 53 kDa forms of proNGF were detected in LC and astrocyte conditioned medium following serum deprivation experiments.

**Conclusions:** This study demonstrates for the first time that the RGC layer is the predominant cell layer positive for p75NTR. Furthermore, astrocytes in this layer are a potent source of NGF. Astrocyte and LC cells secrete proNGF in vitro. It is possible that NGF secreted from astrocytes in the retina and optic nerve head is in the pro form. This may induce p75NTR-mediated apoptosis of the retinal ganglion cells.

**Sponsor:** *NIH, NSF GK-12*

718 **Presentation Type:** Poster

**Author:** Slobodan Dimitrijevich **Presentor:** Jwalitha Shankardas
**Department:** GRADUATE SCHOOL OF BIOMEDICAL SCIENCES
**Classification:** Faculty (Not for Competition)
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*Vinod Mootha, MD, Ophthalmology, UT Southwestern, Dallas, Texas*
*S.D. Dimitrijevich, UNTHSC, Fort Worth, Texas*

**PROFILE OF PROGESTERONE AND ESTROGEN RECEPTORS IN THE PRIMARY CELLS, CELL LINES AND EPITHELIA OF THE HUMAN CORNEA AND CONJUNCTIVA**

**Purpose:** The objectives of this study were to: a. determine the profile of progesterone and estrogen receptors in the corneal and conjunctival epithelia, b. determine the profile of these receptors in the primary epithelial cells and c. demonstrate that this expression is maintained in the epithelial cell lines.

**Methods:** The corneal and conjunctival epithelia were isolated by treatment of intact tissue with dispase, rinsed in PBS and lysed. The primary cells were subcultured on glass coverslips, fixed-permeabilized and examined by indirect immunoflurescence. Epithelial cell lines were hTERT, transformed while the endothelial cell line was E6/E7 transformed and were also examined by indirect immunofluorescence. The receptor profiles were also determined by western analysis of cell and tissue lysates.

**Results:** In this study cells and tissue from male donors were used. Indirect immunofluorescence showed a variable localization of the estrogen, progesterone and androgen receptors in the wild type corneal and conjunctival cells and their transformed counterparts. The western analysis showed the presence of PRA and PRB and Er? and Er?.

**Conclusions:** Cellular components of the cornea and conjunctiva from male donors show the presence of progesterone (A and B) and estrogen (? and ?) receptors. The presence of the respective proteins was confirmed by western blot analysis cell and tissue lysates.

**Sponsor:** *none*

# GENERAL MEDICINE

**800** **Presentation Type:** Poster

**Author:** Roberto Cardarelli **Presentor:** Roberto Cardarelli
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
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*John C. Licciardone, DO, MS; NorTex Director of Research*
*Karen Wood, MPH; Nortex Senior Research Associate*
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**THE NORTH TEXAS PRIMARY CARE PRACTICE-BASED RESEARCH NETWORK**

**Purpose:** To announce the formation of the first North Texas Primary Care Practice-Based Research Network (NorTex) within the Division of Education and Research of the Department of Family Medicine/ Texas College of Osteopathic Medicine.

**Methods:** NorTex is a collaborative network of family medicine, general internal medicine, geriatric, pediatric, and Ob/Gyn physicians throughout North Texas who perform patient-oriented evidence-based research that ultimately improves the health of this region's communities. The success of NorTex will only be sustainable if new members join and participate in the mission and objectives of the Network. Currently, the Network has 48 members and has recently partnered with the Tarrant County Health Department.

**Results:** None

**Conclusions:** None

**Sponsor:** *None*

**801** **Presentation Type:** Poster

**Author:** Cheng Feng **Presentor:** Cheng Feng
**Department:** TEXAS COLLEGE OF OSTEOPATHIC MEDICINE (TCOM)
**Classification:** TCOM DO Student
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**ZONISAMIDE TOLERABILITY IN INFANTS 12 MONTHS OF AGE AND YOUNGER**

**Purpose:** Zonisamide is a broad-spectrum antiepileptic drug (AED) indicated for the adjunctive treatment of partial seizures in adults. Prior reports suggest that zonisamide is effective in pediatric patients with various seizure types; however, data are limited regarding the use of zonisamide in infants. This study was designed to evaluate the efficacy and tolerability of zonisamide therapy in infants.

**Methods:** A retrospective chart review of infants 12 months of age and younger receiving zonisamide for epilepsy at a university-based pediatric neurology clinic was conducted. Evaluation parameters included seizure recurrence based upon caregiver reports and seizure diaries, and adverse effects.

**Results:** Fifty patients (28 male, 22 female) were included in the study, with a mean age of 7 months. The majority (n=29) had symptomatic generalized epilepsy; others had cryptogenic generalized epilepsy (n=11), symptomatic localization-related epilepsy (n=6), or cryptogenic localization-related epilepsy (n=4). The mean duration of follow-up was 14 months. Mean initial zonisamide dosage was 8.8 mg/kg per day, and mean final dosage was 18.9 mg/kg per day. Twenty-nine patients (58%) experienced at least a 50% reduction in seizure frequency from baseline, including 14 patients (28%) who achieved seizure freedom. No patient discontinued due to rash, and there were no reports of renal stones, oligohidrosis, or hyperthermia.

**Conclusions:** This open-label, retrospective review suggests that zonisamide may be effective and well tolerated in infants with severe epilepsy. Further investigation via randomized controlled trials is warranted.

**Sponsor:** *Eisai Inc.*

**803** **Presentation Type:** Poster

**Author:** Roberto Cardarelli **Presentor:** Roberto Cardarelli
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**Assistant Professor, University of North Texas Health Science Center at Fort Worth, Texas College of Osteopathic Medicine, Department of Family Medicine, Division of Education and Research*

***Professor, University of North Texas Health Science Center at Fort Worth, Texas College of Osteopathic Medicine, Department of Family Medicine, Division of Education and Research*

**FACTORS ASSOCIATED WITH THE SEVERITY OF DISCIPLINARY ACTION BY A STATE MEDICAL BOARD**

**Purpose:** There has been an increase in research in evaluating factors associated with disciplinary action. However, research on factors related to the severity of a disciplinary action is lacking. By looking at factors associated with the severity of disciplinary action while controlling for the type of violation, we were able to demonstrate whether factors unrelated to the case, such as gender or primary specialty, affected the disciplinary action process.

**Methods:** 1129 physicians who were disciplined between January 1, 1989 and December 31, 1998 by the Texas State Medical Board were included in the study. Multivariate logistic regression was used to compute odds ratios (OR) and 95% confidence intervals (95%CI) for factors associated with license revocation, the most severe disciplinary action, compared to any other form of disciplinary action.

**Results:** Disciplined general practitioners (OR, 1.80; 95%CI, 1.01-3.19), anesthesiologists (OR, 2.45; 95%CI, 1.05-5.74), psychiatrists (OR, 2.68; 95%CI, 1.41-5.13) and those with a history of multiple disciplinary actions (OR, 1.91; 95%CI, 1.29-2.83) were more likely to have their license revoked. Disciplined physicians who were practicing for many years were also found to be more likely to have their license revoked (OR, 1.05; 95%CI, 1.04-1.07 for each incremental year in practice).

**Conclusions:** Certain specialties, number of years in practice, and having a history of multiple disciplinary actions are associated with a greater likelihood of license revocation.

**Sponsor:** *None*

**806** **Presentation Type:** Poster

**Author:** Roberto Cardarelli **Presentor:** Roberto Cardarelli
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**Classification:** Faculty (Not for Competition)
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*Department of Family Medicine*
*Division of education & Research*
*Center for Evidence-Based Medicine*

**EVIDENCE-BASED REVIEW OF PHARMACEUTICAL MARKETING AND THEIR STUDIES: IS WHAT THEY ARE TELLING US IMPORTANT AND TRUE?**

**Purpose:** Our study's objective was to answer several questions: Is the marketing advertisement that is presented to the physician based on research that (1) is funded by the pharmaceutical company? (2) utilizes patient-oriented versus disease-oriented outcomes? (3) is valid? We also wanted to determine if the data that was printed in the marketing advertisement material matched with the data published in the original study.

**Methods:** The study was conducted in 5 family medicine clinics within the University of North Texas Health Science Center at Fort Worth. All physicians from these clinics were contacted and asked to collect marketing advertisements (MAs) from pharmaceutical representatives and to mark the graph, figure, or data that were emphasized or discussed the most by the representative. They were asked to start collecting the MAs on October 15th, 2004 and to send them all to a centralized location using intra-departmental mail. The MAs were collected on a continuous basis on any class of medication until 20 MAs were received by at the central location. All clinicians were asked to stop collecting MAs on December 5th, 2004. Once the MA was received, the figure, table, or data were identified and the corresponding original published study was obtained. Two reviewers used an instrument to collect data and perform an evidence-based review of the article, comparing data that was printed on the MA to what was found in the original study.

**Results:** Twenty different MAs were collected from the family medicine clinicians, representing 20 different medications and their respective studies. The greatest number of MAs were on cardiovascular medications (45%). Among the 20 studies, 80% were funded by the pharmaceutical company, 15% were unknown and 5% (1 study) was not funded by industry. Sixty percent of the studies and the corresponding MAs presented patient-oriented outcomes, such as mortality, pain scores, and episodes of urinary incontinence. However, only 8 of 20 medications were compared to another treatment regimen. After reviewing each article, the reviewers found 75% of the studies to be valid. Interestingly, 3 of the 20 (15%) MAs presented data that was different from what was in the original published study. Only 1 MA presented data that was not statistically significant.

**Conclusions:** Further studies are needed to determine not only how pharmaceutical MAs affect physician prescribing practices, but if patient outcomes are associated with such practices.

**Sponsor:** *None*

# GENERAL MEDICINE

**807** **Presentation Type:** Poster

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*Ron Palmer, RN, Clinical Supervisor for Hospice, Universal Health Resources*
*Anada I. Gunn-Sanders, JD, UNTHSC, School of Public Health; Board of Directors, Universal Health Resources*

**COST-EFFECTIVE ANALYSIS OF METHADONE IN HOSPICE SETTING**

**Purpose:** Hospice agencies are under a fixed reimbursment on a per diem basis. A major cost of hospice care is related to medications provided by the hospice for symptom management. A common symptom in end of life care is pain, often requiring opioid pain medications for adequate relief. A cost analysis was performed to determine the cost benefit of utilizing methadone for pain relief compared with long acting morphine and transdermal fently patches.

**Methods:** A literature view was undertaken to obtain average wholesale price (AWP) for methadone (generic only), long acting morphine (generic and trade brand) and transdermal fentanyl patches (trade brand only). The higher doses available were used because these are commonly prescribed in the hospice setting. A model of typical conversions from other opioids to methadone was utilized with the 10% morphine equivalent doses conversion factor. For example, methadone 20 mg a day converts to approximately 200 mg of morphine a day.

**Results:** This model validated cost savings of converting patients to methadone from other opioids utilizing AWP as a cost basis. Methadone 10 mg cost is $8.24 a month. The equivalent dose of morphine sulphate cost $313.46 per month for generic and $328.19 per month for trade brand. Transdermal fentanyl patches cost $320 per month. This reveals a 97% cost savings per patient when using methadone, as compared to morhine sulphate and transdermal fentanyl cost.

**Conclusions:** Significant cost savings can be realized by hospice agencies by utilizing methadone in place of other opioids. However, methadone should be prescribed by an experienced practitioner that is knowledgeable in the pharmacokinetics, side effects and interactions of methadone. More research needs to be performed to describe any increases in other hospice services for patients on methadone to better assess overall hospice cost.

**Sponsor:** *none*

**808** **Presentation Type:** Poster

**Author:** Jeanine DeSocio **Presentor:** Jeanine DeSocio
**Department:** PHYSICIAN ASSISTANT STUDIES (PA Program)
**Classification:** GSBS Student
*Jeanine DeSocio, PA-S; Patti Pagels, MPAS, PA-C; Olive Chen, PhD*

**FACTORS INFLUENCING PHYSICIAN ASSISTANTS TO PRACTICE IN PEDIATRIC SPECIALTIES**

**Purpose:** The purpose of this study was to better understand the factors that influenced clinical PAs to choose work in pediatric specialties.

**Methods:** The sample consisted of 1,241 PAs registered with Louisiana, Oklahoma, or Texas state chapters of the American Academy of Physician Assistants. A survey containing 21 questions was developed to collect the data. The researchers sent out E-mails to invite the above PAs to participate in the research. This cover letter summarized the goals of this study and contained an URL that linked to the survey. The PAs accessed the survey by selecting the URL from within the cover letter. The following week, a Reminder E-mail was sent to the same sample population. Statistical Package of Social Science software v. 11.0 was used to perform descriptive analysis.

**Results:** A total of 402 PAs responded to the survey (response rate was 32.4%). After excluding some uncompleted surveys, the valid surveys were 378. Twenty-nine (7.7 %) respondents were PAs working pediatric jobs, 30 (7.9 %) worked a pediatric job in the past, 279 (73.8 %) had never worked in pediatrics and 40 (10.6 %) respondents did not specify.

Among the 59 respondents that had worked a pediatric job during their PA career, the most popular factors influencing the pursuit of this pediatric job were: Practice Site Location (22.0%), Salary/Benefits (18.6%), and Patient Population (15.3%). The top reasons for terminating pediatric jobs were: Other (19.2 %), Salary/Benefits (15.4 %), and Patient Population (15.4 %).

Almost half (41.9%) of the respondents without prior pediatric job experience reported that they would consider pediatrics for future employment. Nearly all respondents (96.6%) currently working in pediatrics planned to continue their job.

**Conclusions:** The results of this study showed that PAs of various clinical experiences reported a high interest in pediatrics and those PAs currently working pediatric jobs indicated an overwhelming willingness to remain working in pediatric medicine. However, only 4% of clinical Physician Assistants (PAs) have worked in pediatric jobs over the last decade. Revealing the factors influencing PAs to pursue pediatric medicine can provide useful information on recruiting PAs to enter pediatric specialties.

The results indicated that Salary/Benefits and Patient Population are top factors for both accepting and terminating pediatric employment. Offering improved salary /benefits options may be the key to increasing PA employment within pediatric medicine.

**Sponsor:** *none*

**809** **Presentation Type:** Poster

**Author:** Anada Gunn-Sanders **Presentor:** Anada Gunn-Sanders
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**Classification:** SPH Student
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*Ray Clark, RN, BSN, Vice-President, Universal Health Services*
*Elizabeth Palmarozzi, D.O. UNTHSC, Chair of Department of Family Medicine*
*Mark Sanders, D.O., J.D., UNTHSC, Department of Family Medicine, Director of Division of Education and Research, Med. Dir./Dir. of Med. Affairs, Universal Health Resources*

**COST EFFECTIVE ANALYSIS: TELEMEDICINE AND CONGESTIVE HEART FAILURE**

**Purpose:** Health care costs continue to increase in the United States, and as a result cost-saving measures are in need of consideration. One such measure is telemedicine. Therefore, this research analyzes the potential economic impacts of utilizing telemedicine to specifically address and treat the chronic disease of congestive heart failure (CHF).

**Methods:** Review of literature and statistics related to the economics of implementing telemedicine to treat patients with CHF. For example, studies looked at such issues as the specific return on investment associated with the implementation of telemedicine.

**Results:** It is well documented in the health care industry that the cost associated with the length of stay in a hospital continues to be on the rise. Contrary to this correlation, is the fact that studies have shown that the longer a patient is on a CHF telemedicine program financial benefits increase exponentially.

**Conclusions:** The U.S. must continue to move in the direction of legislative policies, which offer higher reimbursement for cost-effective care. Telemedicine is one such method of providing cost-effective, high quality health care to patients that require aggressive chronic disease management. Though telemedicine and its widespread implementation is not without its critics, its potential for national benefits is argued to greatly outweigh its cost, both financially and medically.

**Sponsor:** *none*

# IMMUNOLOGY

900 **Presentation Type:** Oral

**Author:** Swapnil Vaidya **Presentor:** Swapnil Vaidya
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**TO KILL OR NOT TO KILL - THAT IS THE QUESTION**

**Purpose:** Natural Killer (NK) cells are effecters of the immune system that can kill tumor cells and virally infected cells without prior stimulation and in an antigen independent manner. This makes them the first line of defense against cancer and viral infections. To understand this 'natural cytotoxicity' of NK cells we have identified several cell surface receptors. 2B4 (CD244) is one such receptor that is expressed on all NK cells, monocytes, and some subsets of T cells. CD48 is its high affinity ligand and cross-linking 2B4 with anti-2B4 antibody in vitro enhances cytotoxicity of NK cells. CD48 is expressed on all hematopoietic cells, including NK cells. To study the physiological role of 2B4 we have generated, by gene targeting, mice deficient in the expression of this cell surface molecule.
**Methods:** In vitro cytotoxicity assays using lymphokine activated killer (LAK) cells were performed to determine the role of 2B4 in NK cell activation. In vivo function of 2B4 in tumor rejection was studied in a mouse tumor model using B16 melanoma cells. The melanoma cells were stably transfected with CD48 and CD48+ and CD48- cells were used in the tumor experiments.
**Results:** 2B4 knockout NK cells were impaired in activation by IL-2, suggesting that 2B4-CD48 interaction among neighboring NK cells is required for the optimal activation of these cells by IL-2. This indicates that 2B4 acts as an activating receptor in this situation. In the tumor studies, the CD48+ B16 cells produced more tumors than the CD48- B16 cells. This demonstrates an inhibitory role for 2B4-CD48 interaction when the interaction occurs between an NK cell and target cell.
**Conclusions:** These studies demonstrate that 2B4 can be activating or inhibitory depending on the situation in which the 2B4-CD48 interaction is occurring. 2B4-CD48 interaction among NK cells is activating, while 2B4-CD48 interaction between an NK and target cell is inhibitory. This context-dependent functioning allows the 2B4 receptor to resolve the dilemma it faces when it binds CD48 - to activate killing or inhibit killing?
**Sponsor:** *NIH grant CA85753*

901 **Presentation Type:** Poster

**Author:** Jae-Kyung Lee **Presentor:** Jae-Kyung Lee
**Department:** MOLECULAR BIOLOGY & IMMUNOLOGY
**Classification:** GSBS Student
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**CHARACTERIZATION OF NOVEL RECEPTOR CS1 (CRACC) IN THE HUMAN LYMPHOCYTES**

**Purpose:** Immune cell functions are regulated by surface receptors and their interactions with ligands. While natural killer (NK) cells mediate innate immune response, B and T lymphocytes mediate the adaptive response. In order to understand the mechanisms of regulation of the immune response, we have identified several surface molecules expressed on lymphocytes. One of the receptor, CS1 is expressed on NK, B and T cells. CS1 is a self-ligand and homophilic interaction of CS1 regulates NK cell cytolytic activity. In this study we have identified a splice variant of CS1 (CS1-S) and investigated the functional role of CS1 in NK cels and B lymphocytes.
**Methods:** To determine the function of each isoform in NK cells, cDNAs for CS1-L and CS1-S were transfected into the rat NK cell line RNK-16 and functionally tested using redirected cytotoxicity assays and calcium flux experiments.
We generated recombinant soluble CS1 to provide biological ligand to investigate the role of CS1-CS1 interactions in the regulation of B cell function. The Sp2/o myeloma cells have transfected with cDNA encoding the extracellular domain of CS1, which had been subcloned into the pSecTaq/Hygro vector.

**Results:** We identified a novel splice variant of CS1 (CS1-S), which lacks immunoreceptor tyrosine-based switch motifs (ITSMs) in the cytoplasmic domain. Human NK cells expressed mRNAs for both wild type CS1 (CS1-L) and CS1-S and their expression level remained steady upon various stimulation. CS1-L was able to mediate the redirected cytotoxicity of P815 target cells in the presence of anti-CS1 mAb, 1G10, and a rise in intracellular calcium within RNK-16 suggesting that CS1-L is an activating receptor whereas, CS1-S showed no effects. Interestingly, SAP associated with unstimulated CS1-L and dissociated upon pervanadate stimulation.
Human B cells expressed only CS1-L isoform and the levels of CS1 expression has been unregulated after activation in vitro. Importantly, anti-CS1 monoclonal antibody strongly enhanced proliferation of both freshly isolated as well as activated B cells.

**Conclusions:** Our data suggest that CS1 plays an important role in human B cells as well as NK cells and CS1-CS1 homophilic interactions may regulate both innate and adaptive immune responses.
**Sponsor:** *Research supported by NIH grant CA85753*

902 **Presentation Type:** Poster

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**POTENTIAL IMMUNE POLARIZATION OF F4/80+ MACROPHAGES AND CD11C+ DENDRITIC CELLS DURING MYCOPLASMA PULMONIS DISEASE IN MICE**

**Purpose:** The purpose of this study was to determine the nature of F4/80+ and CD11c+ cells in the lung and their response to M. pulmonis infection
**Methods:** F4/80+ and CD11c+ cells were purified by micro-magnetic-beads. Oligo microarray were used to detect the mRNA levels of inflammatory cytokines and receptors and further confirmed by realtime RT-PCR. Some cytokine secreted by F4/80+ and CD11c+ cells in cultured supernatant were measured by ELISA.
**Results:** F4/80+ and CD11c+ cells were shown to have different patterns of cytokine and receptor expression. In particular, F4/80+ cells preferentially expressed IL-10, while IL-12, IL-18 and IFN-? were predominantly expressed by CD11c+ cells. Interestingly, following M. pulmonis infection, there was an increase in IL-10 and a decrease in IL-12, IL-18 and IFN-? expression by CD11c+ cells,suggesting the character of CD11c+ cells shifted from a Th1 toward Th2 phenotype.
**Conclusions:** The results suggest that the two APCs cell population may act differently in modulating immune responses during M. pulmonis infection in the lung. F4/80+ macrophages may drive Th2 type immune responses, while CD11c+ dendritic cells promote a Th1 type response. This may be a possible factor participate in chronic disease due to M. pulmonis infection.
**Sponsor:** *NIH grant 1RO1 HL069431 and NIH-NIAD-1R21 AI055907.*

903 **Presentation Type:** Poster

**Author:** Angela Pirooz **Presentor:** Angela Pirooz
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**Classification:** Dual Degree Student DO/PhD
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**THE MOLECULAR CHARACTERIZATION OF THE LIGAND FOR NATURAL CYTOTOXICITY RECEPTOR NKP44**

**Purpose:** Purpose: A part of the innate immune response, bone marrow-derived natural killer (NK) cells provide a frontline defense against viral infection and tumor transformation. NK cell activation and subsequent target cell lysis is dictated by a delicate balance between inhibitory and activating signals mediated through receptor-ligand interactions. Activating signals are propagated largely through three NK cell specific natural cytotoxicity receptors (NCRs), NKp46, NKp44, and NKp30. These immunoglobulin superfamily receptors cooperate in tumor cell lysis, lack tyrosine motifs in their cytoplasmic tails, and associate with transmembrane adaptor proteins for functional activity. The NCR ligands remain unknown. Their identification and characterization will enable us to further understand the mechanisms by which NK cells mediate killing, and lead to the development of novel pharmaceutical interventions for the treatment of cancer.
**Methods:** Materials/Methods: NKp44 cDNA was PCR amplified by using sequence specific primers and subcloned into the pGEM-T Easy Vector (Promega). A region corresponding to the extracellular V domain of NKp44 was subcloned into the mammalian expression vector pCD5Lneg1, which contains the CH2 and CH3 regions of human IgG1. The sequence was further subcloned into pCI-neo (Promega), used for stable transfection, and soluble fusion protein was isolated. The fusion protein will be used for identification of the ligand.
**Results:** Results: We have cloned the cDNA for human NKp44 by PCR from a human NK cell cDNA library. The cDNA was subcloned into the pCD5Lneg1 vector, and cDNA for a soluble fusion protein was subcloned into pCI-neo (Promega). After stable transfection, the fusion protein was purified by Protein A (Bio-Rad). Fusion protein has been used in FACS analysis to identify cell lines which express the ligand. We have shown that a human B cell line expresses the ligand for NKp44.
**Conclusions:** Conclusions: We have completed the first half of the required steps for the molecular characterization of the ligand for natural cytotoxicity receptor NKp44.
**Sponsor:** *NIH Grant CA85753*

# IMMUNOLOGY

904 **Presentation Type:** Poster

**Author:** Sheetal Bodhankar **Presentor:** Sheetal Bodhankar
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**NK-LIKE CELL DEPLETION PRIOR TO NASAL-PULMONARY IMMUNIZATION LEADS TO BETTER PROTECTION IN RESPONSE TO MYCOPLASMA PULMONIS INFECTION**

**Purpose:** A complex balance between the detrimental and beneficial effects of immunity determines the course of mycoplasma infection. NK-like cells, the major source of IFN-gamma , early in mycoplasma infection have shown to 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 immunity against mycoplasma respiratory disease.
**Methods:** Mice were depleted of NK-like cells using rabbit anti-asialo GM1 antibody treatment, prior to nasal-pulmonary immunization with mycoplasma membrane antigen. Seven days after second immunization, mice were challenged with 105 colony forming units (CFU) of Mycoplasma pulmonis, and CFU number determined 14 days later.
**Results:** There was a decrease in CFU isolated from the lungs and nasal passages of the NK-like cell depleted, immunized mice when compared to control (sham-immunized) mice and immunized mice. There was an increase in mycoplasma-specific IgG2a and IgG1 responses in the NK-like cell depleted, immunized group prior to infection; however, there were no significant differences in antibody responses between groups, post-infection. Correspondingly, prior to infection, an increase in the IFN-gamma and IL-4 responses from lung lymphocytes stimulated with mycoplasma antigen in-vitro, was seen in the NK-like cell depleted, immunized group when compared to the immunized group.

