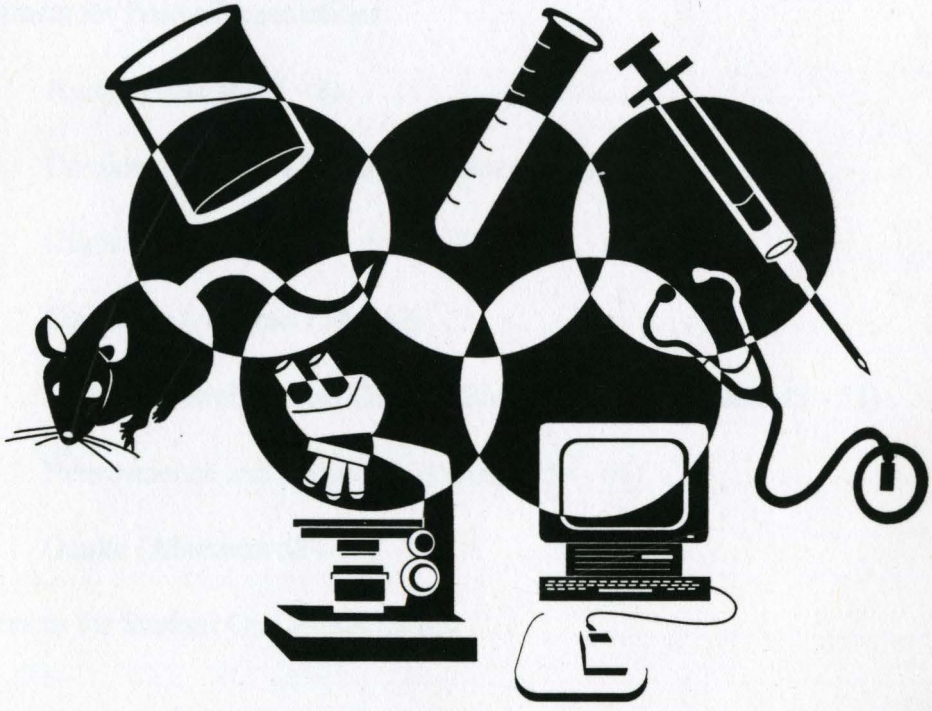
University of North Texas
Health Science Center at Fort Worth

Fourth Annual

Research Appreciation Day

March 20, 1996



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Graduate School of Biomedical Sciences
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University of North Texas Health Science Center at Fort Worth

Research Appreciation Day

March 20, 1996

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AGENDA

8:00 - 9:00 AM	Assemble Posters	Interdisciplinary Lab
9:00 - 10:00 AM	Faculty/Non-Student Poster Session	Interdisciplinary Lab
10:00 - 11:30 AM	Student Poster Competition	Interdisciplinary Lab
12:00 - 1:30 PM	Lunch and Keynote Speaker	Main Auditorium
	Welcome	Benjamin L. Cohen, D.O. Vice President for Health Affairs and Executive Dean
	Overview of RAD '96 Activities	Thomas Yorio, Ph.D. Dean Graduate School of Biomedical Sciences
	Introduction of Keynote Speaker	Robert w. Gracy, Ph.D. Associate Dean Research and Biotechnology
	Calmodulin...Its Role in Cell Regulation and Disease	John Dedman, Ph.D. Professor and Eminent Scholar Molecular and Cellular Physiology University of Cincinnati
1:30 - 4:30 PM	Student Oral Competition	Kiva Classroom
4:30 - 6:00 PM	Alumni Careers Round Table *Sponsored by the Graduate Student Association*	Panoramic Classroom
6:00 PM	Award Ceremony	Kiva Classroom
6:30 PM	Reception *Sponsored by the Graduate Student Association*	Atrium
ALL DAY	Vendor Fair	Kiva Lounge

KEYNOTE SPEAKER

John R. Dedman, Ph.D.
Professor and Eminent Scholar
Department of Molecular and Cellular Physiology
University of Cincinnati

John R. Dedman, Ph.D., Ohio Eminent Scholar in Medicine since June 1991, and one of the top biochemical physiologists in the country, is a pioneer in his field. His research focuses on the mechanisms by which calcium regulates intracellular functions; in short, how calcium acts as a communication link within cells.

Because precise regulation of calcium is basic to biological processes, Dedman works on a variety of disease models and interacts with a broad spectrum of other investigators. His research on the communication process of cells could lead to a better understanding of muscular dystrophy, cystic fibrosis, heart arrhythmia, hypertension and even the damage to brain cells following stroke.

Prior to his position at University of Cincinnati, Dr. Dedman was Professor of Physiology and Cell Biology at University of Texas Health Science Center at Houston. He received his Ph.D. from University of North Texas under mentorship of Ben Harris, Ph.D. Dr. Dedman performed post-graduate training at Baylor College of Medicine.

ALUMNI CAREERS ROUND TABLE

For Research Appreciation Day 1996, the Graduate Student Association (GSA) is sponsoring a discussion with selected alumni on career pathways and opportunities in medicine, industry and academics.

Michael Smith, Ph.D. ('86), recently joined the faculty of the Department of Integrative Physiology at UNT Health Science Center as an Associate Professor. Dr. Smith's research efforts are focused on the neural control of cardiovascular function.

Ray D. Page, D.O, Ph.D. ('91), is a Medical Oncology Fellow at University of Texas M.D. Anderson Cancer Center where he studies Primary Hepatic Lymphoma. Dr. Page is presenting a poster (#31) on his research in today's non-student poster session.

Annita Verstappen, Ph.D. ('92), is Clinical Study Manager for Alcon Laboratories, Inc. Dr. Verstappen oversees clinical trials in Surgical/Anti-Infective Research.

Julie Y. Crider, Ph.D. ('94), is a Senior Scientist with Alcon Laboratories, Inc. in the Molecular Pharmacology Unit. Dr. Crider's efforts focus on drug discovery in the treatment of glaucoma.

UPJOHN RESEARCH ACHIEVEMENT AWARDS

Upjohn is an international pharmaceutical company that has taken an active role in supporting medical and health education. The company provides funding for programs in education, health social welfare, arts and culture, civic development, environmental preservation, public policy research and the sciences.

The Upjohn Research Achievement Awards are given to the top three student poster presentations and the top three student oral presentations as determined by a panel of judges.

The 1996 Research Appreciation Day student poster judges are David G. Bernard, Ph.D., Assistant Professor, Department of Biology, University of Texas at Arlington; Paul Chippindale, Ph.D., Faculty Associate, Department of Biology, University of Texas at Arlington; Jill Van Wart Hood, Ph.D., Allied Health Coordinator, Department of Biology, University of Texas at Arlington; Norman Miner, Ph.D., President, MicroChem Laboratory; Ricardo E. Rodriguez, Ph.D., Associate Professor, Department of Chemistry, Texas Wesleyan University; Arup Sen, Ph.D., Chairman and Chief Executive Officer, Health Tech Development, Inc.; and Reginald Stilwell, Johnson & Johnson Medical.

The 1996 Research Appreciation Day student oral presentation judges are Annita Verstappen, Ph.D., Alcon Laboratories, Inc.; Ray Page, D.O., Ph.D., University of Texas M.D. Anderson Cancer Center; and Julie Y. Crider, Ph.D., Alcon Laboratories, Inc.

SPECIAL CENTERS OF EXCELLENCE

Cardiovascular Research Institute

The Cardiovascular Research Institute, established in 1995, was developed from the multidisciplinary research efforts of molecular biologists, pharmacologists, physiologists, and physicians in the internal medicine subspecialties of cardiology and pulmonary. A key role of the institute is to integrate basic research findings with the clinical therapeutic problems associated with over 50 million Americans who suffer from cardiovascular diseases.

Institute studies focus on heart disease, with special emphasis on understanding the role of exercise in the prevention of and rehabilitation from heart disease. Research is conducted into the fundamental molecular biologic and cellular mechanisms associate with the improved cardiovascular function, cardio-protection from heart attacks and longer life of those people who have moderate- to high- activity lifestyles. Both the basic science and clinical divisions of the institute collaborate with pharmaceutical and biotechnology corporations in order to validate new diagnostic, preventive, therapeutic and corrective procedures. Institute activities involve local, national and international partnerships.

The institute also provides educational and research training opportunities for graduate and medical students, and postdoctoral and clinical fellows.

Center for Osteoporosis Prevention and Treatment

The center was established in 1993 by the Department of Internal Medicine's Division of Rheumatology to foster collaborative research between clinical and basic science faculty dedicated to fighting this debilitating affliction. Osteoporosis is an epidemic in America, resulting in widespread concern about the ability of the health care system to cope with this growing problem.

Basic science departments, the Department of Public Health and Preventive Medicine, the Department of Obstetrics and Gynecology, other departments of the medical school and other health care institutions participate in institute projects.

Goals are: to foster research and clinical efforts to improve the diagnosis, prevention and treatment of osteoporosis; to provide devices and drugs to initiate and validate new preventive techniques and therapies; to forge partnerships with other medical schools since these studies involve large numbers of patients and multi-center research activities; and to develop programs and service models to educate the public and health care providers about osteoporosis. Research efforts are enhanced by the use of a DEXA X-ray densitometer, which facilitates the early diagnosis of bone mineral density abnormalities.

Institute of Forensic Medicine

The Institute of Forensic Medicine, established in the early 1980s, is an academic and research partnership between UNT Health Science Center's Department of Pathology and DNA/Identity Laboratory and the Tarrant County Medical Examiner's Office.

The institute's goals are to increase the quantity and scope of research projects in forensic medicine as well as the number of graduate students studying toxicology, molecular biology and criminalistics. The collaborative strength and variety of the institute's teaching and research activities provide students a comprehensive training arena while building the health science center's forensic medicine research funding.

Institute of Nutrition and Chronic Disease Prevention

The Institute of Nutrition and Chronic Disease Prevention was established in 1995 and represents the combined efforts of the Department of Internal Medicine and the Department of Biochemistry and Molecular Biology, as well as the talents of other interested faculty members.

The long-term mission of this institute is to promote good health by preventing the development and progression of chronic diseases through an emphasis on sound nutritional practices. The institute has three broad areas of focus: higher education, public education and community service, and basic and applied research.

Research activities address the role of nutrition in preventing cardiovascular disease, cancer and diabetes, and the improvement of the quality of life during aging. Efforts focus on the nutritional components and molecular mechanisms of disease processes at the cell, organ and whole organism levels.

North Texas Eye Research Institute

The North Texas Eye Research Institute was formed in 1992 to serve as an academic and research focus for basic and clinical science activities within the visual science community of Fort Worth and north Texas.

The institute faculty consists of basic and clinical scientists who have primary appointments at the health science center, private practice or industry. They are heavily involved in the training of medical students, graduate students and postdoctoral fellows. Their research programs cover aspects of eye disease such as retinal degenerations, glaucoma, diabetic complications, aging and cataracts.

The institute sponsors a monthly Distinguished Visual Scientist Seminar Series, a weekly journal club, continuing medical education courses for health professionals and an annual eye health fair. Institute faculty also conduct clinical trials for testing the safety and efficacy of various therapeutic drugs and devices.

Substance Abuse Institute of North Texas

The Substance Abuse Institute of North Texas, established in 1993 by the Department of Pharmacology and the Department of Psychiatry and Human Behavior, is a consortium of professionals with expertise in substance abuse. Scientists and physicians in physiology, pathology, public health/preventive medicine, general and family practice and medicine also participate.

The institute's missions are to foster clinical and basic science research, train professionals whose efforts focus on the prevention and treatment of substance abuse, and serve as an information resource for area substance abuse treatment programs. The institute hosts research conferences and cosponsors seminars with area substance abuse prevention groups and pharmaceutical industries. The institute also regularly sponsors visits by international scholars to the health science center and the Fort Worth/Dallas Metroplex, and provides faculty consultants to state, federal and international agencies. Outreach programs involving many institutions from the North Texas area are being developed.

Wound Healing Research Institute

A key role of the Wound Healing Research Institute, established in 1992, is to translate research results into viable treatments that minimize the pain and suffering caused by debilitating consequences of problem wounds.

Its five-fold mission includes: expanding knowledge of the process of injury and wound healing using novel *in vitro* models and molecular biology techniques; application and innovative approaches such as the use of hyperbaric medicine, growth factors, tissue replacement therapies to problem wounds to prevent amputation and permanent disability; training graduate and medical students, interns and residents in new and interdisciplinary approaches to problem wounds; disseminating knowledge and experience through courses, seminars, conferences and symposia as a part of continuing medical education; and evaluating new pharmaceuticals and devices through all phases of the FDA approval process.