**Conclusions:** In conclusion, NK-like cells dampen protective immunity in the lungs and nasal passages associated with nasal pulmonary immunization. There is a corresponding influence on humoral and cellular immunity.
**Sponsor:** *NIH grant 1RO1 AI 42075*

905 **Presentation Type:** Poster

**Author:** Stephen Mathew **Presentor:** Stephen Mathew
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**MUTATIONAL AND FUNCTIONAL ANALYSIS OF HUMAN 2B4 (CD244) - CD48 INTERACTION**

**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 recognition is regulated by specific receptors that, upon interaction with their respective ligands, may send stimulatory or inhibitory signals. Interaction between receptors and ligands play critical role in the generation of immune responses. 2B4 (CD244), a member of the CD2 subset of the immunoglobulin superfamily, is the high affinity ligand for CD48. It is the expressed on natural killer (NK) cells, T cells, monocytes and basophils. Recent data indicate that 2B4/CD48 interactions regulate NK and T lymphocyte functions. In human NK cells, 2B4/CD48 interaction induces activation signals, whereas, in murine NK cells it sends inhibitory signals.
**Methods:** To determine the structural basis for 2B4/CD48 interaction, selected amino acid residues in the variable (V) domain of the human 2B4 were mutated by site-directed mutagenesis. Following transient expression of these mutants in B16F10 melanoma cells, their interaction with soluble CD48-Fc fusion protein was assessed by flow cytometry. The functional role of these mutants were determined by chromium release cytotoxicity assays and calcium flux assays.
**Results:** We identified amino acid residues in the extracellular domain of human 2B4 that are involved in interacting with CD48. Our data further demonstrated that Lys68 and Glu70 in the V domain of human 2B4 are essential for 2B4/CD48 interaction.
**Conclusions:** Our study showed that several charged amino acids in the V domain of h2B4 make relative contributions to its interaction with CD48 and the amino acid residues Lys68 and Glu70 are essential for 2B4/CD48 interaction.
**Sponsor:** *NIH grant CA85753*

906 **Presentation Type:** Poster

**Author:** Byung-Jin Kim **Presentor:** Byung-Jin Kim
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**DIFFERENTIATION CHARACTERIZATION OF JAWSII/IMMATURE DENDRITIC CELL LINE WITH STIMULATION BY CYTOKINES.**

**Purpose:** Mycoplasma pulmonis causes chronic lung disease. F4/80+ macrophages and CD11c+ dendritic cells are major cell types of antigen-presenting cells (APC) found in the lungs after M. pulmonis infection. In previous research, we found F4/80+ cells exhibited a greater increase in the lung after M. pulmonis infection as compared to CD11c+ cells. Gene microarray and real time PCR showed that these cells were shown to have different patterns of cytokine and receptor expression. These results suggested that these two APC populations may have differential function against M. pulmonis infection. We also found that expression of IL-6, IL-10 and TNF-alpha was significantly increased and IFN-gamma was slightly increased. There was no change in the expression of IL-4, IL-12 and GM-CSF in total lung tissue. Thus, we hypothesized that the change of micro-environmental conditions such as different cytokine distribution patterns in response to M. pulmonis infection may affect the phenotype of APC forming from common immature precursor cell types which determine their distinct function.
**Methods:** The JAWSII cell line is known as an immature dendritic cell which possesses the characteristics of monocyte/macrophage lineage. We examined the change and maturation of the cell phenotype as functional APC after cytokine treatment.
**Results:** 4 days of treatment of JAWSII cell with cytokines (TNF-alpha, IFN-gamma and IL-4) induced the change of cell morphology and also changes in the expression pattern of cell surface molecules.Flow cytometry data showed that F480+/MHCII+ cells showed a greater increase (about 60%) as compared to CD11c+/MHCII+ cells (less than 6%).
**Conclusions:** These data suggest that a combination of cytokines can influence cell surface marker expression that may determine differentiation in phenotype. In the future study, we propose to test our hypothesis related to phenotype changes of this immature cell line after cytokine stimulation by various combinations and also test functions of each differentiated cells toward T cell population under M. pulmonis stimulation. This work supported by NIH HC069431 grant.
**Sponsor:** *HC069431 grant*

907 **Presentation Type:** Poster

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**FUNCTIONAL ROLE OF THE LLT1 RECEPTOR ON LEUKOCYTES**

**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, 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. All monocytes express LLT1, whereas LLT1 is expressed only on 5-10% of NK cells. A recent report shows that LLT1 is expressed on osteoclasts and it inhibits their formation and function. We hypothesize that LLT1 may function as an immune modulator, possibly linking 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 mAb. A mammalian expression vector encoding the extracellular domain of LLT1 was generated. This plasmid was stable transfected into the SP2/0 cell line and the generated fusion protein was purified on a nickel column.
**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. The nature of its ligand expression may further indicate this.
**Sponsor:** *NIH grant CA85753; NSF Project SCORE*

# MICROBIOLOGY/INFECTIOUS DISEASE

**1001** **Presentation Type:** Poster

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**RHINOCEREBRAL MUCORMYCOSIS WAS ACQUIRED AFTER INITIATING CORTICOSTEROID THERAPY IN A 69 YEAR-OLD DIABETIC FEMALE**

**Purpose:** The purpose of this report is to illustrate the rapidly progressive nature of this disease despite surgical and medical therapies. The report describes a case of rhinocerebral mucormycosis in a 69 year-old diabetic female who was being treated with corticosteroid therapy for bronchospasm prior to her presentation. It is suspected that the patient acquired the illness while hospitalized for the treatment of the bronchospasm.

**Methods:** The patient's medical records, CT scans, and histology slides were reviewed at Plaza Medical Center in Fort Worth, TX. A literature search was performed using an OVID Medline search from 1966 to the present. The keywords rhinocerebral mucormycosis and invasive fungal sinusitis were utilized to locate journals for review.

**Results:** In the review of the literature, I discovered only one other case that was thought to be nosocomially acquired in a patient with Systemic Lupus Erythematous. Long term survival has been documented to be poor. However, I found 2 reports describing long term survival in a 24 and 27 year-old patient. The majority of the cases described patients who died regardless of therapy whether surgical, medical, or both. They were typically older with high risk factors for acquiring mucormycosis.

**Conclusions:** Rhinocerebral mucormycosis is a rapidly progressive invasive sinusitis which can be difficult to diagnose because the disease masquerades as a bacterial sinusitis. Awareness of the high risk factors, signs, and symptoms along with prompt treatment can help decrease the mortality of the illness.

**Sponsor:** *none*

**1002** **Presentation Type:** Poster

**Author:** Nicole Dobbs **Presentor:** Nicole Dobbs
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**Classification:** GSBS Student
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**FIRST DETECTION OF EHRLICHIA CHAFFEENSIS IN AN AMBLYOMMA CAJENNENSE (ACARI: IXODADIE) TICK**

**Purpose:** The Tick-Borne Disease Research Laboratory in the Department of Pathology and Anatomy is the dedicated tick-testing laboratory for the Texas Department of State Health Services (DSHS). Testing is performed to identify diseases present in the tick populations of Texas. Ticks are submitted for DNA-based testing and establishment of pathogen infection and identity. An Amblyomma cajennense tick (also known as the Cayenne tick) submitted to the DSHS Region 11 Zoonosis Control office in Cameron county, Texas was positive for the presence of Ehrlichia chaffeensis, the causative agent of human monocytic ehrlichiosis. Upon review of the literature, this is the first evidence of E. chaffeensis in a tick vector other than its common vector, Amblyomma americanum (the Lone star tick).

**Methods:** Ticks submitted to the Texas Department of State Health Services, are identified to genus, species, life stage, and engorgement state by a DSHS entomologist. The specimens are then sent to the Tick-Borne Disease Research Laboratory at UNTHSC for pathogen screening. DNA is isolated and subjected to polymerase chain reaction (PCR) assays for the detection of Borrelia spp., Ehrlichia spp., and Rickettsia spp. Amplicons produced by the assays are sequenced using an ABI PRISMâ 310 Genetic Analyzer (Applied Biosystems, Foster City, CA.). Pathogen identity is determined.

**Results:** A Cayenne tick, collected in Cameron county, Texas (LAT 26.15650, LON -97.34678), produced amplicons for both the 16s ribosomal DNA gene and the disulfide oxidoreductase gene of the pathogen E. chaffeensis.

**Conclusions:** Upon review of current literature, this is the first discovery of E. chaffeensis in a Cayenne tick. The presence of E. chaffeensis in the Cayenne tick population could pose a significant risk to public health. This risk may extend beyond south Texas and throughout the tick's normal range, which includes much of South America. A detailed investigation to establish the minimum infection rate (MIR) within the tick population, genetic profiles of the pathogen, and risk of transmission to humans, should be performed.

**Sponsor:** *None*

# NEUROSCIENCE

**1100** **Presentation Type:** Poster

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**ETHANOL MODULATES THE DISCRIMINATIVE STIMULUS EFFECTS OF METHAMPHETAMINE: MECHANISMS**

**Purpose:** Methamphetamine is often co-abused with ethanol, yet little is known about the behavioral effects of the two compounds in combination, or which receptors might mediate their interactions. Earlier work showed that ethanol failed to substitute for the discriminative stimulus effects of 1.0 mg/kg methamphetamine, but did produce a left-shift in the methamphetamine discrimination dose-effect curve. Compounds acting at GABAA receptors did not alter the discriminative stimulus effects of methamphetamine, suggesting that GABAA receptors do not mediate the effects of ethanol on methamphetamine-cued responding.
**Methods:** In the present study, the contribution of 5-HT and NMDA receptors to the effects of ethanol were assessed. Sprague-Dawley rats were trained to discriminate methamphetamine (1.0 mg/kg, i.p.) from saline. Mianserin (10 mg/kg, i.p.) and NMDA (30 mg/kg, i.p.) were tested alone and in combination with ethanol (0.5 g/kg, i.p.) and/or methamphetamine (0.1 to 1.0 mg/kg, i.p.).
**Results:** Mianserin failed to alter the ability of ethanol to potentiate the discriminative effects of methamphetamine. Mianserin alone did not substitute for the discriminative stimulus effects of methamphetamine, but acted as a partial antagonist when given in combination with methamphetamine (0.1 to 1 mg/kg). In contrast, NMDA fully reversed the ability of ethanol (0.5 g/kg) to shift the methamphetamine dose-effect curve. NMDA did not alter the methamphetamine dose-effect curve, and did not substitute for methamphetamine.
**Conclusions:** These findings suggest that NMDA receptors mediate at least in part the modulatory effects of ethanol, but do not directly contribute to the effects of methamphetamine. In contrast, although serotonergic antagonists can modulate the discriminative stimulus effects of methamphetamine, 5-HT receptors do not play an important role in the interaction of the discriminative stimulus effects of ethanol and methamphetamine.
**Sponsor:** *N01DA-7-8076*

**1101** **Presentation Type:** Poster

**Author:** Larry Segars **Presentor:** Larry Segars
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**Classification:** SPH Student
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**GEOGRAPHIC VARIATION IN THE PRESCRIPTION OF STIMULANTS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BY U.S. PHYSICIANS**

**Purpose:** To determine the potential geographic variation in stimulant prescriptions for the treatment of ADHD by U.S. physicians from use of the 2001 National Ambulatory Medical Care Survey dataset.
**Methods:** The study utilized the 2001 multi-stage NAMCS dataset. U.S. office-based visits associated wiht ADHD were identified using DSM-IV diagnosis codes. Stimulant treatment was captured by use of the FDA drug classification code. The dependent variable studied was use of a stimulant to treat ADHD with the independent variables assessed including region of country, age group, sex, ethnicity, race, physician specialty and payment type.
**Results:** The 2001 NAMCS randomly sampled a weighted national estimate of 880,486,669 physician office visits in the U.S. A weighted estimate of 4,219,759 office visits associated with ADHD were sampled. Compared to psychiatrists, pediatricians were 66% less likely to have treated a patient with ADHD managed by a stimulant medication (OR=0.339; p=0.048; 95% CI 0.116-0.991). Compared to patients living in the Midwest region of the U.S., those living in the Northeast, South and West were 76% (OR=0.242; p=0.014; 95% CI 0.080-0.734), 78% (OR=0.219; p=0.007; 95% CI 0.075-0.642), and 90% (OR=0.103; p=0.019; 95% CI 0.016-0.670), respectively, less likely to be treated with a stimulant medication.
**Conclusions:** Regional differences existed in the use of stimulant medication for treatment of ADHD, with patients in the Midwest region of the U.S. having the greatest odds of having their ADHD treated with a stimulant medication. In addition, psychiatrists were more likely to treat a patient with ADHD with a stimulant medication.
**Sponsor:** *None*

**1102** **Presentation Type:** Oral

**Author:** Evelyn Perez **Presentor:** John Schetz
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**Classification:** Faculty (Not for Competition)
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**HALOPERIDOL IS NEUROPROTECTIVE AGAINST OXIDATIVE STRESS-RELATED DAMAGE IN VITRO AND IN VIVO**

**Purpose:** Since markers of oxidative stress are elevated in schizophrenic brains we asked whether antipsychotic drugs, in additional to their ability to treat psychosis, might also have a neuroprotective component that could prevent secondary oxidative stress-related brain damage. Our hypothesis is that antipsychotics protect against oxidative stress-related cell death.
**Methods:** Our hypothesis that antipsychotic drugs are protective in cases of oxidative stress was tested with in vitro and in vivo models. Exposure of a pluripotent hippocampal HT-22 cell line to high extracellular concentrations of glutamate served as our in vitro cellular model of oxidative stress cell death. Cell survival in the presence and absence of antipsychotic drugs was assessed by staining cells with the fluorometric vital dye calcein AM. A transient middle cerebral artery occlusion model of cerebral ischemic stroke served as our in vivo model of oxidative stress-induced brain damage. Stroke severity in the absence and presence of antipsychotic drugs was measured by differential triphenyltetrazolium staining to histologically assess the volume of the ischemic lesion.
**Results:** Our data indicates that the butyrophenone antipsychotic haloperidol is strongly neuroprotective in our in vitro HT-22 cell model of glutamate-induced oxidative stress-related cell death, while several other antipsychotics from different structural classes are not. A therapeutically-relevant, acute low dose of haloperidol administered to rats immediately following the induction of a transient ischemic cerebral stroke produces a 50% reduction in ischemic infarct volume.
**Conclusions:** Since the acute dose of haloperidol needed to provide significant neuroprotection corresponds to a dose that is low enough to produce an antipsychotic effect with a minimal risk of extrapyramidal side-effects, the value added potential of haloperidol as an oxidative stress-related protective agent for the treatment of ischemic cerebral stroke and other types of brain trauma warrants further investigation.
**Sponsor:** *F&A Funds*

**1103** **Presentation Type:** Poster

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**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** Postdoctoral Fellow/Resident
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**ETHANOL WITHDRAWAL DECREASES PARVALBUMIN LEVELS AND ESTROGEN PROTECTION**

**Purpose:** Parvalbumin (PA) is a calcium-binding protein that has been implicated in protecting neurons from hyperexcitability by sequestering intracellular calcium. This study examined whether ethanol exposure and/or ethanol-withdrawal (EW) alter the levels of PA in a manner that is protected by 17-beta estradiol (E2).
**Methods:** Ovariectomized rats implanted with E2 (EW/E2) or oil pellets (EW/Oil) received chronic ethanol (7.5% wt./vol., 5 weeks) or control dextrin diets (Dex/Oil and Dex/E2). At 0 hour, 24 hours, and 2 weeks of EW, three brain areas (the cerebellum, hippocampus, and cortex) were prepared for immunoblotting and immunohistological assessment of PA.
**Results:** At 24 hours of EW, the EW/Oil group showed the reduced levels of PA and PA-positive neurons in the cerebellum and hippocampus as compared with the dextrin control or the EW/E2 groups. At 2 weeks of EW, the reduced levels of PA persisted in the cerebellum but recovered toward the control levels in the hippocampus. When tested at 24 hours of EW, the magnitude of EW signs inversely correlated with the levels of PA. Neither ethanol exposed tissues nor brain tissues from the cortex showed alteration to PA levels.
**Conclusions:** These data suggest that EW rather than ethanol exposure reduces PA levels in a manner that is brain region specific and that is protected by estrogen. Disturbed-PA homeostasis is hypothesized to play a role in the hyperexcitability of EW signs.
**Sponsor:** *NIH/NIAAA 013864*

# NEUROSCIENCE

**1104** **Presentation Type:** Poster

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**DEVELOPMENT OF A RELIABLE SCREENING ASSAY FOR SIGMA-1 RECEPTOR LIGANDS**

**Purpose:** The aim of this study is to establish a rapid and reliable screening assay for cloned Sigma-1 receptors. Human breast adenocarcinoma (MCF-7) cells were selected as the host cell line for stably expressing cloned Sigma-1 receptor, because it is the only cell line known not to express this receptor.
**Methods:** General DNA recombination techniques, such as restriction enzyme digestion, T4 DNA polymerase ligation, were used to create a vector containing the Sigma-1 receptor gene. The Sigma-1 receptor gene was transfected into cells using calcium phosphate precipitation. Cloned cell lines were established on the basis of G418 drug selection. Affinity values and receptor densities were determined with a saturation isotherm or inhibition binding assay which was performed using [3H](+)-pentazocine as the radioligand.
**Results:** A MCF-7 cell line stably expressing the Sigma-1 receptor was created. The Sigma-1 radioligand [3H](+)-pentazocine bound a high density (Bmax ~100 pmol/mg) of high affinity (Kd ~3 nM) receptors only in cells transfected with the Sigma-1 receptor, but not untransfected cells. Haloperidol and BD1063, which are known to be Sigma-1 receptor ligands, bound with the expected nanomolar affinities. Remarkably, haloperidol and its metabolite, reduced haloperidol, bind with similar affinities to the Sigma-1 receptor.
**Conclusions:** A reliable screening assay for Sigma-1 receptors was developed and validated. This system allows for rapid screening of compounds that interact with Sigma-1 receptors.
**Sponsor:** *F&A Funds*

**1105** **Presentation Type:** Poster

**Author:** Sebum Lee **Presentor:** Sebum Lee
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**Classification:** GSBS Student
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**ACCUMULATION OF P53 LEADS TO THE DOWN-REGULATION OF PRESENILIN-1 EXPRESSION**

**Purpose:** Neuronal degeneration is a common feature of Alzheimer's disease. Therefore, it is important to understand the nature of the primary insult that prompts this abnormal devastating feature of the disease. Despite of the obscure causes to the neuronal degeneration, p53 accumulation suggests that a lot of cellular stress is going on in the brain of Alzheimer's patients. So far, three genes including PS1 have been linked to the early onset Alzheimer's disease. PS1 was shown to be down-regulated in tumor cells during p53 activation. This suggested a relationship between p53 and PS1. Our lab has shown that the PS1 gene lacks the p53 binding site but p53 can still suppress the transcription of a PS1 promoter-CAT reporter synthetic gene. Therefore, we intend to know if p53 accumulation in the neuroblastoma cell line really down-regulates the level of PS1.
**Methods:** Wild and mutant human p53 genes were constructed into cloning vector pcDNA5/TO. Established vectors were transfected into human neuroblastoma SH-SY5Y cells. Transfected cells had been selected in the presence of appropriate antibiotics. The successful transfections were confirmed by immunohistochemistry. Protein samples from these transfectants were electrophoresed and Western blots were probed with p53, PS1 and actin specific antibodies

**Results:** Immunohistochemistry data showed over-expression of p53 in the cells transfected with wild or mutant p53 genes but not in the cells transfected with vector alone. Subsequent Western blot data showed that over-expression of wild p53 was associated with the decrease in PS1 level but over-expression of mutant p53 did not affect the level of PS1.

**Conclusions:**
Our data suggest that over-expression of p53 is associated with the reduction in PS1 level. Since p53 accumulation is common in human neurodegenerative disorders such as Huntington's disease, Down's syndrome and Alzheimer's disease, our in vitro system can be useful to understand the effects of p53 accumulation on presenilin-1 mediated neuronal functions and to dissect the signal transduction path ways involved in this process.

**Sponsor:** *AG18452 (NIH)*

**1106** **Presentation Type:** Poster

**Author:** Atul Raut **Presentor:** Atul Raut
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** GSBS Student
*Atul Raut, Cheryl Kyser, James W. Simpkins and Anna Ratka, Department of Pharmacology and Neuroscience,IAADR, University of North Texas Health Science Center, Fort Worth, TX.*

**ROLE OF AGE IN SEX AND GENOTYPE DIFFERENCES IN SENSITIVITY TO THERMAL NOCICEPTIVE STIMULUS IN PS1 AND APP-PS1 TRANSGENIC MICE**

**Purpose:** Effective pain relief with analgesics is achieved in less than 50% of elderly patients with neurodegenerative diseases. Clinical reports on pain in old age remain controversial. The effects of neurodegeneration on sensitivity to painful stimuli are not well understood. In this study, an attempt was made to characterize changes in pain perception during progression of a neurodegenerative process.
**Methods:** Two genotypes of male and female mice were studied: mice with over expressed presenilin 1 (PS1 transgenic mice) and mice with over expressed amyloid precursor protein (APP) and PS1 (APP-PS1 transgenic mice). Responses to thermal nociceptive stimulus were tested once a month between 5 to 15 months of age using hot plate (supraspinal response) and tail flick (spinal response) methods. Responses to hot plate were measured at temperatures of 51oC and 56oC. Responses to tail flick were measured at temperature of 500 C.
**Results:** At 51oC, female mice had significantly longer hot plate latencies than male mice at 6, 7, 12, 13, 14 and 15 months of age. APP-PS1 transgenic mice were significantly less sensitive to the hot plate stimulus (longer latency) at age of 5, 6, 13, 14 and 15 months, as compared to PS1 transgenic mice. Hot plate measurements at 56oC showed similar differences but not statistically significant. Tail flick responses showed significant sex differences at only 6 months of age where male mice had higher tail flick latency than female mice. APP-PS1 mice had higher tail flick latency than PS1 mice at 7, 9, 10, 11 and 12 months of age
**Conclusions:** ? The present study showed that in PS1 and APP-PS1 transgenic mice, sensitivity to thermal nociceptive stimulation was dependent on gender and genotype; female sex and the APP-PS1 genotype were associated with significantly higher thresholds to thermal nociceptors.
? Sex-specific and genotype-specific differences in responses to thermal nociceptive stimulus were significantly dependent on the age and most likely, the extent of neurodegeneration in the transgenic mice.
? In the transgenic mouse model relevant to Alzheimer's disease, age plays a role in sex and genotype differences in sensitivity to experimental pain stimulus involving spinal and supraspinal pathways of algesia.
**Sponsor:** *none*

**1108** **Presentation Type:** Oral

**Author:** Amir Ramezani **Presentor:** Amir Ramezani
**Department:** Social & Behavioral Sciences
**Classification:** GSBS Student
*Amir Ramezani*

**UNDERSTANDING THE BIOPSYCHOSOCIAL EFFECTS OF EPILEPSY**

**Purpose:** Clinicians and researchers should focus on the social adjustment of epileptic patients. Understanding the types of interaction styles that derive from social and family systems is essential in an epileptic patient's social adjustment. To facilitate the treatment process, therapists must understand the dynamics of epilepsy and its associations with depression and anxiety.
**Methods:** literature review of anxiety and depressin among epileptic individauls.
**Results:** literature review indicates that social, psychogical and biological factors all effect epilepsy managment or recovery.
**Conclusions:** In conclusion, Social support systems should be taken into consideration for successful treatment outcome. To facilitate the treatment process, therapists must understand the types of mood disorders that are caused by different types of epilepsy. Clinicians must understand the psychological impact of epilepsy, such as depression and anxiety. The effectiveness of psychological and electro-physiological treatment options (cognitive-behavioral, interpersonal, and electric nerve stimulation therapies) should be evaluated before such procedures are implemented.
**Sponsor:** *none*

# NEUROSCIENCE

**1109** **Presentation Type:** Oral

**Author:** Joshua Gatson **Presentor:** Joshua Gatson
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** GSBS Student
*Joshua W. Gatson, Paramjit Kaur, Meharvan Singh*
*University of North Texas Health Science Center at Fort Worth, Department of Pharmacology and Neuroscience, Fort Worth, TX*

**ACTIVATION OF A NOVEL MEMBRANE-ASSOCIATED ANDROGEN RECEPTOR MODULATES THE MAPK AND PI3-KINASE/AKT PATHWAYS AND INDUCES CELL DEATH**

**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 results in distinct effects on the survival-promoting MAPK and PI-3K pathways and cell viability, relative to the effects mediated through the classical (intracellular) AR.
**Methods:** The C6 rat glial cell line was used to evaluate the effects of DHT on ERK and Akt phosphorylation, two key effectors of the MAPK and PI-3K pathways, respectively. A membrane impermeable form of DHT (DHT-BSA) was used to activate the putative membrane AR, and the unconjugated DHT was used to activate the intracellular AR. ERK and Akt phosphorylation were assessed using Western blot analysis, using phosphospecific antibodies. Assessment of cell viability was performed in C6 cells treated with an oxidative insult [iodoacetic acid (IAA)] in the presence or absence of either DHT or DHT-BSA. Cell damage was assessed by measuring the release of lactate dehydrogenase (LDH) into the media (an index of cell damage), and the calcein-AM assay (identifies viable cells).
**Results:** In C6 cells, where we identified the expression of both isoforms of the classical androgen receptor (AR-B and AR-A), DHT elicited a significant increase in phospho-ERK levels. In contrast, DHT-BSA suppressed the phosphorylation of ERK and Akt. Consistent with these effects on cell signaling, DHT modestly protected the C6 cells against IAA-induced toxicity, whereas DHT-BSA exacerbated the toxicity seen with IAA alone.
**Conclusions:** Collectively, these data support the existence of a novel membrane-associated AR in glial cells, and argue for the existence of two, potentially competing, pathways in a given cell or tissue. 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:** *Meharvan Singh, PhD*

**1110** **Presentation Type:** Poster

**Author:** Scott Duncan **Presentor:** Scott Duncan
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**Classification:** GSBS Student
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**DEVELOPMENT OF AN IN VITRO HIGH-THROUGHPUT SCREENING ASSAY FOR TESTING THE PROTECTIVE EFFECTS OF COMPOUNDS AGAINST OXIDATIVE STRESS**

**Purpose:** To establish a rapid and reliable high-throughput method for screening compounds for their possible protective effects against a variety of oxidative stressors. A clonal cell line was selected in an effort to reduce the variability often encountered when using polyclonal cell lines such as pluripotent HT-22 cells.
**Methods:** HEK293 cells were cultured in 96-well plates. Cells were treated with three different types of oxidative stress compounds: L-buthionine sulfoximine (L-BSO), tert-butyl hydroperoxide (tBHP) and sodium nitroprusside (SNP) over a range of concentrations. After induction of oxidative stress, the cells were washed and loaded with a fluorescent cell permeable dye (calcein AM) in order to assess cell viability.
**Results:** Optimal assay conditions were established for adequate cell adherence to plates, optimal calcein-AM concentration, and optimal cell density. Oxidative stress kill curves were fully characterized for L-BSO, tBHP and SNP using the calcein AM assay.
**Conclusions:** We established a reliable high-throughput assay for assessing mechanistically different types of oxidative stress reagents in vitro. The optimized viability assay described here will allow us to rapidly assess the protective effects of compounds against various types of oxidative stress in a cellular system.
**Sponsor:** *F & A funds*

**1111** **Presentation Type:** Poster

**Author:** Akiko Dohi **Presentor:** Akiko Dohi
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**Classification:** GSBS Student
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**THE MITOGEN-ACTIVATED PROTEIN KINASE PATHWAY REGULATES GAMMA-AMINO BUTYRIC ACID-A RECEPTOR GATING**

**Purpose:** The ?-amino butyric acid-A (GABAA) receptor is a ligand-gated chloride channel whose function can be modulated by its phosphorylation. As such, we were intrigued to have found a consensus phosphorylation site for Extracellular-signal Regulated Kinase (ERK), a key effector of the Mitogen-Activated Protein Kinase (MAPK) pathway, on the intracellular loop of all alpha subunits of the GABAA receptor. Thus, we hypothesized that ERK may phosphorylate the GABAA receptor to regulate its function. Using human embryonic kidney-293 (HEK293) cells transfected with the ?6?2?2 or ?1?2?2 configuration of the GABAA receptor, we evaluated the effects of MAPK signaling on GABAA receptor function and assessed, in part, the precise site of action of ERK.
**Methods:** Three HEK293 cell lines were used: ?6?2?2-transfected HEK293 cells, ?1?2?2-transfected HEK293 cells, and HEK293 cells that were transiently transfected with an ?1 subunit in which the putative ERK phosphorylation site was mutated from a threonine residue to an alanine residue (rat ?1(T375A)?2?2). GABAA receptor function was assessed using perforated patch clamp electrophysiology in the presence or absence of two chemical inhibitors of ERK, PD98059 and UO126.

**Results:** Inhibition of ERK with UO126 or PD98059 in either the ?6?2?2- or ?1?2?2-transfected HEK293 cells resulted in an enhancement of GABA-gated currents. In cells where the putative ERK phosphorylation site of the transfected GABAA receptor was mutated [?1(T375A)?2?2 cells], we found that the effect of UO126 was completely reversed. That is, inhibition of MEK (and therefore, ERK) no longer resulted in an enhancement of GABA-gated currents, but instead led to a significant decrease in GABAA receptor function.
**Conclusions:** The ability of the MAPK inhibitors to enhance GABA-gated currents suggests that activation of the MAPK pathway leads to the inhibition of GABAA receptor function. Surprisingly, when the putative phosphorylation site for ERK was mutated, the MAPK inhibitor still had an effect, but now in the opposite direction. Based on these data, our working hypothesis assumes a multi site model for MAPK regulation of the GABAA receptor. Current studies are aimed at characterizing the precise nature of this multiplicity.
**Sponsor:** *National Institute of Health (NIA)-AG022550, AG023330 and a NARSDA Young Investigator Award to M.S.*

**1112** **Presentation Type:** Poster

**Author:** Jaegwon Chung **Presentor:** Jaegwon Chung
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*Jaegwon Chung and James W. Simpkins*
*Department of Pharmacology & Neuroscience, University of North Texas Health Science Center, Fort Worth, TX, USA*

**ROLE OF PKCS IN ESTRADIOL-INDUCED NEUROPROTECTION AGAINST NITRIC OXIDE DONOR-INDUCED APOPTOSIS IN HT-22 CELLS.**

**Purpose:** We previously reported that estrogen and its analogs produce potent neuroprotective effects against various oxidative stress and ischemic stroke. However, the mechanisms by which estrogens promote cell viability in the neurons remain unclear. Several isoforms of protein kinase C (PKC), especially the novel PKC isoforms delta and epsilon, are activated during programmed cell death.
**Methods:** We studied the involvement of PKC isoforms in mediating estrogen-induced neuroprotection against nitric oxide donor (SNP)-induced HT-22 cell death. Treatment with SNP (100 to 500uM) decreased the viability of HT-22 cells in a dose- and time-dependent manner.
**Results:** 17 beta-estradiol produced neuroprotective effect against SNP induced cell death. A PKC inhibitor, bisindolylmaleimide, but not Go6976 suppressed the cell death. In the western blotting, phosphorylation of PKC delta and epsilon was increased after treatment of SNP. Treatment of 17 beta-estradiol prevented SNP-induced cell death through inhibiting phosphorylation of PKC delta and epsilon.
**Conclusions:** These results suggest that NO-induced death of HT-22 is mediated by PKC phosphorylation and 17 beta-estradiol can protect against NO-induced death of HT-22 by a mechanism involving inhibition of PKC phosphorylation.
**Sponsor:** *AG10485 and AG22550*

# NEUROSCIENCE

**1113** **Presentation Type:** Oral

**Author:** Scott Duncan **Presentor:** Scott Duncan
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** GSBS Student
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**POLYCYSTIN-2 ACCELERATES INTRACELLULAR CALCIUM RELEASE FROM THE ENDOPLASMIC RETICULUM IN C. ELEGANS**

**Purpose:** Polycystin-2, encoded by the PKD2 gene in humans, is a member of the TRP family of calcium channels. In this work we compare the calcium signaling mechanisms and electrophysiology of the C. elegans polycystin-2 homologue, Cepc2, in wild-type and pkd-2 knockout strains. By comparing the wild-type and knockout C. elegans strains we have demonstrated that Cepc2 accelerates intracellular calcium release from the endoplasmic reticulum.
**Methods:** We propagated wild-type and pkd-2 knockout C. elegans strains in bulk liquid culture for preparation of microsomes. Microsomes were used for fluorimetric Ca2+ release studies using the Ca2+ indicator dye Fluo-3. Microsomes were also utilized for single channel electrophysiological recordings. To measure intracellular Ca2+ release in intact cells, nematodes were enzymatically treated and tissue was dissociated to yield single cells. Dissociated cells were loaded with the cell-permeable Ca2+ indicator dye Fluo-3 AM for intracellular Ca2+ release measurements.
**Results:** We found that the intracellular Ca2+ channel Cepc2 is required for normal Ca2+ signaling responses involving IP3 and Ryanodine receptors in C. elegans. We demonstrate that Cepc2 activity results in increased amplitude and decreased duration of cytosolic Ca2+ transients.
**Conclusions:** Cepc2 is a major intracellular Ca2+ release channel in C. elegans and its activity is essential for a rapid response to stimuli in excitable cells.
**Sponsor:** *NIH/NIA grant AG022550, PKD Foundation 59a2r*

**1114** **Presentation Type:** Poster

**Author:** Kathryn Gleason **Presentor:** Kathryn Gleason
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** GSBS Student
*Kathryn Gleason 1, Stephanie Selby 1, Evelyn Perez 1, James W. Simpkins 1 and Laszlo Prokai 2*
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**NEUROPROTECTIVE ESTROGEN QUINOLS ARE NON-FEMINIZING**

**Purpose:** Estrogens are well documented as neuroprotective agents and exert their protective effects in several ways; however, the side effects of feminizing estrogens can be undesirable and even detrimental. Estrogens produce free oxygen radicals through redox cycling and can increase pro-thrombotic and pro-mitotic side effects. Prokai et al. (2003) have shown that a nonphenolic quinol with no affinity for the estrogen receptor is produced by the capture of a 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 17?-estradiol-quinol.
**Methods:** Three groups of 16-week-old ovariectomized Sprague-Dawley rats received subcutaneous injections of estrone, estrone-quinol, or vehicle (100?g/kg) every 48 hours for a period of two weeks. 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 takes place in tissues that are not estrogen-sensitive. These quinols appear to be candidates as effective neuroprotective agents.
**Sponsor:** *NIH*

**1115** **Presentation Type:** Poster

**Author:** Jwalitha Shankardas **Presentor:** Jwalitha Shankardas
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**Classification:** GSBS Student
*Jwalitha Shankardas* and S.D. Dimitrijevich****
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****Department of Integrative Pharmacology/ Cardiovascualr Research Institute,Fort Worth, TX-76012*

**DIFFERENTIATION OF NEUROSPHERE CELLS AND CHARACTERIZATION OF THE RESULTING REACTIVE ASTROCYTES**

**Purpose:** The objectives of these studies are a. to show that the in vitro differentiation of neuronal progenitors produces reactive astrocytes, b. determine the PKC profile of the reactive astrocytes and c. Show that reactive astrocytes synthesize extracellular matrix.
**Methods:** Commercially available human neonatal neurospheres are cultured in a medium containing EGF, progesterone, insulin transferrin and fetal bovine serum (FBS, 5%). The resulting reactive astrocytes were examined by indirect immunofluorescence and western blot analysis for expression of characteristic marker proteins, PKC isoforms and collagen type I.
**Results:** : In addition to glial fabrillary protein (GFAP) and neuronal markers a-internexin, b -tubulin, reactive astrocytes also express vimentin, nestin and neuron specific enolase (NSE) and myosin light chain. The PKC profile consisted of string expression of PKC a, bI and z, and weak expression of PKC b II, h __d e; PKC d ___ q were not expressed. Astrocytes were also shown to obtain collagen and synthesize and excrete it.

**Conclusions:** Differentiation of neurosphere cells into astrocytes is an attachment dependent process that involves PKC a, bI and z. Less prominent in this process are PKC b II, h __d e. The presence of a cytoskeletal profile similar to that of the fibroblasts suggests that astrocytes could assemble a cytoskeleton that is appropriate for cell migration and matrix contraction.
**Sponsor:** *Tobacco Grant & Global Medical Research*

# PSYCHOLOGY

**1200** **Presentation Type:** Poster

**Author:** Susan Frensley **Presentor:** Susan Frensley
**Department:** FAMILY MEDICINE
**Classification:** GSBS Student
*Susan Frensley, M.S., Susan F. Franks, Ph.D., James R. Hall, Ph.D., Jerry McGill, Ph.D., Kelley Beck, B.A., Julie Hart, B.S., Sharon Yurvati, M.S., German Berbel, D.O., Adam Smith, D.O.*

**PSYCHOSOCIAL STRESS FACTORS MODERATE ADJUSTMENT DIFFICULTIES IN LAPAROSCOPIC BANDING PATIENTS**

**Purpose:** The purpose of this study was to assess Lap-Band candidates on stress moderator scales of the Millon Behavioral Medicine Diagnostic (MBMD), a psychological evaluation tool designed specifically for use with medical patients

The MBMD is a 165-item, self-report questionnaire designed to assess the psychological factors that can influence the course of disease and treatment of medically ill patients. Numerous studies have demonstrated its usefulness in predicting the course of disease and treatment outcomes, and in providing guidance for clinical management.

**Methods:** Participants included 115 (21 men, 94 women) morbidly obese patients who presented for pre-operative evaluation to the Bariatric Surgical Clinic and UNT-HSC. Participants ranged in age from 22 to 69 years (M=44.8). The range of Body Mass Index (BMI) was 27 to 82 (M =47.4). Each participant completed the MBMD as part of a standard pre-operative assessment battery.
**Results:** Mean prevalence scores for six MBMD stress moderator scales were compared for two groups (High Prevalence Adjustment Difficulties, Low Prevalence Adjustment Difficulties).
Significant group differences were found in stress 4 stress moderators (Illness Apprehension, Functional Deficits, Pain Sensitivity and Future Pessimism). See figures for prevalence scores for stress moderators (Illness Apprehension, Functional Deficits, Pain Sensitivity, Social Isolation, Future Pessimism, and Spiritual Absence).

**Conclusions:** The hypothesis that psychosocial stress factors contribute to post surgical adjustment difficulties was supported. Significant group differences were found in four stress moderators (Illness Apprehension, Functional Deficits, Pain Sensitivity and Future Pessimism).

**Sponsor:**

**1201** **Presentation Type:** Poster

**Author:** Richard Kennerly **Presentor:** Julie Hart
**Department:** FAMILY MEDICINE
**Classification:** Dual Degree Student
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*Julie Hart, University of North Texas, Denton, Texas, 76203*
*Genie Bodenhamer-Davis, University of North Texas, Denton, Texas,76203*
**INCIDENTAL VERSUS INTENTIONAL MEMORY WITH THE COMPLEX FIGURE TEST**
**Purpose:** The current study was designed to isolate test-retest effects from the effect of incidental vs. intentional memory to determine if the cueing to the memory task on retest has significant impact on test scores.
**Methods:** This study utilized the MACK Complex Figure (MACK) as an alternate figure to control for test-retest effects with the REY Osterith Complex Figure Test (REY) in 525 undergraduates.
**Results:** Statistically significant increases in mean scores were found as a test-retest effect on repeat administration of the REY. No statistically significant differences were found in mean scores on the REY or MACK for initial administration. When the MACK was substituted for the REY on retest, there were no statistically or clinically significant differences in mean scores.
**Conclusions:** When test-retest effects were controlled for, no statistically significant differences were found for the incidental vs. intentional memory tasks on the REY or on the MACK.
**Sponsor:** *none*

**1202** **Presentation Type:** Poster

**Author:** Elizabeth Begyn **Presentor:** Elizabeth Begyn
**Department:** FAMILY MEDICINE
**Classification:** GSBS Student
*Elizabeth L Begyn, Susan F Franks, PhD, James R. Hall, PhD, Susan Frensley, MS, Kelley Beck, BA, Sharon Yurvati, MS, German Berbel, DO, and Adam Smith, DO*
*University of North Texas Health Science Center*
**EATING BEHAVIORS IN PEOPLE WITH HIGH VERSUS LOW RISK EATING BEHAVIORS**
**Purpose:** Obesity affects approximately one-third of the American population, operating as a significant risk factor for diabetes, hypertension, and heart disease. This study researched whether people with low versus high risk eating patterns employ different coping styles.
**Methods:** A total of 73 patients completed the Millon Behavioral Medicine Diagnostic (MBMD) and Eating Inventory (EI) for a presurgical health and behavioral assessment for bariatric surgery. Patients included 59 women, 63 Caucasian, 3 African American, 4 Hispanic, and 1 Asian American, ages 29-69.
**Results:** Patients included 59 women, 63 Caucasian, 3 African American, 4 Hispanic, and 1 Asian American, ages 29-69.One-Way ANOVAs revealed patients with low cognitive restraint employ more cooperative and less respectful coping strategies. Patients with high disinhibition eating patterns utilize more inhibited, dejected, and cooperative coping styles. Also, people with low cognitive restraint employ more cooperative and less respectful coping strategies
**Conclusions:** This study reveals the influential cognitive, behavioral, and interpersonal strategies that affect eating behaviors. This information can be useful to understand the complexity of eating behaviors and to maximize treatment goals both pre and post-operatively.
**Sponsor:** *none*

**1203** **Presentation Type:** Poster

**Author:** Kathryn Kaiser **Presentor:** Kathryn Kaiser
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**Classification:** GSBS Student
*Kathryn A. Kaiser, B.S., MT(ASCP), Susan F. Franks, Ph.D., James R. Hall, Ph.D., Jerry C. McGill, Ph.D., German Berbel, D.O., F.A.C.O.S., and Adam B. Smith, D.O., F.A.C.O.S. University of North Texas – Health Science Center, Fort Worth, TX 76107*
**CHANGES IN PSYCHOLOGICAL DIMENSIONS OF EATING BEHAVIOR AFTER LAPAROSCOPIC BANDING: A PRELIMINARY ANALYSIS**
**Purpose:** Patients who have undergone laparoscopic banding surgery (lap-band) commonly report a distinct reduction in appetite, however the mechanism underlying this shift remains obscure. This study presents pilot data for a broader investigation designed to determine psychophysiological aspects of appetite, specifically as related to changes occurring after lap-band.
**Methods:** Subjects were 13 female patients (age X= 42.4, SD = 9.41). The Eating Inventory (EI) was administered pre- and post-surgery to assess three psychological dimensions of eating behavior: Cognitive Restraint (CR), Disinhibition (DI) and Hunger (H). Fasting ghrelin was measured pre- and post-surgery. Post-surgery measures occurred after at least one tightening of the band, with a time span between surgery and second measure (in days) of X= 54.8, SD = 16.7.
**Results:** Results indicate significant changes in EI subscales between published clinical ranges in paired difference t-tests (see table). There was a significant reduction in BMI but not in fasting ghrelin t(12)= 1.72, p=.11. Relationships between BMI change and EI subscale changes were not significant.
**Conclusions:** Results of pilot data demonstrate significant change in psychological dimensions of appetite that appear to be independent of weight loss and fasting ghrelin. The EI appears to be a valuable standardized tool for quantifying psychological aspects of eating behavior in investigations of appetite regulation. Future studies designed to determine mechanisms of appetite change reported after the lap-band should consider psychophysiological interactions.
**Sponsor:** *HSC Faculty Grant/Inamed*

# PSYCHOLOGY

**1204** **Presentation Type:** Poster

**Author:** Swati Varshney **Presentor:** Swati Varshney
**Department:** GRADUATE SCHOOL OF BIOMEDICAL SCIENCES
**Classification:** GSBS Student
*Swati Varshney, M.A.,Kimberly Kelly, Ph.D.,University of North Texas,Michael Ennis,M.A.,University of California at Davis*

**SEX DIFFERENCES IN SALIVARY CORTISOL EXCRETION DURING ANTICIPATION OF A PSYCHOLOGICAL STRESSOR**

**Purpose:** The study tested the hypothesis that differential neuroendocrine elicitation is prompted by the subjects' cognitive expectations of an anticipated stressor. Participants making a 'threat appraisal' of an academic examination were predicted to have increased hypothalamic-pituitary-adrenal (HPA) activation, while this activation was expected to be unchanged in those making a 'challenge appraisal'. Self-reported anxiety in relation to these variables was also examined.
**Methods:** HPA activation was assessed via salivary cortisol at baseline (at least one week before the examination) and at pre-test (immediately before the examination).
**Results:** Findings suggested that salivary cortisol was not related to cognitive appraisal or to self-reported anxiety as hypothesised. Additionally, results did not demonstrate differential sex effects on the cognitive appraisal of an acute psychological stressor and salivary cortisol output. However, interesting results emerged for the level of anxiety experienced by the participants. The results indicated that the overall level of anxiety differed significantly from baseline to pre-test with anxiety increasing immediately before the exam. Males manifested increased cortisol excretion whereas females manifested a higher level of anxiety.
**Conclusions:** The results indicated a novel finding that females in the luteal phase experienced significantly greater anxiety than females in the follicular phase or male participants.
**Sponsor:** *none*

**1205** **Presentation Type:** Poster

**Author:** LaDonna Saxon **Presentor:** Kathryn Kaiser
**Department:** UNT SYSTEM
**Classification:** GSBS Student
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**THE COMMUNITY OF SELVES REPERTORY GRID: STABILITY AND UTILITY IN THE ASSESSMENT OF SPIRITUALITY AND ITS RELATIONSHIP TO COPING**

**Purpose:** This study is an examination of The Community of Selves Repertory Grid (RepGrid; Doster & Watson, 1987) and its application to coping. We report on the test-retest reliability of the RepGrid and its use as an intrinsic measure of spirituality (one of the 15 selves). We also examine this measure of spirituality as it relates to coping strategies.
**Methods:** Eighty-six undergraduates (40% Males, Age M = 21.3 years) completed the RepGrid twice, M = 15.3 days apart. On the second test date, participants also completed a modified Ways of Coping Checklist (Parker & Brown, 1986), which consisted of 47 items. 14 questions are spirituality-related items added from the R-COPE (Pargament, Koenig & Perez, 2000).
**Results:** RepGrid Test/Retest Correlation Coefficients (Pearson's r, $p = <.01$ for all values): [Overall Score, Spirituality Score Only] Percent Zeroes = .83, .86; Functionally Independent Constructs (FIC) = .70, .65; Ordination (ORD) = .75, .44; Constriction = .81, .72.