Funding from federal, state and private agencies and organizations supports various projects conducted within the institute. Faculty from basic science departments and the departments of general and family practice, internal medicine, pathology, surgery and hyperbaric medicine make up the research staff of the institute.

AGING

1.	S. Paranjape	EFFECTS OF AGING ON WOUND HEALING
2.	Anju Dubey	EFFECT OF AGE AND CALORIC INTAKE ON PROTEIN OXIDATION IN DIFFERENT BRAIN REGIONS AND ON BEHAVIORAL FUNCTIONS OF THE MOUSE
3.	Anita I. Zvaigzne	MODELING AGE-RELATED CHANGES IN PROTEIN STRUCTURES
4.	Yaprak Egilmez	EFFECT OF BRETAZENIL ON SHORT-TERM MEMORY PERFORMANCE OF RATS IN A AMORRIS WATER-MAZE PROCEDURE
5.	Doug Gaudette	INVOLVEMENT OF PROTEIN KINASE C ISOZYMES IN T LYMPHOCYTE DYSFUNCTION DURING HUMAN SENESCENCE
6.	Shelley R. McDonald	COGNITIVE AND SENSORIMOTOR PERFORMANCE IN YOUNG APOLIPOPROTEIN E2 DEFICIENT MICE
7.	Douglas Krug	SCOPOLAMINE PRODUCES DEFICITS IN SPATIAL MEMORY PERFORMANCE ON THE CIRCULAR PLATFORM MAZE IN YOUNG B6D2F1 MICE
8.	Shellie Ann Kolavic, DMD, MPH	DENTAL NEEDS OF COMMUNITY - DWELLING ELDERS

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: S. Paranjape

Department: Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff X

Read instructions and fit abstract inside the space given below:

EFFECTS OF AGING ON WOUND HEALING

S . Paranjape, T.J. Reese, J. Moore, C. Henderson, R. Agarwal, J. Wilson, J.G. Mills, R.W. Gracy and S. D. Dimitrijevich,

Departments of Biochemistry and Molecular Biology, Surgery, and Physiology; Wound Healing Research Institute, UNTHSC at Ft. WORTH

It is well recognized that wound healing is compromised in the aged organisms. However, it is not clear if this is due to a loss of intrinsic cellular capacity for repair, or if changes in the microenvironment are a more significant factor. We have developed Human Tissue Equivalents, based on a three dimensional non-contracted connective tissue matrix populated with appropriate fibroblasts, to model human skin, cornea and conjunctiva. Such multicellular systems are useful for studies of epithelialization and other phases of wound healing, and for comparing responses of developmentally or functionally related tissues. In order to study some cellular events non-intrusively (e. g. confocal microscopy), we have developed models populated with fluorescently labeled component cells. These labeled models have a useful life span for many experimental protocols. Current studies utilizing Tissue Equivalents include the role of hyperoxygenation on cell proliferation, differentiation and matrix biosynthesis; mechanisms of matrix contraction, and the role of growth factors. Cells from older donors appear more responsive to hyperbaric oxygen treatment, and epithelialization is enhanced in the Human Skin Equivalent. Although bFGF (FGF2) is less prominently detected in the skin (but not corneas) form older donors, there appears to be no age related effect on its expression in the component cells from this tissue. Our studies are being expanded to include wound healing in tissues other than skin.

Supported by the Texas Adv. Tech. Program (09760008), Texas Inst. for Res. and Education in Aging, and NASA Biotechnology Program (NAG 9-813-Basic)

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Anju Dubey

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow_X_ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

EFFECT OF AGE AND CALORIC INTAKE ON PROTEIN OXIDATION IN DIFFERENT BRAIN REGIONS AND ON BEHAVIORAL FUNCTIONS OF THE MOUSE

Anju Dubey, Michael J. Forster, Douglas E. Krug, Harbans Lal and Rajindar S. Sohal. Department of Biological Sciences, Southern Methodist University, Dallas, TX 75275, and Department of Pharmacology, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX 76107.

Using the aging mouse as a model system, the present studies addressed the hypothesis that oxidative stress/damage is a causal factor in senescence-related loss of brain functions. Based on this hypothesis, it was expected that oxidative protein damage would increase with age within regions of the brain associated with senescence-related functional loss, and that dietary restriction, an intervention which retards certain aspects of age-associated functional loss, would reverse such increases. Dietary restriction was found to retard age associated decline of sensorimotor coordination and improve performance of aged mice on an avoidance learning problem. Protein carbonyl concentration, one measure of protein oxidation, increased from 8 to 27 months of age in most regions of the mouse brain, with the most notable increases occurring in the striatum and hippocampus, regions of the brain strongly implicated in age-associated functional loss. Age-associated loss of protein sulfhydryl was more uniform across brain regions, and did not involve the hippocampus. Dietary restriction resulted in reversal of the age-associated regional trends in carbonyl and sulfhydryl concentration, with the largest changes occurring within the striatum. Crossover studies in aged diet restricted and ad libitum fed mice indicated that lowering of carbonyl content by diet restriction could be induced or reversed within a time frame of three to six weeks. These findings suggest that the beneficial effects of dietary restriction upon brain function and lifespan may depend upon its ability to acutely reduce steady-state levels of oxidative stress. [Supported by NIA grants AG07695 and AG07657.]

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM (POSTER)

First Author: Anita I. Zvaigzne

Department: Department of Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow X Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

MODELING AGE-RELATED CHANGES IN PROTEIN STRUCTURES

Anita I. Zvaigzne and Robert W. Gracy; Department of Biochemistry and Molecular Biology; University of North Texas Health Science Center at Fort Worth; 3500 Camp Bowie Boulevard; Fort Worth, TX 76107

Modified proteins accumulate in aging cells and tissues, and are thought to impede normal homeostasis. This may account for such problems of the elderly as impairment of cognitive function, vision, immune response, wound healing and the ability to respond to environmental and metabolic stresses.

Most of these "aged" proteins result from post-synthetic, covalent modifications such as deamidation and oxidation. These modifications label a protein for degradation, and may therefore be considered as "terminal marking" reactions. It is believed that such marking may be affected by the interactions of the protein with ligands and other proteins. The accumulation of modified proteins appears to be primarily due to age-related alterations in their degradation rather than abnormal synthesis.

Current work is centered on determining how these post-translational events are influenced by the interactions of these proteins with other ligands and/or with other proteins. One of the questions to be answered by this study is whether or not computational methods can be used to predict or support experimental observations and provide better insight into mechanisms of terminal marking.

The systems examined are native and modified triosephosphate isomerases. Triosephosphate isomerase was chosen as the model protein, because it is the best structurally characterized of all housekeeping enzymes, and because specific deamidated and oxidized isoforms have been shown to accumulate in aging cells and tissues.

Abstract #3

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Yaprak Egilmez

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow X Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

EFFECT OF BRETAZENIL ON SHORT-TERM MEMORY PERFORMANCE OF RATS IN A AMORRIS WATER-MAZE PROCEDURE. Y. Egilmez, C.J. wallis, J. Grewal, H. Lal. Department of Pharmacology and SAINT, University of North Texas Health Science Center, Fort Worth, TX 76107.

Bretazenil is a partial benzodiazepine receptor agonist which is known to have potent anxiolytic and anticonvulsant effects. In the present experiments, we studied the effect of bretazenil on short-term memory and motor performance of rats at doses that are effective to alleviate ethanol-withdrawal symptoms. Male Long Evans rats were trained to find a hidden platform in a Morris Water Maze (1.8 m in diameter and 60 cm high, filled with opacified water and maintained at 24 °C) during four consecutive training sessions. Following the acquisition period, rats were given a nutritionally balanced liquid diet with or without (control) ethanol (4.5%) for 10 days. Twelve hours after removal of the ethanol/control diet, rats were tested for their performance at the water maze on three consecutive test days. Each day, the platform was placed in a different location, and subjects were given an initial information trial to locate the platform. The effect of bretazenil (0.08, 0.32 and 1.25 mg/kg) was tested at 15, 30 and 60 min. following the information trial on measures of "latency to reach the platform", "path length" and "speed". There was no significant difference between ethanol and control groups in any of the performance measures used. In the control group, bretazenil did not produce any significant effect in any of the measures whereas in the ethanol group, the lowest dose of bretazenil induced a significant decrease in speed. These findings suggest that bretazenil does not impair short-term memory performance in rats at effective against withdrawal. (Supported by NIAAA #AA09567).

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Doug Gaudette

Department: Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow X Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

INVOLVEMENT OF PROTEIN KINASE C ISOZYMES IN T LYMPHOCYTE DYSFUNCTION DURING HUMAN SENESCENCE

Douglas C. Gaudette and Robert W. Gracy

Dept. of Biochemistry and Molecular Biology, University of North Texas Health Science Center, Fort Worth, Texas 76107

A pilot project grant application has been submitted in response to a request for applications by the National Institute of Aging. The hypothesis of the proposed study is: Structural and/or functional alteration(s) of protein kinase C (PKC) isozyme signalling pathways is a major contributing factor to the impaired T lymphocyte functioning in the elderly. A recent study (Fulop et al. Febs Lett., 1995) has indicated an altered distribution (ie. decrease in cytosol, increase in membrane fractions under resting conditions) and impaired translocation following stimulation of PKCα,δ and ε, but not PKCβ, in peripheral blood T lymphocytes from elderly donors. The aims of the proposed study are to 1) to confirm these observations and to extend the analysis to include PKCθ and η, two isoforms recently identified as being particularily prominent in T lymphocytes. 2) to accurately determine the protein content of all PKC family members present in T lymphocytes, both under resting and stimulated conditions, as well as in the cytosolic and membrane containing fractions. 3) To evaluate whether any of the PKC isozymes present in T lymphocytes from the elderly subjects are structurally modified. 4) To measure isozyme specific catalytic activity in the cytosolic and particulate fractions of resting and T cell receptor stimulated T lymphocytes from young versus elderly donors.

Abstract #5

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: McDonald, Shelley R.

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

COGNITIVE AND SENSORIMOTOR PERFORMANCE IN YOUNG APOLIPOPROTEIN E2 DEFICIENT MICE. McDonald, S.R., Smith, J., and Forster, M.J. Department of Pharmacology, UNTHSC, Fort Worth, TX 76107 and Department of Biochemical Genetics and Metabolism, The Rockefeller University, New York, NY 11021.

Epidemiological studies suggest a strong association of apolipoprotein E (apoE) with Alzheimer's disease (AD). The E4 allele is found in higher frequency among AD patients by many independent studies, and the E2 allele is found less frequently. Thus, it is postulated that E4 confers increased risk of AD; whereas, E2 is apparently protective. If apoE2 exerts an important neuroprotective function, it would be expected that the absence of E2 would be associated with neural damage and functional loss. The purpose of this study was to test this hypothesis by evaluating cognitive and sensorimotor performance of E2 deficient mice (EO) as compared with background controls (E2). Separate groups of five-month-old EO and E2 mice were obtained from the Rockefeller University and tested for cognitive and sensorimotor performance using a water maze, a T-maze, and a battery of motor skill tests. Weight and food intake were also recorded. Learning and memory capacities for spatial discrimination were determined using a place learning task in which mice were required to swim to a platform hidden in a tank of opacified water. The speed of the swimming response was significantly faster and the path length significantly longer for the E2 group. However, no differences were apparent in the amount of time to locate the platform. The ability of the mice to learn discriminated avoidance in a T-maze also did not differ between the 2 groups. Sensorimotor capabilities were measured by maximum running capacity on an accelerating rotorod, ability to tread on a suspended wire, and ability to walk on an elevated path without falling. No differences were apparent in any of the sensorimotor tests. The EO weighed significantly more than the E2, however there were no food intake differences between the groups. Generally, the current findings fail to indicate substantial effects of apoE2 deficiency in young mice. While this suggests that apoE2 is not important for maintaining CNS function in young mice, apoE2 may be important for protection against age-associated functional loss. Aged apoE2 deficient mice need to be evaluated for the effects of any age-associated declines in cognitive or sensorimotor abilities.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Douglas Krug

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow XX Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

SCOPOLAMINE PRODUCES DEFICITS IN SPATIAL MEMORY PERFORMANCE ON THE CIRCULAR PLATFORM MAZE IN YOUNG B6D2F1 MICE. Douglas E. Krug, Christine Hoover, Brian Koller, Christina Hulet, Tiffany Richardson, Rayburn Reynolds, Cassandra Beeny, Harbans Lal, and Michael J. Forster. University of North Texas Health Science Center, Fort Worth, Texas 76107-2699