Participants who exhibited a higher level of spiritual interdependence (FIC) with the larger community of selves had a higher number of coping strategies endorsed as "effective" ($r = .27$, $p = .05$, one tailed). Participants who had a more narrow range of convenience (higher percent zeroes for spirituality) reported a lower proportion of effective coping strategies ($r = -.36$, $p = .01$, one-tailed).
**Conclusions:** The RepGrid displayed a high degree of reliability and is a useful tool for assessing the construct of spirituality. Further, there appears to be a significant relationship between spirituality and the number of effective strategies used to cope with stress.
**Sponsor:** *none*

**1206** **Presentation Type:** Poster

**Author:** Desiree Muse **Presentor:** Desiree Muse
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**SPIRITUALITY AND COPING STYLE IN TYPE 2 DIABETES PATIENTS**

**Purpose:** The role of spirituality as it impacts health and overall well-being is being examined more closely in traditional medicine and mental health settings. However, there is little research on the degree to which spirituality is related to known coping styles. The purpose of the study was to examine the relationship between degree of spirituality and the methods of coping with type 2 diabetes. It was hypothesized that patients with a higher degree of spirituality would be more likely to engage in distraction coping methods.
**Methods:** The study consisted of 51 participants, (30 female and 21 male) ranging in age from 18 to 89, at a medical university-based family medicine clinic. The Coping with Health Injuries and Problems (CHIP) was administered to measure 4 different methods of coping with illness: Distraction, Palliative, Instrumental, and Emotional Preoccupation. The Multidimensional Health Profile (MHP) was administered to assess the degree of reliance on spiritually-related involvement when ill. Subjects were divided into high and low Spirituality based on a one standard deviation scores above or below the mean. Participants falling within a standard deviation of the mean were not included in the analysis. A MANOVA was used to determine the differences between high and low Spirituality for three coping styles.
**Results:** Results indicated a significant difference between coping styles $F(1, 49) = 63.605$, $p = .000$.
**Conclusions:** Diabetes patients who rely very little on spiritual resources for dealing with their illness utilize more instrumental coping and less distraction coping than patients who rely heavily on spiritually-related help. Future studies should examine the degree to which these differences impact positive and negative health behaviors and overall management of the disease, with implications for designing behavioral health interventions.
**Sponsor:** *none*

**1207** **Presentation Type:** Poster

**Author:** Nyaz Didehbani **Presentor:** Nyaz Didehbani
**Department:** FAMILY MEDICINE
**Classification:** GSBS Student
*Nyaz Didehbani, B.S., Susan Franks, Ph.D., Scott Hilborn, B.A ., Margaret Budd, B.A., A. Clifton Cage, D.O, Elizabeth Palmarozzi, D.O.*

*University of North Texas Health Science Center at Fort Worth*

**PREDICTING PSYCHOLOGICAL DISTRESS IN TYPE II DIABETES: STRESS, COPING, AND HYPERTENSION**

**Purpose:** The objective of the study was to determine whether perceived stress, total coping, and hypertension are predictive of psychological distress in clients with diabetes. This study examined the relationship between perceived stress (MHP-PST), medical conditions (hypertension), total coping (MHP-COP), and total psychological distress (MHP-DIS). Total psychological distress includes depressed affect, guilt, motor retardation, anxious affect, somatic complaints, and cognitive disturbances as measured on the Multidimensional Health Profile.
**Methods:** Participants ($N = 74$) were recruited at the University of North Texas Health Science Center in Fort Worth. Particpants included 34 males and 40 females. They ranged in age from 18 to 60 ($M=54.3$).
**Results:** Perceived Stress factors were associated with psychological distress: ($t= 3.79$, $p<.001$). Coping factors ($t=2.53$, $p=.014$) were positively associated with our outcome variable as was the addition of having hypertension ($t= 2.35$, $p=.022$), and informational support from family ($t=-2.48$, $p<.01$). These variables accounted for a significant amount of variance in psychological distress (R Square = .30, $F(4,69)=7.26$, $p<.001$).
**Conclusions:** The study showed that percieved stress, coping, and hypetension predict psychological distress in type II diabetes. Interventions that focus on managing coping styles with diabetic patients with hypertension may be useful when working with this population.

**Sponsor:** *none*

# PHYSICAL MEDICINE/OCCTIC

**1300** **Presentation Type:** Poster

**Author:** Amy Zidron **Presentor:** Amy Zidron
**Department:** Social & Behavioral Sciences
**Classification:** Dual Degree Student DO/PhD
*Amy M. Zidron Ohio University College of Osteopathic Medicine Athens, Ohio 45701*
*Amanda M. McConnell Ohio University College of Osteopathic Medicine Athens, Ohio 45701*
*Gillian H. Ice Ohio University College of Osteopathic Medicine Athens, Ohio 45701*

**PREVALENCE OF SOMATIC DYSFUNCTION AMONG ELDERLY KENYAN POPULATION**

**Purpose:** Although the phrase somatic dysfunction (SD) is one that is well known throughout the osteopathic community, the concept is not often addressed in research. Due to the HIV/AIDS crisis in Africa crisis in Africa, many Luo elders are given the responsibility of caring for one of the 890,000 orphans now living in Kenya, in addition to performing daily activities. The Luo population is thus ideal for research involving SD.

We hypothesized that SD would be more prevalent among caregivers than noncaregivers and more present in women than men. It was also predicted that prevalence of SD would be unique to the type of farming performed in a community and that SES would be inversely proportional to SD. It was expected for SD to be positively association with the body systems addressed in a clinical history.

**Methods:** This study assessed the prevalence of SD and its association with caregiving status, sex, type of farming and socioeconomic status in a population of 103 Kenyan elders. An osteopathic screen performed by a trained osteopathic medical student determined SD. An interview and a complete physical examination were utilized to determine the other variables of interest.

**Results:** SD was prevalent among all participants and was associated with caregiving intensity, perceived burden, waist-to-hip ratio and occupation. Women and farmers had more SD at the costal cage than men and nonfarmers respectively. Significant associations were found among millet and rice farmers and SD in a particular region. The relationship between SES and SD was insignificant. SD was not found to be of clinical significance in this population, but more research is needed to verify the results determined by the clinical history.

**Conclusions:** This study has expanded knowledge of the prevalence of SD in the Kenyan population. SD was found to be prevalent among all members of the population. More information is required to draw more definitive conclusions regarding the associations between the type of farming performed and the presence or absence of SD. Furthermore, the reliability of this study needs to be increased in order to increase the significance of the results. The importance of researching the prevalence of SD in any population cannot be understated as it will help add to the growing bank of knowledge regarding the validity of the practice of osteopathy.

**Sponsor:** *OU-COM Research Award and Scholarly Advancement Fellowship*

**1301** **Presentation Type:** Poster

**Author:** John Licciardone **Presentor:** John Licciardone
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*John C. Licciardone, D.O., M.S., M.B.A., Kimberly G. Fulda, M.P.H., Scott T. Stoll, D.O., Ph.D., Russell G. Gamber, D.O., M.P.H., Clifton Cage, D.O.; University of North Texas Health Science Center, Fort Worth, TX 76107.*

**OSTEOPATHIC PALPATORY FINDINGS IN TYPE 2 DIABETES MELLITUS: A CASE-CONTROL STUDY**

**Purpose:** Osteopathic palpatory findings are hypothesized to reflect organic disorders such as diabetes mellitus. Such findings may represent viscerosomatic manifestations of disease. This study was performed to identify osteopathic palpatory findings associated with type 2 diabetes mellitus.

**Methods:** A case-control study was conducted at the University of North Texas Health Science Center during 2002-2003. A total of 60 type 2 diabetes mellitus cases and 33 controls were included. Standardized osteopathic palpatory examinations were performed by predoctoral osteopathic manipultive medicine fellows who were blinded to each subject's case-control status. These examinations determined the presence or absence of skin changes, trophic changes, tissue changes, tenderness, and immobility at spinal segments T5-T7, T8-T10, and T11-L2 on either the left or right side. Multiple logistic regression was used to compute age- and sex-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for osteopathic palpatory findings associated with type 2 diabetes mellitus.

**Results:** Three osteopathic palpatory findings were significantly associated with type 2 diabetes mellitus: tissue changes at T11-L2 on the right side (OR, 4.49; 95% CI, 1.69-11.96; P=.003); tenderness at T11-L2 on the left side (OR, 4.28; 95% CI, 1.13-16.20; P=.03); and immobility at T5-T7 on the right side (OR, 2.71; 95% CI, 1.09-6.75; P=.03).

**Conclusions:** The significant findings observed in this case-control study support the concept of viscerosomatic manifestations of type 2 diabetes mellitus. The observed associations must be interpreted in light of the complex pathogenesis of type 2 diabetes mellitus. Additional research is warranted to: (1) replicate these findings in a prospective manner; (2) determine if, and how, such changes are caused by type 2 diabetes mellitus; and (3) determine if osteopathic manipulative treatment may have a role in complementing the standard treatment of type 2 diabetes mellitus.

**Sponsor:** *Supported by a grant from the American Osteopathic Association (# 01-11-526) to Dr. Licciardone.*

**1302** **Presentation Type:** Poster

**Author:** John Licciardone **Presentor:** John Licciardone
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*John C. Licciardone, D.O., M.S., M.B.A., Kimberly G. Fulda, M.P.H., Scott T. Stoll, D.O., Ph.D., Russell G. Gamber, D.O., M.P.H., Clifton Cage, D.O.; University of North Texas Health Science Center, Fort Worth, TX 76107.*

**INTEREXAMINER RELIABILITY OF OSTEOPATHIC PALPATORY FINDINGS**

**Purpose:** The study of intra- and interexaminer reliability of osteopathic palpatory findings continues to be a research priority. Previous studies often have been limited by various methodological issues and have yielded conflicting results. This study was performed to measure the interexaminer reliability of basic osteopathic palpatory findings.

**Methods:** Subjects in this study were recruited for subsequent participation in a case-control study of osteopathic palpatory findings in type 2 diabetes mellitus to be conducted at the University of North Texas Health Science Center during 2002-2003. Standardized osteopathic palpatory examinations were performed by two independent predoctoral osteopathic manipultive medicine fellows who were blinded to each subject's case-control status. Six fellows (three non-overlapping pairs) performed these examinations at various times during the study. The examinations were used to determine the presence or absence of skin changes, trophic changes, tissue changes, tenderness, and immobility at spinal segments T5-T7, T8-T10, and T11-L2 on either the left or right side. Interexaminer agreement between the fellows who examined a given subject was summarized both as a crude proportion and the chance-adjusted kappa-value.

**Results:** A total of 91 subjects were included in the analysis: 46, 34, and 11 subjects examined by each of the three fellow pairs, respectively. Overall, the proportional agreement was 0.68 (kappa, 0.35). Similar levels of proportional agreement (and kappa) were observed according to spinal segment and laterality: 0.67 (0.34) for T5-T7; 0.67 (0.35) for T8-T10; 0.69 (0.36) for T11-L2; 0.67 (0.34) for left-sided findings; and 0.68 (0.36) for right-sided findings. Overall proportional agreement (and kappa) for each of the five palpatory elements were: 0.69 (0.16) for skin changes; 0.66 (0.28) for trophic changes; 0.58 (0.05) for tissue changes; 0.84 (0.54) for tenderness; and 0.62 (0.09) for immobility.

**Conclusions:** The observed overall level of chance-adjusted agreement of osteopathic palpatory findings in this study is comparable to that reported for other commonly used diagnostic tests, such as electrocardiograms to identify ST-T responses and peripheral blood films to diagnose iron-deficiency anemia. Although interexaminer agreement between fellows does not vary substantially according to spinal segment and laterality, it does vary according to the element of osteopathic palpation being performed.

**Sponsor:** *Supported by a grant from the American Osteopathic Association (# 01-11-526) to Dr. Licciardone.*

**1303** **Presentation Type:** Poster

**Author:** John Licciardone **Presentor:** John Licciardone
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*John C. Licciardone, D.O., M.S., M.B.A, Professor, Department of Family Medicine, University of North Texas Health Science Center, Fort Worth, TX 76107.*

**OSTEOPATHIC PALPATORY FINDINGS IN HYPERTENSION, TYPE 2 DIABETES MELLITUS, AND DEPRESSION: A CASE-CONTROL STUDY**

**Purpose:** Osteopathic palpatory findings may represent viscerosomatic manifestations of disease. This study was performed to identify osteopathic palpatory findings associated age, sex, and common clinical entities in primary care.

**Methods:** This study was performed as a secondary analysis of data acquired from a case-control study of type 2 diabetes mellitus conducted at the University of North Texas Health Science Center during 2002-2003. Standardized osteopathic palpatory examinations were performed by predoctoral osteopathic manipultive medicine fellows who were blinded to each subject's case-control status. These examinations determined the presence or absence of skin changes, trophic changes, tissue changes, tenderness, and immobility at spinal segments T5-T7, T8-T10, and T11-L2 on either the left or right side. Multiple logistic regression was used to compute odds ratio (ORs) and 95% confidence intervals (CIs) for osteopathic palpatory findings associated with age, sex, hypertension, type 2 diabetes mellitus, and depression.

**Results:** Of the 93 subjects included, 39 (42%) had hypertension, 60 (65%) had type 2 diabetes mellitus, and 30 (32%) had depression. The over-representation of type 2 diabetes mellitus cases reflects the purpose of the primary study. Generally, age was not significantly associated with osteopathic palpatory findings. Men were more often found to have skin and trophic changes than women, but men were less often found to have tenderness than women. Hypertension was significantly associated with bilateral trophic changes in each of the three spinal segments (OR, 3.73; 95% CI, 1.28-10.83 for left T5-T7; OR, 5.55; 95% CI, 1.93-15.90 for right T5-T7; OR, 3.91; 95% CI, 1.37-11.20 for left T8-T10; OR, 3.49; 95% CI, 1.25-9.75 for right T8-T10; OR, 12.33; 95% CI, 3.25-46.74 for left T11-L2; and OR, 4.83; 95% CI, 1.59-14.67 for right T11-L2).

**Conclusions:** Hypertension is strongly associated with bilateral trophic changes at T5-T7, T8-T10, and T11-L2. This study is unique in controlling for age, sex, and other comorbid conditions. Additional research is warranted to: (1) replicate these findings in a prospective manner; (2) determine if, and how, trophic changes are caused by hypertension; and (3) determine if osteopathic manipulative treatment may have a role in complementing the standard treatment of hypertension.

**Sponsor:** *Supported by a grant from the American Osteopathic Association (# 01-11-526) to Dr. Licciardone.*

# PHYSICAL MEDICINE/OCCTIC

## 1304 Presentation Type: Oral

**Author:** Marisa Wynne **Presentor:** Marisa Wynne
**Department:** OCCTIC
**Classification:** OCCTIC Student/Resident
*M.M. Wynne, J.M. Burns, D.C. Eland, R.R. Conatser, J.N. Howell*
*Departments of Biomedical Sciences and Family Medicine, Ohio University College of Osteopathic Medicine, Athens, Ohio 45701*

### EFFECTS OF COUNTERSTRAIN ON REFLEXES AND CLINICAL OUTCOMES IN SUBJECTS WITH PLANTAR FASCIITIS

**Purpose:** Previous work (Cabell et al, JAOA, 98:390, 1998) suggested that counterstrain produces a decrease in the amplitude of the soleus stretch reflex in Achilles tendonitis subjects. The current study was designed to study the effects of counterstrain on stretch reflex activity and clinical outcomes in subjects with plantar fasciitis.
**Methods:** The study compared the effects of counterstrain with placebo in a randomized, single blind study of cross-over design, in which adult subjects (N=20) with plantar fasciitis were led to believe that both the counterstrain and placebo were therapeutic measures whose effects were being compared. Subjects were assigned to begin with either counterstrain or placebo. Each treatment period was three weeks in duration with a two to four week interval between treatments. Clinical outcomes were assessed with questionnaires administered daily during the study. Stretch and Hoffman (H) reflexes in the soleus muscle were assessed electromyographically twice during each lab visit, before and after treatment in the manipulation phase.
**Results:** No significant changes in the electrically recorded stretch or H-reflexes of the soleus muscle were observed in response to treatment. However, changes in the twitches resulting from the electrical responses were observed. Peak torque and time to peak torque both increased ($P = .05$) in the post-treatment measurements, the increase being more significantly pronounced in the manipulation group ($P = .05$). A comparison of symptom severity pre- and post-treatment demonstrated significant relief of symptoms that was most pronounced immediately following treatment.
**Conclusions:** These results indicate that there are significant clinical responses to counterstrain in plantar fasciitis subjects, and that mechanical changes in the lower leg accompany the clinical responses. The causative relation between the mechanical changes and the clinical responses remain to be explored.
**Sponsor:** *Research and Scholarly Advancement Program, Ohio University College of Osteopathic Medicine*

## 1305 Presentation Type: Poster

**Author:** Patricia Meyer **Presentor:** Patricia Meyer
**Department:** MANIPULATIVE MEDICINE
**Classification:** TCOM DO Student
*Patricia M. Meyer, B.S., Scott T. Stoll, D.O., Ph.D., des Anges Cruser, Ph.D. MPA., Heath D. White, B.S., Rebecca Whitesell, B.S.*
*Texas College of Osteopathic Medicine, University of North Texas Health Science Center at Fort Worth, Department of Manipulative Medicine.*
*3500 Camp Bowie Blvd. Fort Worth, TX 76107*

### EFFECTS OF OSTEOPATHIC MANIPULATIVE TREATMENT ON SYMPTOM SEVERITY AND FUNCTIONAL STATUS IN CARPAL TUNNEL SYNDROME

**Purpose:** Carpal tunnel syndrome (CTS), caused by compression of the median nerve within the carpal canal, affects up to 10% of the adult population in the United States with medical costs exceeding $2 billion annually. Complaints include pain and restricted movement of the wrist and hand. The goal of this prospective, randomized, blinded clinical trial is to evaluate the benefits of Osteopathic Manipulative Treatment (OMT) on the symptom severity and daily functioning of subjects with CTS.
**Methods:** A power analysis indicated that 25 individuals in each of two groups, an OMT and a placebo control group (sub-therapeutic ultrasound) would be adequate. Eligibility criteria include individuals between 21 and 70 with a clinical diagnosis of CTS and specific nerve conduction values that validated the presence of nerve impingement. Primary outcome measures for this study are symptom severity and functional status scores, with secondary outcomes of strength measures. Subjects receive six treatments with measures taken prior to beginning treatment, prior to the fourth treatment, and one week following the last treatment.
**Results:** wenty-one subjects have completed the study to date. Preliminary analysis, using paired T-test, shows a significant difference between pre and post treatment measures for the symptom severity ($p=0.003$) and functional status scores ($p=0.017$) in the OMT group and are not significant in the sham ultrasound group. Strength findings were mixed due to further division of groups to account for gender differences in strength.
**Conclusions:** Trends based on initial analysis are positive. Final data analysis will include ANOVA with repeated measures and analysis of strength measures. This study is supported by a grant from the American Osteopathic Association Bureau of Research and the Osteopathic Research Center.
**Sponsor:** *AOA*

## 1306 Presentation Type: Poster

**Author:** Heath White **Presentor:** Heath White
**Department:** MANIPULATIVE MEDICINE
**Classification:** Dual Degree Student DO/MS
*Heath D. White, B.S.1, Scott T. Stoll, D.O., Ph.D.1,2, des Anges Cruser, Ph.D. MPA1,2, Patsy M. Meyer, B.S.1*
*Department of Osteopathic Manipulative Medicine1 and the national Osteopathic Research Center2 University of North Texas Health Science Center*
*3500 Camp Bowie Blvd. Fort Worth, TX 76107*

### PHYSIOLOGIC AND ANATOMIC CHANGES IN CARPAL TUNNEL SYNDROME: IS OSTEOPATHIC MANIPULATIVE TREATMENT AN EFFECTIVE NON-SURGICAL ALTERNATIVE THERAPY?

**Purpose:** Carpal tunnel syndrome (CTS), caused by compression of the Median nerve within the carpal tunnel, affects up to 16% of the adult population in the United States with medical costs exceeding $2 billion annually. The goal of this randomized, blinded, placebo controlled clinical trial was to determine the ability of Osteopathic Manipulative Treatment (OMT) to effect physiologic and anatomic changes in subjects with CTS, using nerve conduction studies (NCS) and magnetic resonance imaging (MRI).
**Methods:** Subjects were randomized between two groups: OMT and Placebo Sub-therapeutic Ultrasound. Eligibility criteria included adults between 21 and 70 with a clinical diagnosis of CTS and increased latency in the median nerve on NCS. Outcome measures were Median motor and sensory nerve conduction distal latencies, carpal tunnel A/P and transverse dimensions, cross sectional area, and edema within the carpal tunnel and median nerve. Subjects received six treatments at a frequency of one treatment per week. NCS were conducted at baseline, prior to the fourth treatment, and one week following the last treatment. A MRI of the wrist was taken pre and post treatment protocol.
**Results:** Thirty-seven of a planned 50 subjects have completed the study to date and no further subject recruitment is planned. Preliminary analysis indicates that there are important differences between the two experimental groups at baseline to the study, in some of the NCS values. Because this is a preliminary study, and because the available published literature offers little reliable data for precedent, the analysis is primarily exploratory. The analysis is providing insights into the nature of the population, the merits of using NCS and MRI to assess the efficacy of OMT, and areas of focus that should be addressed in a larger OMT clinical trial. This study has led to the submission of a research proposal to the NIH-NCCAM for an R21 exploratory/developmental project.
**Conclusions:** As an initial, exploratory study of the utility of repeated NCS to detect changes in nerve conduction and MRIs to detect anatomic changes and the presence of fluid/edema in the carpal tunnel, this study is promising. An in-depth assessment of clinical results and the issues related to both placebo effects and outcome measure validity and reliability is currently underway. This study was approved by the UNTHSC IRB and supported through intramural funding by the Osteopathic Research Center.
**Sponsor:** *Osteopathic Research Center*

## 1307 Presentation Type: Poster

**Author:** Mousumi Som **Presentor:** Mousumi Som
**Department:** OCCTIC
**Classification:** TCOM DO Student
*Mousumi Som, BS, MS IV; Carolyn Pickett, BS, MS IV; Kimberly Fulda, BS, MPH; des Anges Cruser, Ph.D.; Scott Stoll, D.O., Ph.D.; Osteopathic Research Center, UNTHSC-TCOM, Fort Worth, Texas 76107*

### THE EFFICACY OF OSTEOPATHIC MANIPULATIVE MEDICINE ON A COPD POPULATION

**Purpose:** We are conducting a randomized, blinded, and controlled pilot study to determine if Osteopathic Manipulative Medicine (OMM) can improve pulmonary function and quality of life in a COPD patient.