Spatial memory is a biological process that is thought to diminish during aging. The circular platform maze is a task requiring the animal to identify spatial cues that locate the position of the escape alley from the maze. Scopolamine, a muscarinic cholinergic antagonist that has produced amnesia in rats and mice in prior research on learning and memory, was used to examine the potential of the circular maze to detect amnesia in the mouse. Sixteen young B6D2F1 mice were compared on 4 doses of Scopolamine (0.0, 0.16, 0.32, 0.64 mg/kg) using a Latin Square design. The circular platform was scaled to the mouse based on the design of the Barnes Circular Platform (Neurobiology of Aging, 12:47-53). During the acquisition phase, all mice were trained to escape the platform by entering the 1 hole out of 18 possible holes that had the escape alley (8 session of 3 trials). During the reversal phase, the escape location was moved to position on the opposite side of the maze (4 sessions of 3 trials). During the drug evaluation phase, the escape alley was moved to a new location each session the drug was given. Scopolamine doses were given on 4 test days (each dose being given to 4 subjects). Each animal was observed on the maze 15 minutes post injection, trials 2 and 3 followed a 10 minute ITI. Retention sessions were done 24 and 30 hours post injection. Scopolamine produced dose-dependent amnesia as measured by total number of errors at the 0.64 and 0.32 mg/kg dose. The latency to escape was also significant at the 0.64 mg/kg dose. These results suggest the circular platform maze is a useful method to evaluate spatial memory deficits in mice. Future evaluation of aged mice for age related declines is necessary. (Supported by NIH-NIA Grant A607695).

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

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ABSTRACT FORM

First Author: Shellie Ann Kolavic, DMD, MPH Geriatric Dental Fellow

Department: Medicine - Geriatrics

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow X Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

DENTAL NEEDS OF COMMUNITY- DWELLING ELDERS.

Shellie Kolavic,DMD,MPH* Geriatric Dental Fellow, University of North Texas Health Science Center, Fort Worth, TX & Baylor College of Dentistry, Dallas, TX. Janice Knebl, DO, UNT Health Science Center, Fort Worth, TX. Linda Niessen,DMD, MPH, Ingrid Guo,PhD, Gretchen Gibson,DDS and Becky DeSpain, BSDH, MS, Baylor College of Dentistry, Dallas, TX.

This study was planned to determine the oral health status of community-dwelling elders who participate in three programs sponsored by a local Area Agency on Aging. A Geriatric Dental Fellow interviewed and examined fifty-one elders aged 59-95 years. Results suggest a lack of dental care and presence of untreated oral conditions. Seventy percent reported no current access to dental care, 53% had not seen a dentist in over 10 years and 20% reported oral pain. Forty-nine percent expressed a need to see a dentist immediately. Forty-five percent reported trouble chewing food, while nearly one-third had difficulty swallowing or had a dry mouth. Abnormal soft tissues were noted in over half of the subjects. Root caries and/or mobility was observed in over half of those with at least one tooth. The results confirm the need for dental care and improved access to care for this group. This information can be used to develop oral health programs for community-dwelling low income elders. The implementation of comprehensive, integrated health care services that includes oral health care is possible because the population is currently served by a coalition of social service agencies. This study was supported by Title IIIB of the Older Americans Act.

Abstract #8

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28. A. J. Mia, Ph.D. — ENDOCYTOSIS BY CAVEOLAE AND COATED PITS IN TOAD URINARY BLADDER GRANULAR CELLS

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Bhalchandra J. Kudchodkar

Department: Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

FACTORS MODULATING SERUM PARAOXONASE ACTIVITY.
Bhalchandra J. Kudchodkar and Andras G. Lacko. Dept of Biochem and Mol Biol, UNTHSC at Fort Worth, Ft Worth, Texas 76107-2699.

Paraoxonase (POX) is a serum enzyme that hydrolyses toxic organo phosphates. In humans the enzyme shows polymorphism and recently the prevalance of low activity phenotype has been found to be significantly higher in subjects prone to atherosclerosis. These findings, combined with the observation that POX protects LDL against oxidation has led to the suggestion that POX activity may be anti atherogenic. The ultimate goal of this investigation is to study the relationship between POX and atherosclerosis. Currently, we have investigated the effects of diet and exercise on serum POX activity in humans and in experimental animals. POX activity in Baboons (15-170 nmol/ml/hr) was found to be similar to humans (18-211 nmol/ml/hr) indicating that the baboon may represent a suitable experimental model. In humans changes in serum unesterified fatty acid levels, brought about by acute exercise, were found to stimulate (at concentration < 0.5 meq/L) as well inhibit (at concentration > 0.5 meq/L) serum POX activity. Studies in rabbits indicated that a high fat, high cholesterol diet inhibited (-20 to -70%) POX activity. POX was found to be transported in serum lipoproteins, specifically in a very high density lipoprotein subfraction (VHDL, d > 1.15 g/ml) along with the enzyme lecithin cholesterol acyltransferase(LCAT). Both the levels of VHDL and LCAT correlated positively with POX activity ($p<0.05$), indicating that factors affecting the synthesis and secretion of VHDL and LCAT may also affect the synthesis and secretion of POX. POX activity correlated negatively ($p<0.05$) with the levels of lipid peroxides in plasma suggesting that lipid peroxides may inhibit POX activity or

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Pamela Brett

Department: Medicine & Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

DOT BLOT, AN ALTERNATIVE APPROACH FOR THE QUANTIFICATION OF APOLIPOPROTEINS Pamela L. Brett and Walter J. McConathy. Departments of Medicine and Biochemistry & Molecular Biology. UNTHSC, Fort Worth, Texas 76107

Changes in apolipoproteins\lipoprotein levels have been associated with many pathological conditions. Therefore their quantification can be important in the treatment and prevention of diseases. Traditionally, quantification of apolipoproteins has involved the use of ELISA or electroimmunoassays. These methodologies are time consuming, require expensive equipment, and have inherent technical problems associated with quantitating lipoproteins. The dot blot immunoassay is a variation of a micro ELISA assay. Dot blotting involves applying samples (0-2 mL) to nitrocellulose (NC) membrane using a 96-well dot blot manifold. Prior to or after application, samples can be treated (detergents, solvents) to expose masked epitopes. Addition of primary antibody is followed by secondary antibody conjugated to alkaline phosphatase. Color development occurs with BCIP/NBT with an optimal development time of 5-7 minutes. The image is scanned and stored as a computer true image file (TIF). ZeroD-Scan, (Scanalytics) generates levels automatically from the standard curve. The first apolipoprotein to be quantified using this method is apo(a). Lp(a) is an independent risk factor for coronary heart disease. Using secondary standards, sensitivity and range of this assay is from 0.4ng/dot to 3.5ng/dot. The standard curve is the expected sigmoidal curve. Preliminary results for other apolipoproteins (AI, AII, B, CI, CII, CIII, D and E) yielded a similar sigmoidal response. The dot blot method is time efficient, results can be easily obtained in eight hours. Much of the needed equipment is standard to many laboratories, except for the dot blot manifold, scanner and the computer software program. Therefore this sensitive method can be used in many laboratories and has general applicability for all antigens, including detergent solubilized antigens such as membrane proteins.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

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ABSTRACT FORM

First Author: Bhalchandra J. Kudchodkar

Department: Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

ATTENUATION OF ATHEROSCLEROSIS IN CHOLESTEROL FED RABBITS BY HYPERBARIC OXYGEN TREATMENT. **Bhalchandra J. Kudchodkar and Judy R. Wilson* Depts of Biochemistry & Molecular Biology and Integrative Physiology.*, UNTHSC, Fort Worth, Texas 76107-2699.**

Oxidative modification of lipids in plasma lipoproteins and tissues is believed to be important in the genesis of atherosclerosis. Since hyperoxia is known to promote lipid oxidation, it was felt important to evaluate the effect of hyperbaric oxygen (HBO) on the development of atherosclerosis because of the expanding use of this treatment in clinical and sports medicine. New Zealand white rabbits were randomly divided into three groups (Gr.). Gr. I (n=3) was fed chow while Gr. II (n=5) and Gr. III (n=6) were fed chow supplemented with 10% coconut oil + 1% cholesterol. In addition, rabbits in Gr. III received 90 minutes of 100% 0_2 at 2.5 ATA, 5 days/week. In Gr. II 3/5 animals died between 8 and 9 weeks while only 1/6 animals in Gr. III died at the end of 10 weeks at which time all animals were sacrificed and aortas were removed. Atherosclerosis was assessed in sections taken from the aortic arch and by determining cholesterol content of the arch, abdominal and thoracic segments of the aorta. Massive atherosclerotic lesions were seen in both the animals in Gr. II. On the other hand, in Gr. III animals, atherosclerotic lesions were absent in three, minimal in one and moderate in the other. Aortic cholesterol content (Gr. II vs Gr. III: mg/g) was Arch: 17.0 vs 5.8; Abdominal 4.3 vs 1.9 and Thoracic: 7.9 vs 2.7. The effect was independent of serum and lipoprotein cholesterol which were elevated to the same extent in both groups. Serum and tissue levels of TBARS in the HBO treated Gr. III were lower compared to Gr. II but were higher compared to Gr. I. These results indicate that HBO treatment was effective in suppressing atherosclerosis especially in abdominal and thoracic aortic segments.

Abstract #11

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Leslie Napier

Department: Physiology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ALTERATIONS IN AUTONOMIC FUNCTION AND MYOCARDIAL ENKEPHALINS IN MORPHINE-ADDICTED DOGS

L.D. Napier, Z. Mateo, D.A. Yoshishige, T.S. Noecker, B.A. Barron, J.L. Caffrey. University of North Texas Health Science Center, Dept. of Physiology, Fort Worth, Texas 76107.

Opiate abuse continues to be a significant public health concern. Post-mortem studies have revealed substantial cardiovascular abnormalities in opiate addicts. Endogenous opioids increase in some types of heart disease and may be altered as a result of opiate addiction. Since little information is available regarding the cardiovascular adaptations to chronic opiate administration, morphine pellets (75 mg) were implanted subcutaneously in dogs. Plasma morphine rose through Day 3 and remained relatively stable thereafter. After 7 days, dogs were anesthetized for cardiovascular evaluation. Hypertensive responses to naloxone administration (an average of 35.6 mmHg) served to verify drug dependence. The bradycardic response to vagal stimulation was significantly reduced in addicted dogs when compared to controls. The arterial pressor response to bilateral carotid occlusion (BCO) appeared to be blunted. Naloxone did not reverse the reduced responsiveness in addicted animals and acute morphine did not suppress the response in controls indicating that the attenuated responses were due to chronic exposure to morphine and not to its acute influence. Following the experiments, the heart tissue was homogenized. Enkephalins were extracted, separated by molecular weight and assayed with antibodies specific for C-terminal met-enkephalin (ME) and met-enkephalin-arg-phe (MEAP) sequences. ME-immunoreactivity was unchanged as a result of addiction but immunoreactivity eluting with MEAP and the N-terminal extended precursor, Peptide-B, was decreased in addicted animals compared to controls. The results indicate that chronic morphine alters autonomic control of the heart and circulation. Parallel reductions in cardiac enkephalins suggest that endogenous opioids contribute to this adaptation. Technical concerns associated with repeated pellet implantation during longer protocols have led us to begin using ambulatory infusion pumps to deliver morphine. This method provides for better control of the dose administered and early results are promising with plasma morphine reaching the desired steady state within eight hours. This method will be used to evaluate the cholinergic mechanisms responsible for the alterations in autonomic function.

Abstract #12

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Geoffrey Kline

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ISCHEMIA-INDUCED α-ADRENERGIC MEDIATED CORONARY CONSTRICTOR TONE DURING SUBMAXIMAL EXERCISE IN DOGS

Geoffrey Kline and Patricia A. Gwirtz, Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, Texas 76107.

Under normal coronary flow conditions a coronary α_1-adrenergic mediated constrictor tone is small during mild levels of exercise. This study examined the hypothesis: a coronary artery stenosis during mild exercise results in myocardial ischemia and exacerbates the coronary α_1-constrictor tone. Seven dogs were chronically instrumented with a flow probe and occluder on the left circumflex coronary artery. The selective α_1-adrenergic antagonist, prazosin (0.5 mg, i.c.) Was given during exercise at 6.4 kph, 4% incline to remove the constrictor tone while the dogs were running. Coronary blood flow (CBF) increased by 25±3% during exercise. In the absence of a coronary artery stenosis, CBF increased only 4±3% after prazosin. When CBF was prevented from increasing above baseline resting flow levels by partial inflation of the occluder, CBF increased by 23±4% after prazosin. These data suggest that an ischemia-induced increase in the sympathetic adrenergic coronary constrictor tone occurred. (Supported by NIH HL-34172 and HL-29232, and a grant from the Texas Affiliate of the American Heart Association)

Abstract #13

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Kristin Bryant

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ACTIVATED INTRAMUSCULAR MECHANORECEPTORS (IMR) INHIBIT HUMAN CAROTID BAROREFLEX (CBR) FUNCTION.