This poster will present the study design and rationale, relevant background and importance and the lessons learned about conducting clinical research
**Methods:** We are recruiting 50 individuals with COPD between the ages of 40 and 80 from the Patient Care Center at UNTHSC-TCOM . Subjects are included if they have a clinical diagnosis of COPD and no contraindications to participating. After receiving informed consent, we randomly assign the subject to either an OMM intervention or resting period of 30 minutes. The IRB approved the study in November 2004.

Subjects perform two respiratory tests: 1) spirometry and 2) plethysmography. Subjects complete the St. George's Respiratory Questionnaire, The American Thoracic Society Dyspnea Index, and the Borg Scale. After completing the questionnaires and providing basic demographic information, the subjects perform a six minute walk. The following observations are recorded: 1) Distance walked 2) Heart Rate and 3) Oxygen Saturation. Following the six minute walk, subjects complete a second Borg Scale.

After receiving either OMM or resting for 30 minutes, subjects perform a second set of pulmonary function tests and complete a third Borg Scale. We also administer a short questionnaire to test for blinding effectiveness after the second set of tests. Subjects perform a second six minute and complete a fourth Borg scale.
**Results:** As of March 11, ten subjects have completed the trial. Statistical analysis will be performed on the collected data after subject recruitment is completed.
**Conclusions:** Based on research conducted on healthy populations there is evidence supporting positive changes in pulmonary function as measured by spirometry and plethysmography after an OMM treatment. Currently, there are no known published prospective, randomized, blinded, controlled clinical trials to evaluate the clinical actions and effects of OMM on COPD.

We will use statistical analysis for small samples to determine if there is an immediate effect of OMM on the following outcomes: 1.) Pulmonary Function Values and 2.) Perceived quality of life and confidence in treatment. If statistical significance is present in the clinical outcomes, we anticipate the Osteopathic Research Center will seek support for a larger clinical trial.
**Sponsor:** *Osteopathic Research Center*

# PHYSICAL MEDICINE/OCCTIC

**1308** **Presentation Type:** Poster

**Author:** John Licciardone **Presentor:** John Licciardone
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*John C. Licciardone, D.O., M.S., M.B.A., Professor, Department of Family Medicine, University of North Texas Health Science Center, Fort Worth, TX 76107.*

**MIDCAREER INVESTIGATOR AWARD IN CAM-OSTEOPATHIC MEDICINE (K24)**

**Purpose:** The purpose of the Midcareer Investigator Award in CAM-Osteopathic Medicine (K24) is to provide protected time and resources for the author/presenter to: (1) undertake career development activities involving osteopathic manipulative treatment (OMT), including its mechanistic aspects and clinical applications; (2) mentor beginning clinician investigators; and (3) conduct a randomized clinical trial of OMT for chronic low back pain.

**Methods:** Career development activities will be available on the campus of the University of North Texas Health Science Center through: (1) health professional and graduate courses offered by the Texas College of Osteopathic Medicine, the Graduate School of Biomedical Sciences, and the School of Public Health; and (2) research collaborations with other investigators within the national Osteopathic Research Center. Off-campus education and training will be available through various osteopathic organizations. Mentoring relationships will be established with beginning clinician investigators, including postdoctoral clinical research fellows and junior faculty members in osteopathic manipulative medicine and osteopathic primary care specialties. Investigators will have the opportunity to participate in ongoing patient-oriented research.

**Results:** The randomized clinical trial will address the efficacy of OMT for chronic low back pain with respect to the following primary outcomes: (1) visual analogue scale for low back pain; (2) Roland-Morris Disability Questionnaire; (3) Medical Outcomes Study Short Form-36 scales; (4) work disability; and (5) satisfaction with back care.

**Conclusions:** The Midcareer Investigator Award in CAM-Osteopathic Medicine (K24) represents an important mechanism for the national Osteopathic Research Center to leverage its current funding to support faculty development, mentoring of beginning clinician investigators, and expansion of OMT research.

**Sponsor:** *Application under review, NIH-National Center for Complementary and Alternative Medicine*

**1309** **Presentation Type:** Poster

**Author:** John Licciardone **Presentor:** John Licciardone
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
*John C. Licciardone, D.O., M.S., M.B.A., Steve Buchanan, D.O., Kendi Pim, D.O., des Anges Cruser, Ph.D., Scott T. Stoll, D.O., Ph.D., University of North Texas Health Science Center, Fort Worth, TX 76107.*

**A PILOT CLINICAL TRIAL OF OSTEOPATHIC MANIPULATIVE TREATMENT IN PREGNANCY**

**Purpose:** The purpose of this pilot clinical trial is to explore the efficacy of osteopathic manipulative treatment (OMT) in women during the third trimester of pregnancy, labor and delivery, and the post-partum period.

**Methods:** Subjects for this randomized clinical trial have been recruited since August 2003 in the Department of Obstetrics and Gynecology at the University of North Texas Health Science Center-Texas College of Osteopathic Medicine. Approximately 100 subjects are expected to complete the trial. Subjects are enrolled at the 28th week of pregnancy. Exclusion criteria include any of the following: (1) presentation for obstetrical care following the 28th week of pregnancy; (2) intent to deliver at a non-designated hospital; (3) high-risk pregnancy as determined by the attending obstetrician. The latter category includes, but is not limited to, maternal age, vaginal bleeding, gestational diabetes, pre-eclampsia/eclampsia, placenta previa, and abruptio placenta. Each subject is randomized to one of three groups: (1) usual obstetrical care and OMT; (2) usual obstetrical care and sham ultrasound treatment; and (3) usual obstetrical care only. The OMT and sham ultrasound treatments are provided by licensed physicians during seven prenatal visits (assuming a full-term pregnancy) and two post-partum visits. The primary outcomes include: (1) a visual analogue scale for low back pain; (2) the Roland-Morris Disability Questionnaire; and (3) the Medical Outcomes Study Short Form-12 scales. Secondary outcomes include maternal and fetal complications during pregnancy, labor, and delivery.

**Results:** Of the first 900 clinic patients screened through March 2005, 351 (39%) were eligible for inclusion in the trial and 99 (28% of eligibles) elected to participate and were randomized. Of these, 48 (49%) have completed the trial; 20 (20%) are currently enrolled, and 31 (31%) withdrew of their own volition or because of the incidence of a high-risk pregnancy complication.

**Conclusions:** The trial continues to recruit and follow subjects. Comprehensive data analyses will be performed at the trial's conclusion. If favorable outcomes are observed, a larger clinical trial will be warranted.

**Sponsor:** *Osteopathic Heritage Foundation*

**1310** **Presentation Type:** Poster

**Author:** Jeremy Russell **Presentor:** Jeremy Russell
**Department:** FAMILY MEDICINE
**Classification:** TCOM DO Student
*Jeremy W. Russell MS 4 - TCOM*
*Jaclyn C. Jones MS 4 - TCOM*
*Kimberly G. Fulda MPH - ORC*
*Ben Adams MS 2 - TCOM*
*Krystal Faifer MS 1 - TCOM*
*Susie Quintana B.S. - Family Medicine*
*Samuel T. Coleridge D.O. - Family Medicine*

*Ft.Worth, TX 76017*

**PREDICTABILITY OF MARATHON RUNNERS UTILIZING OSTEOPATHIC MANIPULATIVE TREATMENT AND CHIROPRACTIC TREATMENT**

**Purpose:** To determine our ability to predict the use of manual medicine (osteopathic manipulative / chiropractic treatment) among marathon runners based on age, gender, race / ethnicity, and total number of running related injuries.

**Methods:** A 19-item survey was presented to marathon runners participating in the Cowtown Marathon on February 26, 2005 in Fort Worth, TX. Survey items pertaining to age, gender, race/ethnicity, number of running related injuries, and manual medicine (either osteopathic manipulative treatment or chiropractic treatment) were analyzed. Statistical analyses included descriptive analysis, chi-square for group comparison, and multiple logistic regression to predict use of manual medicine. The UNTHSC Institutional Review Board approved the survey methodology.

**Results:** The total number of surveys completed was 277 of 722 registered marathon runners for a 38% response rate. On average, participants were 42 years of age (sd = 10.84) and had 1.41 total running related injuries (sd = 1.53). Of the sample, 201 (72.6%) were male, 234 (84.5%) were Caucasian, 191 (69.0%) had a running related injury, and 46 (16.6%) had ever received manual medicine. Those who reported an injury were significantly more likely to have had manual medicine, OR = 5.779; 95% CI (2.001, 16.686). The total number of injuries reported was a significant predictor of having had manual medicine ($p < 0.001$). Age, gender, and race / ethnicity were not statistically significant predictors.

**Conclusions:** Runners of the 2005 Fort Worth Cowtown Marathon, who reported running related injuries, were 5.8 times more likely to have received osteopathic manipulative or chiropractic treatment than those who did not report injuries. Additionally, for every increase in the total number of running related injuries, the odds of having received manual medicine increased 1.7 times. A significant number of marathon runners with injuries are utilizing manual medicine. Further research should be conducted to determine the potential efficacy of manual medicine in the treatment of running related injuries.

**Sponsor:** *Family Medicine*

**1311** **Presentation Type:** Poster

**Author:** Kimberly Fulda **Presentor:** Kimberly Fulda
**Department:** OCCTIC
**Classification:** SPH Student
*Kimberly G. Fulda, MPH, Osteopathic Research Center, Texas College of Osteopathic Medicine, University of North Texas Health Science Center at Fort Worth, TX 76107; Turner Slicho, DO, MS, Plaza Medical Center, Fort Worth, TX; Khiya Marshall, MPH, School of Public Health, University of North Texas Health Science Center at Fort Worth, TX 76107; Daisha Cipher, PhD, School of Public Health, University of North Texas Health Science Center at Fort Worth, TX 76107; Scott T. Stoll, DO, PhD, Osteopathic Research Center, Texas College of Osteopathic Medicine, University of North Texas Health Science Center at Fort Worth, TX 76107*

**ATTITUDES TOWARDS TREATMENTS COMMONLY USED IN OMM CLINICAL RESEARCH TRIALS**

**Purpose:** The purpose of this study is to determine attitudes towards three different treatments (HVLA, placebo light touch, placebo subtherapeutic ultrasound) commonly used in OMM clinical research trials.

**Methods:** This pilot study utilized a randomized, cross-over design. Subjects were recruited from the Family Medicine Clinic, Texas College of Osteopathic Medicine. Participants were asked to watch a video with 2 minute demonstrations of a High Velocity Low Amplitude (HVLA), placebo light touch (LT), and placebo subtherapeutic ultrasound (ULTRA) treatment for low back pain. The order of the demonstrations was randomized to control for order effect bias. Subjects were asked if they Strongly Agree, Agree, Disagree, or Strongly Disagree with 4 statements after each demonstration: 1. I believe this treatment would allow me to get better quicker; 2. I believe this treatment would decrease my low back pain; 3. I believe this treatment would make me more able to do the things I want to do; 4. This seems like a logical way to treat low back pain. Repeated measures analysis of variance was performed to determine the differences in responses to each question. A partial Eta squared is presented for each question. Cohen's d was calculated for 2 groups at a time. Study procedures were approved by the UNTHSC Institutional Review Board.

**Results:** Twenty of 29 eligible subjects participated. Of the participants, 15 (75%) were female, 12 (60%) were Caucasian, and 8 (40%) had completed college. The mean age was 43.6 years (sd=14.87). Repeated measures ANOVA revealed no significant differences for responses after each demonstration. The partial Eta squared was 0.03, 0.05, 0.04, and 0.002 for each statement, respectively. For statement 1, Cohen's d=-0.21 for HVLA and ULTRA, -0.196 for HVLA and LT, and 0 for ULTRA and LT. For statement 2, Cohen's d=0 for HVLA and ULTRA, -0.25 for HVLA and LT, and -0.28 for ULTRA and LT. For statement 3, Cohen's d=-0.24 for HVLA and ULTRA, -0.23 for HVLA and LT, and 0 for ULTRA and LT. For statement 4, Cohen's d=-0.06 for HVLA and ULTRA, -0.06 for HVLA and LT, and 0 for ULTRA and LT.

**Conclusions:** A lack of statistical significance could be due to a small sample size or no true differences between groups. Small effect sizes were found when examining the proportion of variance for the 3 treatments. Effect sizes were also small when examining 2 treatments at a time. When selecting an effective placebo, the effect sizes between HVLA and either placebo group is similar.

**Sponsor:** *ORC*

# PHYSICAL MEDICINE/OCCTIC

■ 1312 **Presentation Type:** Oral

**Author:** Janet Burns **Presentor:** Janet Burns
**Department:** OCCTIC
**Classification:** Faculty (Not for Competition)
*Janet M. Burns, D.O., Jillian S. Pleskow, MS III, Robert R. Conatser, M.S., David C. Eland, D.O., John N. Howell, Ph.D., and Robert L. Williams II, Ph.D.; Departments of Biomedical Science and Family Medicine, Ohio University College of Osteopathic Medicine and Department of Mechanical Engineering, Russ College of Engineering & Technology, Ohio University; Athens, OH 45701.*

**CONTRIBUTION OF CUTANEOUS AND PROPRIOCEPTIVE INPUTS TO OSTEOPATHIC PALPATORY DIAGNOSIS**

**Purpose:** The issue of which receptors are involved in medical palpation has been discussed in the literature; with some practitioners emphasizing the role of cutaneous receptors and others emphasizing the role of muscle proprioceptors. The relative importance of these modalities in osteopathic palpatory diagnosis is unknown, and objective methods of measuring palpatory skill have been lacking.

We investigated the importance of cutaneous feedback from the index finger and proprioceptive feedback from the upper extremity to osteopathic medical students' ability to identify: Tissue texture change, Asymmetry, and Resistance to motion; utilizing a virtual reality simulation of somatic dysfunction, the Virtual Haptic Back (VHB), currently under development at Ohio University.

**Methods:** Subjects' ability to identify randomly selected thoracic vertebrae, rotated out of position, or stiff to rotation, at 3 successive levels of difficulty was tested on 4 different days over 2 weeks. Following orientation, 2 trials of each task were run each day. On day 1 both trials were run without anesthesia. On days 2 & 3 the first trial was without anesthesia and the second was with either topical anesthesia (EMLA cream - lidocaine + prilocaine), or with digital block (2% lidocaine). On day 4 both trials were without anesthesia. Muscle spindles in the muscles controlling the palpating fingers were presumably unaffected. Computers recorded elapsed time and the number of errors before the correct vertebra was identified. Subjects were provided voice feedback as to whether or not they chose correctly.

**Results:** There were no statistically significant increases in number of incorrect responses or time required to perform either task, with either form of anesthesia.

**Conclusions:** Palpatory information needed to perform these 2 tasks on the VHB appears not be dependent upon superficial receptors subject to topical anesthesia, (Meissner's corpuscles and Merkel's disks), nor upon deeper cutaneous receptors subject to digital block, (Pacinian and Ruffini's corpuscles); but on proprioceptive input from the muscles of the upper extremity.

**Sponsor:** *Osteopathic Heritage Foundation, Office of Research & Grants,Ohio Univ. College of Osteopathic Med.*

Although abstracts were not available at press time for these presentations, the following posters will be displayed:

■ 1313 Multicenter Clinical Trial on OMT & Otitis Media in Children

■ 1314 Multicenter Osteopathic Pneumonia Study in the Elderly

■ 1315 Manual/Manipulative Therapy for Back Pain in Active Duty Military Personnel

■ 1316 Mentored Patient-Oriented Research Career Development Award (K23)

■ 1317 Competencies in Research in OMM (R25)

■ 1318 The Effects of Upper Cervical Manipulation on Vagal Tone

■ 1319 Lymphatic Pump Treatments Increase Thoracic Duct Flow

1400 **Presentation Type:** Poster

**Author:** Rafael Alvarez-Gonzalez **Presentor:** Rafael Alvarez-Gonzalez
**Department:** MOLECULAR BIOLOGY & IMMUNOLOGY
**Classification:** Faculty (Not for Competition)
*Rafael Alvarez-Gonzalez, Nils F. Confer, Sunitha R. Kumari, Manfred Frey, Hanswalter Zentgraf and Hilda Mendoza-Alvarez*

*University of North Texas Health Science Center at Fort Worth and*
*Deutsches Krebsforschungzentrum, Heidelberg, Germany*

**ENZYMATIC OLIGOMERIZATION OF PARP-1 WITH ITSELF, DNA POLYMERASE BETA AND P53**

**Purpose:** The purpose of this research project was to compare the ability of poly(ADP-ribose) polymerase-1 (PARP-1) to homodimerize, in the presence or absence of nicked DNA, versus its tendency to herodimerize with other DNA-damage activatable proteins in the mammalian chromosome, such as DNA polymerase beta or the tumor suppressor protein known as p53.
**Methods:** Methods utilized in this project include gene cloning, protein expression, protein denaturation, protein renaturation, protein purification, western blotting, co-immunoprecipitation, affinity chromatography, DNA-binding, immunofluorescence, gel filtration chromatography, HPLC, high resolution polyacrylamide gel electrophoresis, autoradiography, Electrophoretic Mobility Shift Assays (EMSA), enzyme assays, and enzyme kinetics.
**Results:** We observed that PARP-1 has the tendency to form catalytically competent homodimers, both, in the presence or in the absence of active DNA. However, the presence of activated (nicked) DNA significantly stabilized homodimerization and stimulated the enzymatic activity of PARP-1 to synthesize protein-bound ADP-ribose polymers. In addition, we also observed that PARP-1 was able to form catalytically competent heterodimers with DNA polymerase beta and p53. In fact, both DNA-damage dependent proteins were efficient covalent acceptors for covalent poly(ADP-ribosyl)ation as well.
**Conclusions:** Our experimental results are consistent with the conclusion that the formation of multi-enzyme complexes in mammalian chromatin, following the genotoxic exposure of cells in culture, facilitates the repair of damaged DNA. Therefore, the biochemical pathways that are regulated by these DNA/Protein macromolecular complexes may directly contribute to the prevention of carcinogenesis, tumor formation, and cancer.
**Sponsor:** *NIH/NIGMS*

# GENERAL PUBLIC HEALTH

**1500** **Presentation Type:** Oral

**Author:** Thaddeus Miller **Presentor:** Thaddeus Miller
**Department:** Health Management & Policy
**Classification:** SPH Student
*Thaddeus L. Miller,1,2 Peter Hilsenrath, 1,2 Kristine Lykens, 1,2 Scott J.N. McNabb,3 Patrick K. Moonan,1,2 and *Stephen E. Weis 1,2,4*

*Department of Medicine, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX; 1*
*School of Public Health, Fort Worth, TX; 2*
*Centers for Disease Control and Prevention, Atlanta, GA; 3*
*Tarrant County Health Department, Fort Worth, TX 4*

**HOW CAN THE UNITED STATES PRIORITIZE THE TARGETED TESTING OF TUBERCULOSIS?**

**Purpose:** Evaluation improves efficiency and effectiveness. Current U.S. tuberculosis (TB) control policies emphasize the treatment of latent TB infection (LTBI). However, this policy, if not targeted, may be inefficient. Our objective was to determine the efficiency of a state-law mandated TB screening program and a non state-law mandated one in terms of cost, morbidity, treatment, and disease averted.
**Methods:** We conducted an evaluation of two publicly funded metropolitan TB prevention and control programs through retrospective analyses and modeling in Tarrant County, Texas.
Study programs were Tarrant County homeless person and jail inmate TB screening programs, and main outcome measures were TB incidence and prevalence, TB cases averted, and cost.

**Results:** A non state-law mandated TB program for homeless persons in Tarrant County screened 4.5 persons to identify one with LTBI and 82 persons to identify one with TB. A state-law mandated TB program for jail inmates screened 109 persons to identify one with LTBI and 3,274 persons to identify one with TB. The number of patients with LTBI treated to prevent one TB case was 12.1 and 15.3 for the homeless and jail inmate TB programs, respectively. Treatment of LTBI by the homeless and jail inmate TB screening programs will avert 11.9 and 7.9 TB cases at a cost of $14,350 and $34,761 per TB case, respectively.
**Conclusions:** Mandated TB screening programs should be risk-based, not population-based. Non mandated targeted testing for TB in congregate settings for the homeless was more efficient than state-law mandated targeted testing for TB among jailed inmates.
**Sponsor:** *CDC*

**1501** **Presentation Type:** Poster

**Author:** KAREN WOOD **Presentor:** Karen Wood
**Department:** FAMILY MEDICINE
**Classification:** Staff (Not for Competition)
*KL Wood, MPH. University of North Texas Health Science Center, Department of Family Medicine, Divsion of Education and Research. Ft. Worth, Texas 76107*
*B Walsh, MPH. Parkland Memorial Hospital, Strategic Planning and Population Medicine. Dallas, Texas 75235*
*M Bayona, MD, PhD. University of North Texas Health Science Center, Department of Epidemiology, School of Public Health. Ft. Worth, Texas 76107*

**A PRIMARY CARE-BASED EDUCATIONAL INTERVENTION: ANALYSIS OF THE "BABIES FIRST" TRIAL**

**Purpose:** The research was designed with two goals. The first goal was to determine whether this program significantly and positively impacted parents' and infants' health outcomes compared with standard care provided at the community-oriented primary care (COPC) clinics. The second goal was to determine whether there was a difference when services were provided by a professional RN or by a paraprofessional client advocate.
**Methods:** The study design is a randomized, controlled trial. Eligible patients were infants born to parents receiving care at two Parkland primary care clinics. randomly assigned to two intervention groups and a control group.
The interventions consisted of providing parents with information through verbal interaction, distribution of written materials, and hands-on demonstrations. Either a professional (RN) "nurse" or paraprofessional client "advocate" gave home visits and enhanced services at the clinics. The control group received standard care at the clinics. The study follow-up period lasted 24 months. Intervention groups' parents and infants received 13 interventions beginning at birth and ending at 24 months.
**Results:** Mothers in the advocate group breast-fed their babies an average of 2.2 months longer than controls mothers did ($p = 0.04$), and 1.4 months longer than the nurse group did ($p = 0.33$).Both advocate and nurse groups completed more well-child visits than did the controls (8.4 vs. 7.3, $p < 0.01$; 7.3 vs. 4.7, $p = 0.01$), and the advocate group completed more visits than the nurse group (8.45 vs. 7.26, $p = 0.01$). Compared to controls, advocate group infants were 2.4 times more likely to be enrolled in CHIP/Medicare at birth (OR = 2.4, 95% CI 0.8 - 6.7), and nurse group infants were three times more likely to be enrolled in CHIP/Medicare at birth (OR = 3.0, 95% CI 1.2 - 7.2). Advocate group children were six times more likely than control group children were to have their immunizations up-to-date by age two (OR = 6.0, 95% CI 0.5 - 74 $p = 0.20$).
**Conclusions:** The initiative should continue and can serve as a model for all primary-care practices, as it has demonstrated its potential for success in benefiting this highly vulnerable population and increasing the chance of success later in life. For this type of educational intervention, paraprofessional advocates, for the most part, are more likely to effectively deliver the intervention because they are more culturally similar to the mothers, and may be more cost-effective.
**Sponsor:** *none*

**1502** **Presentation Type:** Poster

**Author:** MICHAEL COY **Presentor:** Karen Wood
**Department:** FAMILY MEDICINE
**Classification:** Postdoctoral Fellow/Resident
*M Coy, DO.*
*L Velasco, MD.*
*M Kieger, NP.*
*KL Wood, MPH.*
*University of North Texas Health Science Center, Department of Family Medicine. Ft Worth, Texas 76107.*

**THE PREVALENCE OF OVERWEIGHT IN AN INDIGENT PEDIATRIC POPULATION IN THE DIAMOND HILL/JARVIS AREA, FORT WORTH**

**Purpose:** The purpose of this study is to examine any differences between the national BMI figures and a pediatric sample from the Diamond Hill Clinic in northwest Fort Worth. Specifically, this study aims to determine 1) what ethnic/racial and age groups are "at risk of being overweight" or being "overweight", 2) the ethnic/racial and age groups' risk factors for diabetes and coronary artery disease, and 3) whether the Diamond Hill pediatric sample's BMI values mirror the national sample's values within certain age, gender, and ethnic groups.
**Methods:** This study used data from pediatric medical charts from the Diamond Hill Clinic during June through mid September, 2004. One hundred thirty-four pediatric (two to eighteen years old) patient charts were reviewed. The patient variables captured included height, weight, ethnicity, presence of acanthosis nigricans, and family history of coronary artery disease and diabetes mellitus. Height and weight measurements collected were then used to obtain the body mass index (BMI) and BMI percentile.
**Results:** Eighty-four percent of patients represented in the sample are Mexican-American. The BMI was compared to the different age groups and gender within the Mexican-American group. Among the males, the combined prevalence of at risk for overweight and overweight for each of the two younger age groups was over 23 percent. Seventeen percent of the 12-18 year old males were overweight. Females in the 6-11 age group had a combined prevalence of at risk for overweight and overweight of almost 30 percent. Results from the overall comparison of all age groups show that 65 percent of the males and 68 percent of the females were at risk for overweight or overweight. Acanthosis nigricans is most prevalent in both male and female children with a BMI greater than 95 percent,and overweight children between the ages of six and eighteen have the highest percentage of diabetes mellitus and coronary artery disease family history. Compared to the national averages, our sample had much fewer children at risk of overweight, but was comparable in distribution of overweight children.
**Conclusions:** Knowledge gained from the prevalence data will allow us to create educational programs and interventions that specifically target the low-income, predominantly minority population in this area of Fort Worth. These results are generalizable to an urban, predominantly Mexican-American, low-income population, a common demographic in large Texas cities.
**Sponsor:** *none*

**1503** **Presentation Type:** Poster

**Author:** Cathy Spranger **Presentor:** Cathy Spranger
**Department:** Social & Behavioral Sciences
**Classification:** SPH Student
*Cathy B Spranger, UNTHSC-SPH, Fort Worth, TX*
*Ruth Ann Carpenter, The Cooper Institue, Dallas, TX*
*Ximena Urrutia-Rojas, UNTHSC-SPH, Fort Worth, TX*

**IMPLEMENTATION OF A STANDARDIZED HEART HEALTH CURRICULUM: HOW AND WHY RE-INVENTION OCCURS**

**Purpose:** This study was to describe how communities adapt and re-invent a standardized heart health curriculum.
**Methods:** Twenty-nine local rural and urban community agencies that had received grants from the Illinois Department of Public Heath Office of Women's Health (OWH) to promote heart health using a standardized lifestyle change curriculum—Heart Smart For Women (HSFW) comprised the study population. Grantees received training, support materials, and technical assistance from the OWH and The Cooper Institute (CI), the developer of the curriculum during the grant year. Approximately 10 months after the end of the grant year, a semi-structured, audio-recorded telephone interview was administered to key grantee personnel to ascertain the degree of re-invention. The survey assessed the number of elements in the curriculum that were similar to or different from the original version. A single interviewer conducted the phone interviews. Upon completion of the phone interviews, audiotapes were transcribed and the data were analyzed using NVivo software.
**Results:** Seventy-nine percent of the agencies awarded HSFW grants in 2002-2003 participated in this study. Of these twenty-three sites, all but one made modifications to the curriculum to both essential and non-essential elements of the curriculum. Analyses of these data revealed that how grantees re-invented the HSFW curriculum could be grouped within five categories (culturally-population relevant changes, change in session sequence, omitted 'stuff', modified tools/forms; change in presentation, and additions/supplemental info). The question of why these modifications were made was answered through the main themes that emerged from these data.
**Conclusions:** According to Rogers (1995), at least some degree of re-invention occurs at the implementation stage for many innovations/interventions. This study confirmed Rogers' diffusion process theory. Thus, the modifications made were likely primarily related to Roger's point that local pride of ownership may cause re-invention. This study provides information that may be useful to program developers and implementers alike as they work to disseminate more evidence-based lifestyle interventions into community settings. In addition, it is recommended that future research be done to further explore the influences on re-invention especially within rural communities and communities of minority populations.
**Sponsor:** *none*

# GENERAL PUBLIC HEALTH

**1504** **Presentation Type:** Oral

**Author:** Nykiconia Preacely **Presentor:** Nykiconia Preacely
**Department:** Epidemiology
**Classification:** SPH Student
*Nykiconia Preacely, MPH. University of North Texas Health Science Center, Fort Worth, TX 76107*
*Tess Cruz, PhD, MPH. Keck School of Medicine, University of Southern California, Alhambra, CA 91803*

**PROJECT SPONSORSHIP MISSION AVOID RELIANCE ON TOBACCO MONEY: ORGINS, EVOLUTION AND OUTCOMES**

**Purpose:** This study explored efforts made by the state of California to counter tobacco sponsorship, and to document related outcomes in tobacco promotions through sports and community events. Project SMART (Sponsorship Mission: Avoid Reliance on Tobacco) Money (PS$) was created in the late 1990's by a consortium of public health and tobacco education organizations to counter tobacco sponsorship of sporting and community events and organizations. Sponsorship of organizations and events serves as an opportunity for tobacco companies to gain community acceptance and respect. By associating their name through sponsorship of credible events or organizations, the tobacco industry is discretely targeting their products to specific populations, including new smokers or potential smokers.

**Methods:** Data for this study were obtained from the Tobacco Industry Monitoring Evaluation (TIME) project at the University of Southern California and through interviews conducted with key informants. Data on tobacco sponsored events occurring in the state of California from 1999-2003 were drawn from the TIME project's event census database.

**Results:** Master Settlement Agreement violations -there were a total 191 violations reported, with SCENE Magazine, a weekly publication of NASCAR having the highest number (56) of violations observed. Policies – as a result of PS$'s efforts, 484 anti-tobacco policies have been developed to either create a smoke free environment, counter tobacco sponsorship, and/or refuse corporate donations from tobacco companies. Changes over time in sponsorship- the frequency of tobacco sponsorships, regardless of brand or corporate sponsor, decreased significantly in California from 1999-2003. Key informant interview responses- PS$ has evolved with the tobacco industry's changing tobacco marketing focus areas.

**Conclusions:** The results of this case study show that PS$ has been instrumental in reducing and eliminating tobacco industry sponsorships in California, but more work needs to be done. Anti-tobacco sponsorship trainings, toolkits, and communication systems have proven to be effective in providing organizations and events with strategies to reject or get rid of existing tobacco sponsorships; however new innovative approaches need to be developed to continue the fight against tobacco sponsorship of events and organizations.

**Sponsor:** *NCI*

**1505** **Presentation Type:** Poster

**Author:** CAROL STEHLY **Presentor:** CAROL STEHLY
**Department:** FAMILY MEDICINE
**Classification:** Faculty (Not for Competition)
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*M Sanders, DO, JD*
*KL Wood, MPH*
*University of North Texas Health Science Center, Department of Family Medicine. Ft. Worth, Texas 76107*

**WILL A HEALTHLY LIFESTYLE EDUCATIONAL INTERVENTION REDUCE CHOLESTEROL IN TEXAS FOOTBALL OFFICIALS?**

**Purpose:** The purpose of this research project is to compare baseline cholesterol levels to one-year follow-up screenings following an educational intervention.

Objective 1: Determine the baseline cholesterol levels of a sample of Texas State Football Officials. Reassess the sample's cholesterol levels one year later.

Objective 2: Determine whether a healthy lifestyle educational intervention delivered by Texas College of Osteopathic Medicine students to State Football Officials reduced the officials' cholesterol levels.

**Methods:** A brief, one-on-one educational instruction on cardiovascular disease prevention and healthy lifestyle promotion, provided by D.O. medical students, was presented to a sample of State football officials attending the Annual Football Meeting of Texas Association of Sports Officials (TASO) in July 2004 at Arlington Convention Center, Arlington, Texas. We assessed the baseline cholesterol levels and self-reported health status of the officials, and will reassess those measures in a one-year follow-up screeing in July 2005.

**Results:** The results of this study should determine the value of a healthy lifestyle, community-based, education in changing State Football Officials' cholesterol levels. We anticipate an improvement in the sample's cardiovascular health, as evidenced by lower cholesterol levels in the follow-up screening.

**Conclusions:** One effective method of reducing the risk of cardiovascular disease is by adopting a physical activity and healthy-eating regimen. Through an individual educational instruction, individuals may learn to adopt these healthy lifestyle changes. This one-on-one approach has been to shown promise in workplace settings.

**Sponsor:** *none*

**1506** **Presentation Type:** Poster

**Author:** Patrick Moonan **Presentor:** Patrick Moonan
**Department:** Epidemiology
**Classification:** SPH Student
*Stephen E. Weis 1,3,7; Patrick K. Moonan 1,2,3; Teresa N. Quitugua 4; Janice Pagoda 5; Gary Woo 6; Gerry Burgess 1,3; Behzad Sahbazian 1,3; and Charles Wallace 7.*

*University of North Texas Health Science Center at Fort Worth, 1. Department of Medicine, 2. Department of Epidemiology, Fort Worth, TX 76107-2699; 3. Tarrant County Health Department, Fort Worth, TX 76104; 4. Texas University of Texas Health Science Center at San Antonio, Department of Microbiology, San Antonio, TX 78245; 5. STATOLOGY, Ventura, CA 93003; 6. Dallas County Health And Human Services Dallas, TX 75207-2710; 7. Texas Department of State Health Services Austin, Texas 78756-3199.*

**DOES UNIVERSAL DIRECTLY OBSERVED THERAPY (DOT) REDUCE TRANSMISSION OF DRUG RESISTANT TUBERCULOSIS?**

**Purpose:** To evaluate the role of universal directly observed therapy in the transmission and acquisition of drug resistant tuberculosis.

**Methods:** We conducted an ecological study of two north Texas Tuberculosis Control Programs with identical programmatic structures, population demographics, and funding support. The only difference was the management and utilization of universal directly observed therapy (Tarrant County) and selective directly observed therapy (Dallas County). These programs were compared using standardized molecular genotyping and drug suspectibilties as part of their participation in the National Tuberculosis Genotyping and Surveillance Network, sponsored by the Centers for Disease Control and Prevention. Differences in proportions were tested by Fisher's exact test. Maximum-likelihood estimates of odds ratios (ORs) and 95% confidence intervals (CIs) were computed by logistic regression to analyze factors associated with molecular clustering. Multiple logistic regression was used to determine factors independently associated with molecular clustering by a stepwise approach. All tests were two-sided with a 0.05 significance level.

**Results:** Anti-tubercular drug resistance to isoniazid, rifampin and ethambutol in the initial isolate was 1.7 times more common in Dallas County than Tarrant County [OR = 1.7 95% CI: 1.1 – 2.6]. Clusters containing at least one isolate resistant to isoniazid, rifampin, and/or ethambutol were 2 times more likely in Dallas County than Tarrant County [OR = 2.0, 95% CI: 1.5, 2.6]. Genotype clusters having 2 or more members with matching drug resistance profiles were 4 times as common in Dallas County than in Tarrant County [OR = 4.0, 95% CI: 2.5, 6.5].

**Conclusions:** This is the first study to demonstrate that universal directly observed therapy is associated with less acquisition of initial drug resistance and less transmission of drug resistant isolates.

**Sponsor:** *Centers for Disease Control and Prevention*

**1507** **Presentation Type:** Oral

**Author:** Carolina Alvarez-Garriga **Presentor:** Carolina Alvarez-Garriga
**Department:** Epidemiology
**Classification:** SPH Student
*Carolina Alvarez-Garriga, M.D., S.C.P., Dr. P.H., Raghbir Sandhu, M.B.B.S., D.T.M. & H., D.P.H., Dr.P.H., Antonio Rene M.P.H., Ph.D., Daisha Cipher, M.S., Ph.D., Federico Montealegre, D.V.M., M.S., Ph.D., Marco Marruffo, M.D., M.S., Dr.P.H., Manuel Bayona, M.D., M.S., Ph.D.*

**RISK FACTORS FOR CHILDHOOD ASTHMA IN THE UNITED STATES**

**Purpose:** The purpose of this study was to assess risk factors by using NHANES 1999-2000 data in children one to six years of age comparing 158 asthmatics with 1,104 non-asthmatics regarding selected factors.

**Methods:** Cases of asthma were compared to non-cases of asthma regarding the frequency of selected factors. The logistic regression adjusted odds ratio was used as a measure of association between presence of asthma and the selected factors.

**Results:** Results indicated that a higher prevalence of 12.5 per 100 population was found for the United States while those reported in previous NHANES surveys ranged from 5 to 9 per 100 population. Males were 1.9 times more likely to have asthma. Likelihhod to have asthma increased with age. Mexican Americans were 37% less likely to have asthma while other Hispanics were 2.4 times more likely ($p = 0.008$). African Americans were 61% more likely to have asthma ($p = 0.014$). Breastfeed children were found to be 41% less likely to have asthma ($p = 0.014$) with a clear dose-response relationship with the length of breastfeeding. Starting foods other than breast milk after four months of age decreased 54% the likelihood of asthma ($p = 0.009$). Smoking during pregnancy increased 45% the probability of asthma, while quitting decreased it by 54% ($p < 0.03$). Those that attended day care were 44% more likely to have asthma, and those that did not have newborn care had two times more probability for asthma ($p < 0.05$).

**Conclusions:** These findings indicate that childhood asthma is still increasing, and provide information about high risk groups and protective factors that can be used for public health interventions to prevent disease.

**Sponsor:** *None*

# GENERAL PUBLIC HEALTH

**1508** **Presentation Type:** Poster

**Author:** Marco Marruffo **Presentor:** Marco Marruffo
**Department:** Epidemiology
**Classification:** SPH Student
*Marco Marruffo, M.D., M.S., Dr.P.H., Antonio Rene M.P.H., Ph.D., Raghbir Sandhu, M.B.B.S., D.T.M. & H., D.P.H., Dr.P.H., Daisha Cipher, M.S., Ph.D., Federico Montealegre, D.V.M., M.S., Ph.D., Carolina Alvarez-Garriga, M.D., S.C.P., Dr. P.H., Manuel Bayona, M.D., M.S., Ph.D.*

**PREDICTORS FOR THE SEVERITY OF ASTHMA IN THE HOSPITAL SETTING. A CLINICAL EPIDEMIOLOGY STUDY BASED ON HOSPITAL RECORDS FROM TEXAS HEALTH CARE INFORMATION COUNCIL.**

**Purpose:** The purpose of this research was to identify and assess prognostic factors for severity and risk of death due to asthma.
**Methods:** This research identifies and assess prognostic factors for severity and risk of death among 27,383 hospitalized asthma patients in the state of Texas during 2002, by using the public available Texas Hospital Inpatient data, collected by The Texas Health Care Information Council (TCHICC). Severity and risk of death were assessed at three levels (minor, moderate and major) regarding selected factors. Data was analyzed by means of multinomial logistic regression using minor risk as the reference group. The SPSS 13.0 statistical package was use to analyze the data.
**Results:** Among other results, severe asthma cases were 2.0 times more likely to be males, 8.1 times to be obese, 1.4 times more likely to be smokers, 4.6 times more likely to be hypertensive, and 29 times more likely to have diabetes as compared to those without severe asthma ($p < 0.001$). Males were 2.4 times, obese 2.7, hypertensive 2.8 and diabetics 5.7 times more likely to have major risk of death due to asthma ($p < 0.001$).
**Conclusions:** Patients of male gender, smokers, obese, hypertensive, and diabetics are at higher risk for severity and mortality due to asthma. The results of this study can be used to identify high risk groups to plan and applied control measures for tertiary prevention of severity and death due to asthma.
**Sponsor:** *None*

**1509** **Presentation Type:** Poster

**Author:** Neda Moayad **Presentor:** Neda Moayad
**Department:** Epidemiology
**Classification:** SPH Student
*Neda Moayad, M.A., Dr.P.H.; Héctor Balcázar, M.S., PhD; Janet Marruffo, M.D.; Guadalupe Munguia-Bayona M.D., M.P.H.; Luis Velasco, M.D.; and Manuel Bayona, M.D., M.S., Ph.D.*

**DO FAMILY COHESIVENESS, ACCULTURATION AND OTHER SOCIAL FACTORS INFLUENCE THE SEVERITY OF DIABETES AMONG HISPANICS IN FORT WORTH? A CROSS-SECTIONAL STUDY.**

**Purpose:** The prevalence of type II diabetes in Latinos ages 45-74 is three times higher than in the non-Latino whites of the same age group. The goal of this research was to assess the importance of selected potential prognostic factors as related to severe type II diabetes in Latino patients. Among other findings, the results of this study showed that severe diabetes was associated to family history of diabetes, born, having spent childhood or being educated in Mexico, preferring Spanish as the spoken language, receiving food stamps, smoking, being overweight and obese, and having high acculturation and/or low family cohesiveness among respondents with less than sixth grade of education were associated with severe diabetes. These findings can be used to identify high risk groups for severe diabetes, and risk factors that can be modified to prevent diabetes severity.
**Methods:** This study was conducted by using a cross-sectional design in which 275 Latino diabetes patients were interviewed. Data was analyzed by comparing patients with severe diabetes (Hg A1c > 7) with patients with non-severe diabetes (Hg A1c < 7) by using multiple logistic regression adjusted odds ratios.
**Results:** Among other findings, the results of this study show that family history of diabetes, born in Mexico and having spent childhood in Mexico, preferring Spanish as the spoken language, having been educated in Mexico, receiving food stamps, smoking, being overweight and obese, and high acculturation and low family cohesiveness among respondents with less than sixth grade of education were associated with severe diabetes.
**Conclusions:** The results of this study can be used to identify high risk groups for severe diabetes in which preventive measures should be emphasized such as in males born in Mexico with low family cohesiveness and/or high acculturation. Modifiable risk factors identified in this study such as obesity and low level of education can be modified or eliminated to prevent diabetes severity.
**Sponsor:** *None*

**1510** **Presentation Type:** Oral

**Author:** Godavari Patil **Presentor:** Godavari Patil
**Department:** Biostatistics
**Classification:** SPH Student
*Godavari Patil*
*University of North Texas Health Science Center School of Public Health*

*Francisco Soto Mas, MD, MPH, PhD*
*University of North Texas Health Science Center School of Public Health*

*Holly Jacobson, PhD*
*University of North Texas Health Science Center School of Public Health*

*C. Ed Hsu, MS, MPH, PhD University of Maryland, College Park*

**PHYSICIANS OF NON-PARTICIPATING COUNTIES IN NORTH TEXAS: A STUDY IN PUBLIC HEALTH PREPAREDNESS AND RESPONSE TO BIOTERRORISM**

**Purpose:** Bioterrorism (BT) represents an emerging threat to the public health in North Texas since many counties are ill prepared to coordinate response management efforts due to the absence of a local or county health department. This study was undertaken to evaluate the experiences, skills and attitudes that North Texas physicians have with diagnosis and treatment of biological, chemical, or radiological diseases or conditions (including psychological and behavioral) that result from a bioterrorism-related event. The second purpose was to create a database with this information in order to maintain a current record of physicians with the willingness, skills, and experience to assist with local emergency bioterrorism response efforts.

**Methods:** Data were collected through a survey instrument was developed and piloted by the research team. Data was collected using this survey instrument. The study population comprised licensed Physicians practicing or retired within 37 non-participating North Texas counties in Public Health Region 2/3. Contact information of these physicians was obtained from the Texas State Board of Medical Examiners (TSBME). The survey was mailed to the entire study population -- 841 licensed physicians. Collected data were transformed to a database using Microsoft Access and statistical analysis was performed using SPSS.
**Results:** Chemical exposure was the most commonly seen and/or treated BT-related event among physicians with experience. Most reported neither having seen nor treated the other types of exposure. A majority (72.4%) of the respondents had not participated in any bioterrorism preparedness and response training. Of those who reported receiving training, most (73.2%) had received training after September 11, 2001. More than 43% of the respondents reported being willing and available to collaborate with TDH in the event of a bioterrorism incident.
**Conclusions:** Physicians in these regions are receptive to participating in TDH bioterrorism preparedness and response efforts. In response to the physicians' receptiveness, it is suggested to collects data on other health professionals such as nurses, physician assistants,etc. This will facilitate strategic planning and will improve bioterrorism preparedness and response in North Texas.

**Sponsor:** *None*

**1511** **Presentation Type:** Poster

**Author:** Marco Marruffo **Presentor:** Marco Marruffo
**Department:** Epidemiology
**Classification:** SPH Student
*Marco Marruffo 1,2,3; Patrick K. Moonan 1,2,3; Mark Lobato 4; Manuel Bayona 1, 2; Stephen E. Weis 1,3; University of North Texas Health Science Center at Fort Worth, 1. Department of Medicine, 2. Department of Epidemiology, 3. Centers for Disease Control and Prevention 4.*

**EPIDEMIOLOGIC ASSESSMENT OF TUBERCULOSIS IN CHILDREN**

**Purpose:** Four aims are included: (a) identify current risk factors for children under 6 years of age with latent TB infection (LTBI) to develop TB; (b) calculate the prevalence of BCG immunization in U.S. born children, the extent unnecessary treatment, and the overestimation of the LTBI prevalence; (c) calculate the frequency of chest x-ray radiological findings and their correlation with clinical findings; and, (d) evaluate the influence of the country of birth of the "source case" in the childhood TB yield ratio between associate and contact investigations.
**Methods:** This is a cross-sectional study based on a TB case-series study. A record review was conducted at three sites of the Centers for Disease Control and Prevention (CDC) TB Epidemiology Consortium (TBESC, 2003). Data includes childhood patients with LTBI and active TB (TBESC, 2003). (1) The active/latent TB ratio will be measured by demographic and ethnic characteristics in children to identify high risk groups for infection; (2) A comparison of active and latent TB will be conducted in regards to selected variables to identify high risk groups and potential risk factors; (3) the prevalence of BCG immunization in U.S. born children will be assessed to measure the potential overestimation of the LTBI prevalence and unnecessary treatment; (4) a case-series analysis will be conducted to measure the frequency and percentage of each different chest x-ray radiological finding in TB cases and compare each finding with the symptomatology to clinically characterize the type of radiological abnormality; and, (5) the childhood TB yield rate and yield rate ratio of associate/contact investigations will be calculated by country of origin. This will be carried out to investigate if the country of origin of the source case has any influence on the TB yield rate.
**Results:** Information about diagnosis and risk factors for TB in children will become available. Learning more about the diagnosis of TB in children will help to improve screening for the detection of new cases and diagnostic practices.
**Conclusions:** Study of risk factors is useful for the identification of high risk groups, as well as to implement better preventive measures for this vulnerable population. Learning more about the diagnosis of TB will help to improve case-finding as well as diagnostic procedures.
**Sponsor:** *None*

# GENERAL PUBLIC HEALTH

**1512** **Presentation Type:** Poster

**Author:** Minyong Uhm **Presentor:** Minyong Uhm
**Department:** Biostatistics
**Classification:** Faculty (Not for Competition)
*Minyong Uhm, RN, MS, Sejong Bae, Ph.D., and Karan Singh, Ph.D, University of North Texas Health Science Center at Fort Worth, Fort Worth, Texas, 76107*

**ASSESSING NITROUS OXIDE EXPOSURE IN OPERATING ROOM**

**Purpose:** A large population of health care workers is potentially exposed to nitrous oxide which can cause harmful health effects including decrease in mental performance, audiovisual ability, and reduced fertility, neurological, renal, and liver disease. Nitrous oxide exposure assessment in operating room has been not been done in Korean hospitals. Study objective is to assess nurses' possible hazardous exposure to nitrous oxide before and during operation and to compare passive and active sampling methods.