K.H. Bryant, I.P. Reese, X. Shi, and P.B. Raven. Departments of Integrative Physiology and Medicine, University of North Texas Health Science Center at Fort Worth, Texas.

The aim of this study was to differentiate whether lower body positive pressure (LBPP) induced diminution of CBR was associated with the activated IMR or the increased central venous pressure (CVP). Heart rate (HR) and mean arterial pressure (MAP) responses were assessed using a train of pulsatile neck pressure and suction (+40 to -65 torr) in 7 normal healthy male volunteers (age:25±1yr). The maximal gains of CBR-HR and CBR-MAP were compared during supine rest, LBPP 30 torr, and volume expansion (VE) with 6% dextran in saline by increasing 5.8±0.2% (3.6±0.2 ml/kg, VE-I) and 9.5±0.3% (6.1±0.3 ml/kg, VE-II) of total blood volume, respectively (see table). Though CVP was similarly increased

	CVP (mmHg)	HR (bpm)	MAP (mmHg)	CBR-HR (bpm/mmHg)	CBR-MAP (mmHg/mmHg)
Baseline	6.6±0.8	57±3	93±4	0.455±0.078	0.313±0.037
LBPP	8.1±0.5*	57±3	95±4	0.272±0.055*	0.235±0.026*
VE-I	8.4±0.3*	56±2	88±3	0.424±0.090	0.360±0.122
VE-II	10.2±0.5*	59±4	97±3	0.343±0.084*	0.197±0.063

*** indicates a significant change from the baseline.**

by LBPP and VE-I; LBPP, not VE-I, significantly decreased CBR, indicating that the LBPP induced CVP increase could not exclusively explain the diminished CBR. We concluded that an activated IMR resulted in a reduced CBR gain.

(Supported by AHA-TX Affiliate Grant-in-Aid 93R-146 and NIH grant #HL45547)

Abstract #14

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Patrick Hayes

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student ✓ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ELIMINATION OF POST-EXERCISE HYPOTENSION IMPAIRS PLASMA VOLUME RECOVERY.

Patrick M.Hayes, Jason C.Lucas, Peter B.Raven, H.Bart Robbins, and Xiangrong Shi. Department of Integrative Physiology, UNT Health Science Center, Fort Worth, TX 76107.

The aim of this study was to test the hypothesis that PV recovery following exercise was facilitated by post-exercise hypotension. Six volunteers (age: 27.5±1.2 years) performed 2 bouts of cycling exercise (2.0±0.2 watts/kg) for 60-min (≥1 week apart) followed by 90-min seated recovery without intervention (Exp.1) or with phenylephrine infusion (PE, 60 - 90 μg/min to maintain normotension at the baseline) started at the 10th-min through the end of recovery (Exp.2). At time 0, 5, 15, 30, 45 and 60-min of exercise, and at 5, 15, 30, 45, 60 and 90-min of recovery, blood samples were taken for the analyses of hematocrit (Hct, by Microhematocrit), hemoglobin (Hb, by Co-Oximeter), total plasma protein (TP, by Refractometry), and plasma albumin (PA, Colormetric method). PV was determined using Evans blue dye dilution method prior to exercise and ΔPV was calculated from the changes in Hb and Hct during the experiments. There was no difference in any baseline variable between the two experiments (see table):

Exp.	Wt. (kg)	PV (l)	Hct (%)	Hb (g/dl)	TP (g/dl)	PA (g/dl)
1	82.2±2.9	4.00±0.26	42.7±0.8	14.1±0.3	7.1±0.2	4.4±0.1
2	83.6±4.0	3.95±0.31	42.2±1.3	13.9±0.4	7.0±0.1	4.3±0.1

Started at the 30th-min of recovery, ΔPV approached the baseline in Exp.1, -1.8±1.2% (P=0.18), which was significantly different from that in Exp.2, -6.2±1.0% (P=0.01). However, ΔTP content was +0.2±4.6g and +9.5± 3.5g with and without PE, respectively. We concluded that post-exercise gain in TP was impaired by PE during recovery from acute exercise and that recovery of PV was associated with post-exercise hypotension.

Partially supported by AHA-TX Affiliate Grant-in-Aid 93R-146

Abstract #15

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Patrick Hayes

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student ✓ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

INCREASE IN PLASMA PROTEIN DURING RECOVERY FROM EXERCISE.

Patrick M.Hayes, J.C.Lucas, H.Bart Robbins, Xiangrong Shi, and Peter B.Raven. Department of Integrative Physiology, UNT Health Science Center, Fort Worth, TX 76107.

The aim of this study was to test the hypothesis that there was a net gain of plasma protein following one bout of exercise. Six volunteers (age: 27.5±1.2yrs, wt.: 80.5±3.2kg, ht.: 180±3cm) performed cycling exercise for 60 minutes at 65% of their individual maximal aerobic capacity (power output: 2.0±0.2 watts/kg) followed by 90 minutes of recovery in the seated body position of the exercise. Before exercise (≥60-min seated rest), and at 5, 15, 30, 45 and 60 minutes of exercise, and at 5, 15, 30, 45, 60 and 90 minutes of recovery, blood samples were taken for the analyses of hematocrit (Hct, by Microhematocrit), hemoglobin (Hb, by Co-Oximeter), total plasma protein (TP, by Refractometry), and plasma albumin (PA, Colormetric method). Plasma volume (PV, 4.07±0.18L) was determined using Evans blue dye dilution method prior to exercise and the change in PV was calculated from the changes in Hb and Hct during the experiment. At the end of 60-min of exercise, PV was significantly decreased by -14.5 ±2.4% accompanied by significant increases in TP (+12.9±2.7%) and PA (+16.5±3.8%). The increased TP and PA were explained by the exercise induced hemoconcentration. At the end of recovery, ΔPV was -2.1±2.4% (P=0.42). However, TP and PA remained above baseline, TP: +6.6 ±1.9% (P=0.045) and PA: +7.9±2.7% (P=0.061). We conclude that moderate prolonged exercise stimulates a gain of plasma proteins during the recovery from exercise.