**Methods:** To explore the nitrous oxide exposure level among nurses in operating room, we studied the exposure level in two different operating rooms before and during the operation. Passive sample and active sampling methods were used to assess nitrous oxide level in operating room.

**Results:** An investigation was made of possible hazardous exposures to nitrous oxide at operating rooms in a hospital. Air samples were taken while nitrous oxide was in use for over six hours where the surgeon and assistants were present for operation. The active air-sampling results revealed a range of nitrous oxide concentrations in the room air from 27 to 283 parts per million (ppm) while the passive air-sampling nitrous-oxide concentration ranged from 1 to 86 ppm.

**Conclusions:** : There was a significant difference in nitrous oxide concentration by sampling methods. A possible health hazard from excessive exposures to nitrous oxide exists in the operating room. Adjustment of the ventilation system each time nitrous oxide is going to be used is recommended. Routine maintenance checks should be performed on all anesthetic and suction equipment. The installation of a larger fan in the room as well as on the roof of the building is suggested. Patients should be watched carefully during the administration of nitrous oxide for a possible leakage.

**Sponsor:** *none*

**1513** **Presentation Type:** Poster

**Author:** Tuan Le **Presentor:** Tuan Le
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**Classification:** SPH Student
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*Chiehwen Ed Hsu, Ph.D.,University of Maryland, College Park*
*Sue Lurie, Ph.D., University of North Texas Health Science Center, Fort Worth, Tx, 76107*
*Raghbir Sandhu, Dr. PH, University of North Texas Health Science Center, Fort Worth, Tx, 76107*

**BARRIERS TO HEALTH CARE ACCESS AMONG VIETNAMESE REFUGEES**

**Purpose:** The previous studies in the literature reviewed showed that Vietnamese refugees have accessed health care services to a lesser degree than their Caucasian or English speaking counterparts, even other refugee communities. The purpose of this study is to determine the barriers that are keeping the Vietnamese refugees away from accessing the health care system in North Texas.

**Methods:** This study used a cross-sectional survey data collected from Vietnamese refugees at community-based sites in North Texas between February 12, 2004 and February 29, 2004. The 201 qualified participants, who are 18 years old or older, voluntarily participated in this study. This study focused on four main kinds of barriers such as language, legal, socioeconomic, and cultural to determine whether they were some of the perceived barriers that Vietnamese refugees have been facing when accessing health care.

**Results:** About 87% of the respondents said that they had problems with spoken English in utilizing health care with varying levels from moderate to severe problems (very much problem). Lack of understanding of the medical system was a barrier for 15% of the respondents. A large majority of respondents (82.6%) reported that they have never gone to any kind of preventive or health clinics in the last two years. Around 17% of respondents reported that legal issues were barriers to accessing health care. Sixty-eight percent of Vietnamese refugee women have no health insurance, and 31.5% of Vietnamese refugee men have no health insurance.

**Conclusions:** Reducing these barriers to accessing health care among refugees is significant not only in the enhancement of refugee health to produce a healthy labor force and healthy community by preventing the potential for communicable disease transmission, but also for cost-savings in the long-run. This study illustrates that Vietnamese refugees did not emphasize health prevention, so health promotion and education should be implemented in the Vietnamese refugee community. This would help to reduce health disparities and increase health in society

**Sponsor:** *None*

# RECEPTOR PHARMACOLOGY & DRUG DELIVERY

**1600** **Presentation Type:** Poster

**Author:** Rashmi Lote **Presentor:** Rashmi Lote
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** GSBS Student
*Rashmi Lote, Ran Zhang, Heather Rhubottom, Jay J. Gadhiya, and Tina K. Machu, Dept. of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, TX 76107-2699*

**LOOP C RESIDUES IN 5-HT3A RECEPTORS INTERACT TO CONFER CURARE POTENCY.**

**Purpose:** Mouse and human 5-HT3A receptors are competitively antagonized by d-tubocurarine (curare), with IC50s of 12 nM and 1800 nM, respectively. We are using differences in curare potencies to characterize amino acid residues involved in ligand binding.
Previous work by our laboratory demonstrated that a human chimera, in which Loop C residues were replaced by the mouse orthologs (H-Loop C), has a curare IC50 of 40 nM. These results suggest that Loop C accounts for part of the curare potency in these two receptors.

**Methods:** Mouse and human 5-HT3A receptor mediated currents were measured in Xenopus oocytes in the two-electrode voltage clamp configuration in the absence and presence of curare.

**Results:** Seven residues are different between mouse and human receptors in Loop C, and the human receptor residues were sequentially mutated to the corresponding mouse orthologs and tested for curare potency. All seven have been tested, with five reducing the curare IC50, (H-Y217Q, 1100 nM; H-R219K, 660 nM; H-M223I, 930 nM; H-Y228S, 920 nM; and V237I, 382 nM). The H-S225I mutant has a slightly higher IC50 of 2100 nM, whereas, the H-E224D mutant has an IC50 of 8900 nM. These results suggest that two or more residues interact to confer curare potency. A human chimera containing all six of these mouse receptor residues has a curare IC50 of 40 nM, suggesting that V237 is not required for curare potency. Human chimeras containing three or four mouse orthologs were tested. The human chimera, Hch-LC-mini 217, 223, 228 has an IC50 of 175 nM. The human chimera, Hch-LC-mini 217, 219, 223, 228, which has all four of the mouse orthologs that individually enhance curare potency, has an IC50 of 100 nM. Adding the mouse ortholog E224D to the three point mutant chimera produced a chimera, Hch-LC-mini 217, 223, 224, 228 that has an IC50 of 40 nM.
**Conclusions:** Multiple interactions among the amino acid residues in Loop C produce curare potency. It is likely that several combinations of four or more point mutations will produce human chimeras with curare IC50s equal to that of the Hch-Loop C. These results suggest redundancy in Loop C in conferring curare potency in the mouse 5-HT3A receptor.

**Sponsor:** *NINDS*

**1601** **Presentation Type:** Poster

**Author:** Christina Floresca **Presentor:** Christina Floresca
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** Postdoctoral Fellow/Resident
*Christina Z. Floresca, Sandhya Kortagere, and John A. Schetz, Dept. of Pharmacology and Neuroscience, UNTHSC, Ft Worth, TX 76107 and Dept. of Physiology & Biophysics, Weill Medical College of Cornell University, NY, NY 10021.*

**RECIPROCAL MUTATIONS IN A DOPAMINE D2 BACKGROUND REVEALS A CRITICAL SELECTIVITY MICRODOMAIN**

**Purpose:** Mutant D4 receptors constructed by substituting nonconserved amino acids in the second and third transmembrane domain (TM2 and TM3) with the corresponding amino acid from the D2 receptor had lower affinity for several D4-selective compounds. In order to extend these previous results, reciprocal mutant D2 receptors were constructed by substituting the corresponding amino acids from the D4 receptor into a D2 receptor background, and then tested with the same compounds. We hypothesize that favorable and unfavorable aromatic interactions with amino acids in TM2 and TM3 are critical for selective interactions with the D2 receptor subtype.
**Methods:** All D4-selective drugs were tested by inhibition of specific [3H]methylspiperone binding to wild type and mutant D2 receptors transiently expressed in COS-7 cells. In an effort to explain our experimental results and derive new hypotheses concerning ligand-receptor interactions, ligand structures were manually docked into a molecular model of the binding site.
**Results:** In all cases, a moderate to large increase in binding affinity was seen by removal of the steric clash produced by phenylalanine in TM3 concomitant with the introduction of a favorable pi-stacking interaction with another phenylalanine in TM2. A remarkable finding is that these ligands can be classified into two subgroups based on a) the pattern of sensitivity to D2 mutants and b) the nature of substituents on the aromatic ring of the ligands.
**Conclusions:** A combination of favorable and unfavorable aromatic interactions between the ligands and their receptor accounts for a significant proportion of their receptor subtype selectivity. Specifically, a favorable interaction between the ligand and phenylalanine in TM2 and the absence of a phenylalanine in TM3 makes the pharmacology of the ligand more D4-like. In addition, the unique pattern of sensitivity for subclasses of these ligands suggests an additional interaction of the orthoelectronegative aromatic groups with the D2 receptor.
**Sponsor:** *NIH/NIMH*

**1602** **Presentation Type:** Poster

**Author:** Andrew Wilson **Presentor:** Andrew Wilson
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** Staff (Not for Competition)
*Andrew Wilson, James Simpkins, Mridula Rewal, and Marianna Jung*

**THE STIMULUS EFFECTS OF ETHANOL WITHDRAWAL IS MORE TOXIC THAN ETHANOL PER SE: CELLULAR MECHANISMS**

**Purpose:** Studies suggest that ethanol withdrawal (EW) stimulus can cause more severe brain damage than ethanol exposure itself. To further elaborate this issue, we compared the stimulus effects of EW with those of ethanol exposure per se at the cellular levels using in vitro and in vivo models of ethanol dependence.
**Methods:** In an in vitro model, HT-22 cells were exposed to ethanol at the concentrations of 0 to 500 mM for 4 to 12 hours. Using a calcein assay, the cell viability was measured at 4, 8, and 12 hours of ethanol exposure or during EW. In an in vivo model, rats received ethanol diet for 5 weeks (6.5% w/v) and the cerebellar tissues were collected during ethanol exposure or during EW. The levels of lipid peroxidation and protein kinase C (PKC) signaling profiles were assessed using the TBASR (thiobarbituric acid reactive substances) assay and the ATP[?32 P] phosphorylation assay, respectively.

**Results:** Ethanol exposure decreased cell viability in a manner that depends on dose and duration of ethanol exposure: a high dose and a longer exposure resulted in a greater cell death. As compared to ethanol exposure or control groups, EW resulted in a greater cell death, higher levels of TBARS, and higher levels of PKC?.
**Conclusions:** These data suggest that the toxicity of ethanol depends on dose and length of exposure. Our data also strengthen the idea that EW is more toxic than ethanol exposure per se at the levels of cell viability, oxidative balance, and PKC signaling.

**Sponsor:** *none*

**1603** **Presentation Type:** Poster

**Author:** Robert Luedtke **Presentor:** Robert Luedtke
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** Faculty (Not for Competition)
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**PHARMACOLOGICAL SURVEY OF MEDICINAL PLANTS FOR ACTIVITY AT LIGAND-GATED ION CHANNELS: SELECTIVE INTERACTION WITH 5-HT3 RECEPTORS.**

**Purpose:** The ligand-gated anion-selective ion channels are part of a superfamily of ligand-gated ion channels (LGICs) that are responsible for a majority of inhibitory signaling in the central nervous system and are the targets of numerous therapeutics.
**Methods:** Aqueous, organic and alcoholic extracts of 47 Chinese, Bolivian and Pakistani medicinal plants were evaluated for the ability to modulate the activity of GABAA receptors. Extracts were initially screened for their ability to modulate activity of a1b2g2 GABAA receptors expressed in HEK 293 cells.
**Results:** . Based on the initial screen, two extracts derived from members of the Asteraceae family, Xanthium spinosum and Senecio mathewsii, were chosen for more detailed analysis. Xanthium spinosum inhibited GABAA receptor function, with an IC50 of 50 ± 10 mg/ml, while Senecio mathewsii inhibited GABAA receptor activity with an IC50 of 35 ± 3.0 mg/ml. To assess the selectivity of interaction, these extracts were also tested on two other members of the LGIC superfamily a) glycine receptors, a distinct inhibitory neurotransmitter receptor and b) 5-HT3A receptors, a cation-selective receptor. At a concentration of Xanthium spinosum that blocked 70% of GABA-activated current, only 15% of glycine-gated current, recorded from recombinant a1 glycine receptors, was blocked, suggesting a lower affinity of Xanthium spinosum for glycine receptors. Senecio mathewsii had larger inhibitory effects on glycine receptors than Xanthium spinosum, although the apparent affinity still was estimated to be three-fold lower than that seen for GABAA receptors. Xanthium spinosum and Senecio mathewsii also inhibited 5-HT3A receptor function. Notably, the IC50 of both extracts was seven to ten-fold lower than that observed for GABAA receptors.
**Conclusions:** The rank order of potency for organic extracts from both Xanthium spinosum and Senecio mathewsii was 5-HT3A receptors > GABAA receptors > glycine receptors. Therefore, these extracts may be a source of novel compounds that may serve as lead molecules for the development of novel 5-HT3 receptor antagonists.
**Sponsor:** *NIH/NIDA*

# RECEPTOR PHARMACOLOGY & DRUG DELIVERY

1604 **Presentation Type:** Poster

**Author:** Eric Gonzales **Presentor:** Eric Gonzales
**Department:** PHARMACOLOGY & NEUROSCIENCE
**Classification:** GSBS Student
*Eric B. Gonzales* and Glenn Dillon, Ph.D., UNTHSC-Fort Worth, Dept. of Pharmacology and Neuroscience, Fort Worth, Texas 76107*

**ANALYSIS OF THE TM2 7' POSITION IN HOMOMERIC GLYCINE ALPHA 1 RECEPTOR GATING**

**Purpose:** The cys-loop family of receptors is responsible for rapid neurotransmission in the central nervous system and spinal cord. Members of this family, which include the gamma-aminobutyric acid type A, glycine (GlyRs), nicotinic acetylcholine, and serotonin type-3 receptors (5-HT3Rs), share similar structural homology and are targets for numerous therapeutics. Each receptor is composed of five protein subunits, with four transmembrane domains each. Previously, our lab has demonstrated that the TM2 7' position in the Glycine alpha 1 receptor influences channel kinetics. We extended these investigations by using a higher resolution solution exchange system.

**Methods:** Wild type and mutant glycine alpha 1 homomeric receptors were expressed transiently in HEK293T cells. Mutations (T7' to L, and A) were introduced by site-directed mutagenesis. We used the whole-cell patch clamp recording method to analyze each receptor and generate a glycine concentration response curve. Kinetic properties of the receptor were analyzed with a rapid solution exchange system that had an effective solution exchange time of (10-90% rise time) of 7 ms (Warner Instruments).

**Results:** The T6'A and T6'L mutation in the Gly alpha 1 receptor showed slower activation kinetics than the wild type at EC50 concentrations (T > L,A). Activation rise time at these concentrations could be correlated with amino acid polarity. Activation at 30xEC50 was slower with the T6'L mutation, while the T6'A mutation was not significantly different from the wild type. Deactivation was unique in the T6'A mutation. This mutation increased the deactivation rate of the receptor at the end of a 10 second application of glycine EC50, while deactivation of the Gly alpha 1 (T6'L) mutation was significantly slower

**Conclusions:** This study provides a better picture of what is happening at the TM2 7' position in the cys-loop family of receptors. Amino acid polarity influences the activation of the channel at this position. Future experiments will address the direction in which this residue projects in the channel.

**Sponsor:** *NIH ES 07904; Grass Foundation*

# OTHER

**1700** **Presentation Type:** Poster

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**OSTEOPATHIC TERMINOLOGY, SNOMED CT AND THEIR RELEVANCE IN OSTEOPATHIC RESEARCH**

**Purpose:** Medical terminology refers to the words used to describe medical encounters, diagnoses, and treatments. Medical terminology is the backbone to any patient record and a standardized terminology is of vital importance if data aggregation, data retrieval and outcomes studies are to be successful. SNOMED CT is a controlled medical terminology which has been recommended as the general terminology of choice by the National Committee on Vital and Health Statistics for the development of the electronic medical record1.. Osteopathic terminology is unique to Osteopathic practitioners and must be included in any terminology if the terminology is to meet the needs of the Osteopathic community. The Authorized Osteopathic Thesaurus was used as a resource and compared to SNOMED CT. The purpose is to ensure content needed by Osteopathic practitioners will be present in the Electronic Medical Record (EMR).

**Methods:** In his State of the Union address in 2004 President Bush stated that the need for Computerized health records was one of the "critical issues in healthcare today" 2. The terminology which will support this record must include the words and phrases used by clinicians in all walks of healthcare. SNOMED CT has 364,000 concepts, 984,000 synonyms and 1.45 million relationships. However, when compared with the American Association of Colleges of Osteopathic Medicine's Authorized Thesaurus the following was found: Osteopathic thesaurus - 671 concepts, SNOMED CT 364,000.Overlap of content(%)= 15%.Concepts currently being added to SNOMED- 393; Concpets not to be added- 177.

**Results:** A collaborative agreement was reached and the decision was made to proceed with the integration of the Osteopathic Content into SNOMED CT. Many terms commonly used by Osteopathic practitioners in assessing and describing patient were suprinsingly not present. The decision was made to add these to the core of the terminology.

**Conclusions:** By adding essential Osteopathic terminology to SNOMED the hope is that medical documentation will be better able to reflect and serve the needs of healthcare providers. In the long run this can only lead to an improved ability to retrieve data for research purposes.

**Sponsor:** *College of American pathologists*

**1701** **Presentation Type:** Poster

**Author:** RICHARD VIRGILIO **Presentor:** RICHARD VIRGILIO
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**THE QUANTITY AND QUALITY OF PHARMACEUTICAL ADVERTISEMENTS FOUND IN SUBSCRIPTION VERSUS COMPLIMENTARY MEDICAL JOURNALS**

**Purpose:** To determine if there is a difference in the quantity and quality of pharmaceutical advertisements found in two different categories of medical journals (subscription journals which are purchased and contain mainly original research articles and complimentary journals which are given free of charge and contain mainly articles dealing with the clinical practice of medicine).

**Methods:** The variables used in the study consisted of two groups, quantity and quality. The quantity variable group consisted of continuous variables dealing with the number of advertisements and number of pages per advertisement. The quality variable group consisted of categorical variables dealing with the information that was included in the advertisements. In order to check the reliability of the measures, inter-rater reliability was performed in a 10% random sample. Quantity data were analyzed using analysis of variance (ANOVA). Quality data were analyzed using chi square tests.

**Results:** Good inter-rater reliability was observed. The mean Pearson's product moment correlation coefficient value was 0.94. Complimentary journals had a significantly higher number of advertisements, pages per advertisement, advertisements per journal article and percent of pages in each issue that were advertisements ($p < .001$ for each contrast). No significant differences in the quality of the advertisements were found between the two categories of medical journals.

**Conclusions:** The quantity, but not quality, of pharmaceutical advertisements varies depending on the category of medical journal.

**Sponsor:** *None*

**1702** **Presentation Type:** Poster

**Author:** Suzanne Shaffer **Presentor:** Suzanne Shaffer
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**Classification:** GSBS Student
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*John Planz, Department of Pathology and Anatomy*
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**EFFICACY AND LIMITATIONS OF STR MULTIPLEX SYSTEMS IN LOW COPY NUMBER (LCN) DNA ANALYSIS**

**Purpose:** The aim of this study is to demonstrate the reliability and reproducibility of LCN DNA profiles based on empirical data. We have begun pilot testing of variable LCN DNA amounts performed under differing PCR and electrophoretic parameters.

**Methods:** DNA was isolated from 3 males and 3 females using the DNA IQ™ System (Promega Corporation, Madison, WI). DNA quantities were determined using Quantifiler™ Human DNA Quantification Kit (Applied Biosystems, Foster City, CA). Various LCN amounts of DNA ranging from 3 to100 pg were examined. Each LCN sample dilution was amplified using the PowerPlex® 16 (Promega Corporation, Madison, WI ) multiplex STR system for a total of 10 amplifications in order to determine the reproducibility of the individual profiles. PCR was performed on LCN samples at 30, 32 and 34 cycles. All electropherograms were generated using ABI PRISM® 3100 Genetic Analyzer (Applied Biosystems, Foster City, CA) and GeneScan software.

**Results:** Increasing PCR cycle numbers reduces the quality of the profile, including increased stutter proportions, allelic drop-in, and background contaminants.

**Conclusions:** Our findings suggest that while increasing DNA input amounts and PCR cycle numbers may enhance DNA STR profiles, the relatively high and broad standard deviations are indicative of stochastic effects associated with LCN samples. In addition, incorrect genotype assignments rise with increasing cycle numbers. Although increasing the filtering conditions decreases the number of aberrant alleles, it ultimately reduces the number of true alleles being called, which is the primary goal of LCN analysis.

**Sponsor:** *SCORE grant*

**1703** **Presentation Type:** Poster

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**DEVELOPMENT OF A CONTROLLED VOCABULARY FOR OSTEOPATHIC MEDICINE**

**Purpose:** Osteopathic Medicine has developed a unique terminology to transmit specialized professional knowledge to its members, students, patients, and public. However, this terminology is often idiosyncratic, inconsistent, imprecise, and unstructured. This can lead to confusion and misunderstanding in the teaching and communication of key concepts in osteopathic philosophy, principles, and practice. National and international collaborative programs demand accurate and consistent terminology to collect and manipulate large quantities of data, thus exacerbating this problem.

**Methods:** The Authorized Osteopathic Thesaurus arose from the need for a controlled vocabulary to index the osteopathic literature in OSTMED®. The first edition of the Osteopathic Thesaurus was developed from ECOP's Glossary of Osteopathic Terminology and the subject headings in OSTMED®. Osteopathic physicians then identified and defined these terms and their interrelationships, which a Thesaurus Editor compiled and organized into a structured thesaurus format.

**Results:** In January 2004, the Authorized Osteopathic Thesaurus, containing 413 terms, of which 204 are unique main entry terms, was submitted to the National Library of Medicine for inclusion in the Metathesaurus®. The Thesaurus has also been submitted to SNOMED, the Systematized Nomenclature of Medicine. These large databases have been declared standards for use in developing the national Electronic Medical Record (EMR) and other systems for the electronic exchange of clinical health information. Thus, osteopathic physicians, educators, and researchers will benefit from osteopathic medicine's greatly expanded representation in standard medical information systems.

**Conclusions:** To maintain control, currency, clarity, and consistency of terminology, many professions now maintain their controlled vocabulary in a structured thesaurus format. With the Authorized Osteoapthic Thesaurus, osteopathic medicine is now in a position to use its unique vocabulary to:

- search the osteopathic literature with precision,
- develop standardized core clinical osteopathic curricula,
- analyze and evaluate osteopathic educational programs,
- develop and index test items for standardized examinations,
- develop and implement an osteopathic electronic medical record,
- collect and analyze osteopathic patient data,
- incorporate osteopathic practice in automated office and reimbursement software,
- communicate osteopathic education, practice and research findings clearly.

**Sponsor:** *American Association of Colleges of Osteopathic Medicine, American Osteopathic Association*

# OTHER

1704 **Presentation Type:** Poster

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**Classification:** GSBS Student
*Kathryn A. Kaiser, B.S., MT(ASCP), Susan F. Franks, Ph.D., German Berbel, D.O., F.A.C.O.S., Adam B. Smith, D.O., F.A.C.O.S., and Joan F. Carroll, Ph.D. University of North Texas Health Science Center, Fort Worth, TX 76107*

**METHODOLOGICAL ISSUES IN ELICITING GHRELIN RESPONSE: COMPARISON OF DIFFERENT LIQUID MEAL VOLUMES**

**Purpose:** The presence of the gut peptide ghrelin in the system of hunger and appetite regulation has been a relatively recent discovery. This has led to increasing numbers of investigations attempting to further elucidate its role in weight control as applied to human obesity. Overall results of these studies however, have been largely inconclusive due to low subject number and possibly methodological inconsistencies. This study presents pilot data for a broader investigation designed to determine the role of ghrelin in appetite regulation in morbid obesity. Ghrelin measurements from initial subjects failed to demonstrate a change from fasting to postprandial levels, therefore a pilot investigation was undertaken to study methodology of ghrelin elicitation.

**Methods:** Subjects were 15 morbidly obese females who were scheduled to undergo laparoscopic banding (lap-band) surgery. All subjects had blood drawn for fasting ghrelin levels. Subjects in Group 1 consumed one Slim-Fast® shake for a total volume of eight ounces. Subjects in Group 2 consumed three Slim-Fast® shakes for a total volume of 24 ounces.

**Results:** Ratio of pre- and postprandial ghrelin levels were compared between Group 1 ($M = 0.98$, $SD = .17$) and Group 2 ($M = 1.42$, $SD = .41$) via independent t-test. Results were significant $t(13) = -2.49$, $p = .03$.

**Conclusions:** Results of thus study indicate that caloric content and volume may play an important role in eliciting a measurable ghrelin response to feeding. Future studies should also investigate the role of mastication in ghrelin elicitation. Standardization of methodology in the field will be critical in determining the role of ghrelin in hunger and appetite regulation.

**Sponsor:** *HSC Faculty Grant/Inamed*

1705 **Presentation Type:** Poster

**Author:** Robert Kaman **Presentor:** Robert Kaman
**Department:** GRADUATE SCHOOL OF BIOMEDICAL SCIENCES
**Classification:** Faculty (Not for Competition)
*Robert L. Kaman, JD, PhD, GSBS Outreach, UNTHSC*
*Elizabeth Davis, MEd., GSBS Outreach, UNTHSC*
*Minnie Zavala, GSBS Outreach, UNTHSC*
*Monica Campos, MPH, GSBS Outreach, UNTHSC*
*Rustin Reeves, PhD, Anatomy and Cell Biology, 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, Minority K-12 Initiative for Teachers and Students (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 great success in creating a diverse student population that leads the state in that area.

**Sponsor:** *NIGMS,NHLBI,NSF,DOE,State of Texas Coordinating Board*

1706 **Presentation Type:** Poster

**Author:** Rick Lin **Presentor:** Andrew Racette
**Department:** RESIDENCY PROGRAMS
**Classification:** Postdoctoral Fellow/Resident
*Rick Lin, D.O. Dermatology Institute of North Texas, Duncanville, TX*
*Andrew J Racette, D.O. Plaza Medical Center, Ft. Worth, TX*
*Dan Ladd, D.O. Austin, TX*
*Clay Cockerell, M.D. UT Southwestern, Dallas, TX*
*Whitney High, M.D. UT Southwestern, Dallas, TX*
*Bill Way, D.O. Dermatology Institute of North Texas, Duncanville, TX*

**DO CLINICAL PHOTOGRAPHS ALTER THE HISTOPATHOLOGIC DIAGNOSIS OF DYSPLASTIC NEVI?**

**Purpose:** Although it is crucial that dermatopathologists have as much information as possible when considering the degree of histologic dysplasia in melanocytic nevi, no studies have endeavored to see if the histologic diagnosis of dysplastic melanocytic nevus would be influenced in any way by giving the dermatopathologist both a clinical digital image of the biopsied lesion and a routine H&E specimen to examine.

**Methods:** We reviewed forty-seven pathology reports from a single dermatopathologist over a three year period. Two sets of readings were performed with the first set being without and the second set with the digital photograph.

**Results:** All nine of the melanoma in situ diagnoses remained consistent between the first and second reading. Of the twenty-nine compound dysplastic nevi and junctional dysplastic nevi that were not originally recommended for removal, one of them was recommended for excision after the second reading with the aid of clinical digital images. In the first
reading, there were a total of nine nevi with unusual features and the dermatopathologist recommended excision for all of them. After the second reading with the aid of clinical photographs, only three of the six compound dysplastic nevi and none of the three junctional dysplastic nevi still retained the recommendation for excision.

**Conclusions:** The results of this study suggest that digital clinical images may increase the accuracy with which dermatopathologists interpret melanocytic nevi with varying degrees of atypia. In this small study, there was a trend toward fewer excisions being recommended, which could represent considerable cost savings in the management of dysplastic nevi. Larger studies are needed to confirm this finding.

**Sponsor:** *none*

1707 **Presentation Type:** Poster

**Author:** Rachel Boyer **Presentor:** Rachel Boyer
**Department:** PHYSICIAN ASSISTANT STUDIES (PA Program)
**Classification:** TCOM MPAS Student
*Rachel Boyer, PA-S; Olive Chen, PhD; Laurie Hill, MPAS, PA-C*
*UNTHSC Physician Assistant Studies*
*Fort Worth TX, 76107*

**POTENTIALS AND BARRIERS OF PHYSICIAN ASSISTANTS WORKING IN HOSPICE**

**Purpose:** Purpose: This study intended to identify potentials for Physician Assistants (PAs) to work in hospice and to identify the barriers that maybe preventing PAs from working in hospice.

**Methods:** Method: A total of 7,449 practicing PAs from 16 state chapter PA societies were invited to participate in this cross sectional study. A modified cluster sampling method was used to collect data. The investigators developed a 17-question survey to collect the data. A cover letter was e-mailed to the above prospective participants inviting them to respond to the survey. The prospective participants could access the survey by selecting a URL link within the cover letter. Once the data collection was complete, Chi-Square and ANOVA statistical analysis was performed using SPSS (11.5) software.

**Results:** Results: A total of 6,721 PAs received the e-mail and 1,036 practicing PAs responded (15% response rate). The respondents who had referred a patient to hospice at least six times had more interest in working for a hospice than those who had referred a patient only one to five times ($F = 18.577$, $p < 0.001$). The respondents who felt that they had received adequate training had a higher interest in working for a hospice than those who felt they had not been adequately trained ($t = -3.710$, $p < 0.001$). Almost all (98.8%) of the respondents felt they do not clearly understand the regulations for Medicare reimbursement of PA hospice services.

**Conclusions:** Conclusion: Potentials for PAs to work with terminally ill patients were identified: over 97% of the respondents felt that hospice is a beneficial program and PAs could be a beneficial addition to a hospice team. Some barriers identified for PAs to practice in hospice were: PAs lack formal education in working with terminally ill patients in a hospice setting, dissatisfaction existed with the education received in PA school in working with this patient population, and respondents do not understand the current regulations involving Medicare reimbursement for hospice services. With a few changes in PA school curricula and changes in the reimbursement regulations, there will be a great potential for PAs to work in a hospice setting.

**Sponsor:** *none*

# OTHER

**1708** **Presentation Type:** Poster

**Author:** Paul Moga **Presentor:** Paul Moga
**Department:** MANIPULATIVE MEDICINE
**Classification:** Faculty (Not for Competition)
*Paul J. Moga, D.O., Ph.D.*
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**DOES MANUAL MEDICINE TREATMENT IMPROVE CHRONIC LOW BACK PAIN PATIENTS' LOAD ESTIMATION?**

**Purpose:** Chronic low back pain (CLBP) patients appear to estimate load differently (Moga, MSU-FP Research Day, 2004). Osteopathic treatment may improve both their pain and load estimation. This study will test 2 primary null hypotheses--H01: There is no difference in load estimation between CLBP and pain-free subjects, and H02: There is no difference in load estimation of CLBP subjects pre- and post-treatment. Two secondary null hypotheses will also be tested--H03: There are no differences in anthropometric measurements between CLBP and pain-free subjects and H04: There is no difference in pre- and post-treatment, pain-scale response or torso range-of-motion in CLBP subjects.
**Methods:** Volunteers will be recruited from Michigan State University clinics. CLBP subjects will have had pain of at least 6 months' duration, while exclusion criteria include lower extremity radicular symptoms, gross spinal deformity, or previous spine surgery. To test H01, back-pain and pain-free subjects will be recruited and matched for gender, age, height, and weight. To test H02, back pain subjects will act as their own controls.
All will receive general history and physical examinations, as well as standardized structural examinations and anthropometric measurements that include BMI, sagittal plane spine angles, body segment lengths, and spine- and leg-length ratios. Measurements will be compared between-groups to validate observations that persons having certain spine deformities or complaining of back pain exhibit unique anthropometric characteristics (Moga, Doctoral Dissertation, 2002).
Back pain subjects will respond to standardized pain questionnaires. Pain-scale responses, range-of-motion evaluations, and subjective, palpatory findings will monitor treatment outcome. Load estimation will be determined using a weight belt worn around the waist.
**Results:** It is hypothesized that there will be a between-group, load estimation difference, and that improvement of back pain using osteopathic manipulative therapy will result in improved load estimation.
**Conclusions:** Validation of load estimation differences and objective improvement of these differences may contribute to the understanding of sensory response adaptation and of nervous system plasticity. Verification of unique, anthropometric characteristics in back pain subjects may help to design work stations, training programs, or screening protocols. Manual medicine outcomes validation may interest osteopathic practitioners and researchers.
**Sponsor:** *None*

**1710** **Presentation Type:** Poster

**Author:** Paul Moga **Presentor:** Paul Moga
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**Classification:** Faculty (Not for Competition)
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**DOES CORRECTION OF HAMSTRING SHORTNESS AFFECT THE THORACIC KYPHOSIS ANGLE IN HYPERKYPHOTIC SUBJECTS?**

**Purpose:** Hamstring shortness (HS) has been associated with leg injuries and the spine disorder Scheuermann's Disease, an acquired thoracic hyperkyphosis (TH). Scheuermann's patients have a thoracic angle greater than 40 deg., a cosmetic deformity, restricted trunk motion, and may have localized back pain. HS is linked to restrictions of hip motion, sagittal plane flexion, pelvic tilt, and flattened lumbar lordosis. As one spine level's motion restriction may lead to increased motion at another, perhaps TH is a compensatory mechanism to enhance the restricted torso flexion of HS. If so, then it is reasonable to hypothesize that treatment of HS would improve TH. This study will test 3 null hypotheses--H01: There is no difference in Finger-to-Floor Reach Distance between pre- and post-treatment HS subjects, H02: There is no difference in Thoracic Kyphosis Angle between pre- and post-treatment HS subjects, and H03: There is no difference in Finger-to-Floor Reach Distance or Thoracic Kyphosis Angle in untreated, age-, gender-, height- and weight-matched, untreated HS controls over time.
**Methods:** Volunteers 14-18 years-old will be recruited from area schools and screened for HS using the Finger-to-Floor Reach Test. Subjects will fill out questionnaires concerning their health history and athletic participation. These data will be coupled with anthropometric measurements to validate previously observed relations between spine curvature, athletic training, hamstring shortness, and anthropometry (Moga, Doctoral Dissertation, 2002).

HS subjects, those unable to touch the floor, will be matched to hamstring-normal controls, and all will be screened for TH using a non-radiographic, photogrammetric method developed by Ashton-Miller and Wojtys (University of Michigan). Subjects labeled at spine surface landmarks and illuminated by a reference grid stand on a platform, with digital images recorded and processed to yield spine angles. Manual medicine will be used on the treatment group, with reach distances and thoracic angles re-evaluated at intervals.
**Results:** It is hypothesized that both HS and TH will improve following manual medicine intervention, and that there will be no improvement of these two parameters in untreated controls over time.
**Conclusions:** Correction of HS may help prevent lower extremity injury and may improve TH, preventing its cosmetic and functional changes. Osteopathic practitioners are in a position for both early recognition and treatment of these problems.
**Sponsor:** *None*

**1709** **Presentation Type:** Oral

**Author:** Priscilla Ortiz **Presentor:** Priscilla Ortiz
**Department:** SCHOOL OF PUBLIC HEALTH (SPH)
**Classification:** SPH Student
*Priscilla M. Ortiz*
*HIHAL MPH Student, EAD 713*
*UNTHSC School of Public Health*
*Fort Worth, TX 76107*

**FORT WORTH AND DALLAS HEALTH CARE INTERPRETERS: PERSPECTIVES ON INTERPRETER TRAINING PROGRAMS**

**Purpose:** This study attempts to understand whether the work-related training that health care interpreters have received affects their perceptions of their on-the-job performance. It explores whether healthcare interpreters in the Dallas/Fort Worth area view the training they have had as relevant and if they feel it has equipped them sufficiently for their work and impacted their perceived levels of confidence and competence.
**Methods:** Participants were engaged in semi-structured, conversational interviews using a 50-question interview guide. Interviews were audio taped, transcribed and coded for analysis.

**Results:** The evident diversity in training and educational backgrounds of healthcare interpreters working in the Dallas/Fort Worth area illustrates the extremely broad range of "training programs" for interpreters in healthcare. The data indicates that an overwhelming amount of interpreter training happens on-the-job.
Respondents expressed the idea that health care interpreting involves a complex range of tasks which requires intentional skill development to perform well. The role of the interpreter was a recurring theme for participants. How this role is understood plays a vital part in how they perceive their work. Interpreters felt their training programs were not advanced enough, did not last long enough and did not equip them sufficiently for the complex job they perform. Interpreters seriously need and want more extensive, in-depth training and professional development.
**Conclusions:** The insights of working healthcare interpreters and the identification of current gaps in training will prove invaluable to those who design and improve interpreter educational programs. More research is needed in the area of training development.
Additionally, further research is needed toward understanding the actual role of the health care interpreter. The interpreters interviewed here asserted that having a clear understanding of their role gives them confidence in their work. However, the work of other researchers has shown that the normative understanding of an interpreter's role, expressed by many of the interpreters interviewed, is not effective in fully describing the work an interpreter actually does (Wadensjo 1998). Thus, the foundation on which many interpreters are placing their confidence in their job performance is an understanding which must be further researched, explained, and understood so that it can be usefully applied in new training programs.
**Sponsor:** *None*

**1711** **Presentation Type:** Poster

**Author:** Anada Gunn-Sanders **Presentor:** Anada Gunn-Sanders
**Department:** SCHOOL OF PUBLIC HEALTH (SPH)
**Classification:** SPH Student
*Anada I. Gunn-Sanders, J.D., School of Public Health UNTHSC*

**FROM CRIME SCENE TO COURTROOM: THE EMERGENCE OF MITOCHONDRIAL DNA AS EVIDENCE**

**Purpose:** Research the development of mitochondrial DNA being submitted as evidence in courtrooms across the United States, and its effect on the legal system.
**Methods:** Legal review of pertinent cases tracking the progression of mitochondrial DNA offered as evidence in various court cases. Discussion of relevant genetic issues, including comparisons of DNA (as traditionally viewed) to mitochondrial DNA; analysis of DNA advancements; debates concerning the use of mitochondrial DNA; as well as its legal implications as evidence.
**Results:** From its first offering as evidence in a courtroom, mitochondrial DNA has now found acceptance throughout the United States and beyond. Courts are now recognizing that mitochondrial DNA evidence has met and surpassed threshold tests of admissibility under both Frye v. United States (1923) and Daubert v. Merrill-Dow Pharmaceuticals, Inc. (1993). Through continued education, judges, juries and lawyers have begun to appreciate the significance of mitochondrial DNA evidence.
**Conclusions:** Technological advancements now allow law enforcement officials to have biological evidence (mtDNA) readily available for lawyers and judges to use at trial. It is this technology and efficiency, which assists in expediting the journey of forensic evidence from the crime scene to the courtroom.
**Sponsor:** *none*

# OTHER

**1712** **Presentation Type:** Poster

**Author:** Jongbae Baek **Presentor:** Jongbae Baek
**Department:** Biostatistics
**Classification:** Faculty (Not for Competition)
*JongBae Baek, Ph.D., Sejong Bae, Ph.D., and Karan Singh, Ph.D, University of North Texas Health Science Center at Fort Worth, Fort Worth, Texas, 76107*

**MEASURING A SAFETY CLIMATE IN KOREAN MANUFACTURING INDUSTRY: PRELIMINARY RESULTS**

**Purpose:** Safety climate has been recently recognized as a fundamental and ultimate solution for improving workplace safety in various industries including manufacturing industry such as chemical plant. There have been some movements to improve safety culture and climate among industries as well as government agencies in Korea. But the safety climate study has not been done in Korean manufacturing industries. There is general agreement that creating a safety climate in Korean manufacturing industries, but few if any validated tools measure important elements of a safety climate. Investment of resources in this important facet of safety will be limited as long as the effect of strategies cannot be measured. We explored the validity of Health and Safety Commission (HSC) (2002) instruments in Korean industry to measure safety climate following planned interventions.
**Methods:** The questionnaires, targeted to managers and workers, were developed from the HSC instruments. Respondents indicated relative agreement with each item on a five-point Likert-scale, ranging from 'Fully Agree' to 'Fully Disagree', to measure the level of safety climate. Underlying factors (Management commitment to safety (M1), Merits of the H&S procedures, instructions, and rules (M2), Accidents & Near-misses (M3), Training & Competence (W1), Job security and Satisfaction (W2), Pressure for production (W3), Communications (W4), Perceptions of personal involvement in H&S (W5), Perceptions of organizational & management to H&S (W6), Rule breaking (W7), Workforce view on state of safety & culture (W8)) were evaluated from a total of 184 respondents drawn from managers and workers. To test reliability the internal consistency was assessed by Cronbach's alpha coefficient.
**Results:** With the exception of the Pressure for Production (alpha=0.61), the Cronbach alpha coefficients for most scales were satisfactory. Correlations were calculated for all three managerial level and eight workers' level safety scales. The scales of the HSC scales were moderately correlated ($p < 0.01$).
**Conclusions:** The Safety Climate Questionnaire adapted from the HSC showed a good internal consistency and reliability in Korean manufacturing industry. Further study is needed to measure changes in safety culture following planned interventions. Utilization of a tool to assess dimensions of a safety climate will allow empirical evaluation of manufacturing industry interventions for safer environment.
**Sponsor:** *Korean Occupational Safety and Health Agency*

**1713** **Presentation Type:** Poster

**Author:** Joosik Park **Presentor:** Joosik Park
**Department:** Biostatistics
**Classification:** Postdoctoral Fellow/Resident (Not for Competition)
*JooSik Park, Ph.D.1,2, ChongGyu Lim, Ph.D.2, Sejong Bae, Ph.D.1, and Karan Singh, Ph.D1, 1:University of North Texas Health Science Center at Fort Worth, Fort Worth, Texas, 76107 2:Korean Science and Engineering Foundation*

**FUZZY EXPERT SYSTEM FOR EFFECTIVE SEWAGE DISPOSAL CONTROL UNIT**

**Purpose:** Sewage disposal is an important issue worldwide and problem of pollution of environment by groundwater by domestic and industrial waste. Large inputs of organic matter and nutrients from raw sewage to environment may lead to deterioration of the water quality. Sequential wastewater treatment over time is good but may not be efficient enough in highly industrialized area. Better efficiency can be obtained in sewage treatment system by finding and using the real time dissolved oxygen saturation and pH level to control the activity of micro-organisms in the system.
**Methods:** The sequencing batch reactor (SBR) processes the nitrogen and phosphorus efficiently well and is accepted; more research is being done on nitrogen, phosphorus, and other organic materials in discharged water, ideal condition should be established for the growth of oxygen-using bacteria and other micro-organisms that consume organic materials which pollute the water. Modeling the optimal oxygen saturation "bending point" is a key step in obtaining the ideal condition for biological nitrification, denitrification, and phosphorus removal. To control the process, we rely on past data or measure real time oxygen amounts and use them to find oxygen saturation bending points to control the activity of micro-organisms. The fuzzy expert system was developed to improve existing dissolved oxygen and pH control unit for better sewage disposal control.
**Results:** It is anticipated that (1) by controlling dissolved oxygen and pH levels in a tank the system will maximize denitrification rate, (2) by controlling the production of ammonia in a tank the system will reduce odor, (3) by regulating the waste water discharge amount based on the density of the inlet water based on the exact oxygen saturation bending point, the system will reduce the source water pollutants, and (4) by using the micro-controller, remote investigation, control, and data storage can be achieved and will be effective in reduction of man power costs.
**Conclusions:** Successful wastewater management requires long term data so that baseline conditions and variation within the system can be explored using statistical modeling. This is an ongoing study that started on late 2004. Full seasonal data will be collected. Preliminary results are expected to be available in late 2005. Results of this study will help reduce man power costs as well as reduction in pollution.
**Sponsor:** *Korean Science and Engineering Foundation*

# BIOMEDICAL SCIENCES ORAL PRESENTATIONS

| | | |
|---|---|---|
| 2:00 PM | **Scott Duncan**<br>POLYCYSTIN-2 ACCELERATES INTRACELLULAR CALCIUM RELEASE FROM THE ENDOPLASMIC RETICULUM IN C. ELEGANS | **Abstract# 1113** |
| 2:15 PM | **Everett Nixon**<br>DIFFERENTIALLY DISTRIBUTED IP3 RECEPTORS AND A NEW ROLE FOR GROUP I MGLUR IN THE RETINA | **Abstract# 712** |
| 2:30 PM | **John Fuller**<br>EXPRESSION OF P75NTR AND NERVE GROWTH FACTOR IN HUMAN OPTIC NERVE HEAD AND RETINA | **Abstract# 717** |
| 2:45 PM | **James Flynn**<br>17BETA-ESTRADIOL ATTENUATES MITOCHONDRIAL DEPOLARIZATION IN POLYOL-STRESSED CULTURED LENS EPITHELIAL CELLS | **Abstract# 705** |
| 3:00 PM | **Josh Gatson**<br>ACTIVATION OF A NOVEL MEMBRANE-ASSOCIATED ANDROGEN RECEPTOR MODULATES THE MAPK AND PI3-KINASE/AKT PATHWAYS AND INDUCES CELL DEATH | **Abstract# 1109** |
| 3:15 PM | **BREAK** | |
| 3:30 PM | **Amit Vashist**<br>DIFFERENTIAL EFFECTS OF SHORT-TERM PHYTOESTROGEN SUPPLEMENTATION ON COGNITIVE AND PSYCHOMOTOR PERFORMANCE OF MALE AND FEMALE MICE | **Abstract# 105** |
| 3:45 PM | **Swapnil Vaidya**<br>TO KILL OR NOT TO KILL - THAT IS THE QUESTION | **Abstract# 900** |
| 4:00 PM | **Amir Ramezani**<br>UNDERSTANDING THE BIOPSYCHOSOCIAL EFFECTS OF EPILEPSY | **Abstract# 1108** |
| 4:15 PM | **Arti Sharma**<br>ANTIOXIDANT PRETREATMENT PROTECTS MYOCARDIAL ENZYMES DURING CARDIAC ARREST | **Abstract# 312** |
| 4:30 PM | **Jie Liu**<br>PHOSPHORYLATION PLAYS A ROLE IN REGULATING INTRACELLULAR LOCALIZATION OF HUMAN ANNEXIN II | **Abstract# 400** |

# PUBLIC HEALTH ORAL PRESENTATIONS

| | | |
|---|---|---|
| 9:30 AM | **Thaddeus Miller**<br>HOW CAN THE UNITED STATES PRIORITIZE THE TARGETED TESTING OF TUBERCULOSIS? | **Abstract# 1500** |
| 9:50 AM | **Nykiconia Preacely**<br>PROJECT SPONSORSHIP MISSION AVOID RELIANCE ON TOBACCO MONEY: ORGINS, EVOLUTION AND OUTCOMES | **Abstract# 1504** |
| 10:10 AM | **BREAK** | |
| 10:25 AM | **Carolina Alvarez-Garriga**<br>RISK FACTORS FOR CHILDHOOD ASTHMA IN THE UNITED STATES | **Abstract# 1507** |
| 10:45 AM | **Godavari Patil**<br>PHYSICIANS OF NON-PARTICIPATING COUNTIES IN NORTH TEXAS: A STUDY IN PUBLIC HEALTH PREPAREDNESS AND RESPONSE TO BIOTERRORISM | **Abstract# 1510** |
| 11:05 AM | **Priscilla Ortiz**<br>FORT WORTH AND DALLAS HEALTH CARE INTERPRETERS: PERSPECTIVES ON INTERPRETER TRAINING PROGRAMS | **Abstract# 1709** |

# FIRST AUTHOR/PRESENTER INDEX

# FIRST AUTHOR/PRESENTER INDEX

# KEY WORD INDEX

# KEY WORD INDEX

# KEY WORD INDEX

# KEY WORD INDEX

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