Partially supported by AHA-TX Affiliate Grant-in-Aid 93R-146

Abstract #16

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Ross Querry

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

COMPARISON OF NON-INVASIVE VS. INVASIVE MEASUREMENTS OF ARTERIAL BLOOD PRESSURE DURING PROGRESSIVE DYNAMIC EXERCISE TO FATIGUE.

R.G. Querry, K.M. Gallagher, I.P. Reese, K.H. Bryant and P.B. Raven, FACSM. Dept. of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, TX. 76107

The purpose of the study was to compare systolic arterial pressures (SAP), mean arterial pressures (MAP), and diastolic arterial pressures (DAP) as measured non-invasively by a photoplethysmographic method (Ohmeda Finapres 2300) to pressures measured invasively via radial artery cannula during progressive dynamic exercise to fatigue. Pressures were recorded beat-to-beat on line using both methods simultaneously in four males age 25.2 $\pm$ 2.9 yrs. during four experimental conditions of exercise: a) control - exercise with no intervention; b) exercise with thigh cuff inflation to 90 mmHg; c) exercise with application of lower body positive pressure (LBPP) to 45 mmHg; and d) exercise with thigh cuff inflation + LBPP. The regression equations and coefficient of determination (R^2) on trials where Finapres vs. arterial line placement met established criteria for accurate data collection for the Control condition are as follows: (SAP) $y=1.18x-19.65$, $R^2=0.96$, (MAP) $y=0.99x-0.41$ $R^2=0.95$, and (DAP) $y=1.09x-3.6$, $R^2=0.81$. Although SAP indicated a higher intercept, no significant differences were found with unpaired t-tests. Findings were similar in the experimental conditions. These findings demonstrate that the Finapres can provide an accurate absolute measurement of beat-to-beat changes in systolic, mean, and diastolic arterial pressures during progressive dynamic exercise to fatigue and during conditions of heightened sympathetic nervous system activity. We conclude that the Finapres can be used as a non-invasive substitute for invasive arterial lines to decrease subject risk during physiological experimentation without losing the fidelity of the data as long as the established criteria for Finapres measurements are met. (Supported in part by NIH HL45547.)

Abstract #17

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Scott Alan Smith

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

INTERACTION OF MUSCLE ERGORECEPTORS WITH CENTRAL COMMAND DURING PROGRESSIVE WORKLOAD DYNAMIC EXERCISE TO MAXIMUM IN HUMANS S.A. Smith, K.M. Gallagher, R.G. Querry, K.H. Bryant and P.B. Raven, FACSM Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, TX 76107

Six subjects, mean age 26.8 ± 4.3 yrs, performed an increasing workload (WL) bicycle exercise protocol to maximum to investigate the interaction of central command and muscle ergoreceptors. Measures of central command included electromyographic activity (EMG in μ volts) of the *m. rectus femoris*, heart rate (HR in bpm), and ratings of perceived exertion of leg effort (RPE_L in au.). Each subject performed four bouts of exercise: control-exercise with no intervention; exercise with thigh cuff inflation to 90 mmHg; exercise with application of lower body positive pressure (LBPP) to 45 mmHg; and exercise with combined thigh cuff inflation and LBPP. Mean results are presented below:

WL	Control			Cuffs			LBPP			Cuffs + LBPP		
	EMG	HR	RPE_L	EMG	HR	RPE_L	EMG	HR	RPE_L	EMG	HR	RPE_L
Rest	12	65	-----	11	71	-----	8	62	-----	7	61	-----
100W	35	97	10	55	106	14*	65*	106	13*	43	102	14*
200W	66	128	15	87	134	17	121*	133	16	79	136	18
Max	106	171	18	110	160	19	164	155	19	129	153	19

2 factor ANOVA significance from control is indicated by an * when $p<0.05$

We conclude that activation of the muscle ergoreceptors occurs by recruitment of additional motor units during progressive dynamic resistance exercise as a result of increased central command. This was reflected by significant increases in EMG activity and RPE_L as well as a trend for an increase in HR.

Supported in part by NIH HL45547.

Abstract #18

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Steve Stuewe

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

EXERCISE TRAINING ENHANCES GLYCOLYTIC AND OXIDATIVE ENZYMES IN CANINE MYOCARDIUM. S. Stuewe, P.A. Gwirtz, and R.T. Mallet, Dept. of Integrative Physiology, Univ. North Texas Health Science Center, Fort Worth, Texas 76107-2699

Epidemiological evidence indicates that endurance exercise training renders the myocardium resistant to ischemic injury. However, the mechanisms for exercise-induced cardioprotection are unknown. Exercise training increases activities of glycolytic and oxidative enzymes in skeletal muscle. The goal of this study was to determine whether training can also enhance the metabolic capabilities of cardiac muscle. Mongrel canines were subjected to 9 wk treadmill training; sedentary dogs were cage-rested for 4 wk. Stop-frozen samples of left (LV) and right (RV) ventricular myocardium were obtained from pentobarbital-anesthetized trained (Trn) and sedentary (Sed) dogs. Enzymes (HK: hexokinase; PFK: phospho-fructokinase; GAPDH: glyceraldehyde 3-phosphate dehydrogenase; PK: pyruvate kinase; LDH: lactate dehydrogenase; CS: citrate synthase; α-KGDH: α-ketoglutarate dehydrogenase; MDH: malate dehydrogenase; 3-HADH: 3-hydroxyacyl CoA dehydrogenase) were extracted in phosphate buffer and assayed at 38°C. The table reports enzyme activities (U · mg protein^{-1}); data are means ± SE, $n = 6$ (*: $P < 0.05$ *vs.* sedentary).

Enzyme	LV Sed	LV Trn	RV Sed	RV Trn
HK	0.12 ± 0.03	0.14 ± 0.05	0.10 ± 0.02	0.13 ± 0.04
PFK	0.66 ± 0.06	0.77 ± 0.16	0.50 ± 0.08	0.50 ± 0.09
GAPDH	4.2 ± 0.35	6.3 ± 0.5*	4.5 ± 0.4	6.0 ± 0.4*
PK	2.7 ± 0.5	4.7 ± 0.8*	2.6 ± 0.4	3.3 ± 0.3
LDH	8.3 ± 0.5	9.6 ± 1.2	7.0 ± 0.4	8.6 ± 0.7
CS	0.43 ± 0.05	0.82 ± 0.10*	0.49 ± 0.09	0.57 ± 0.10
α-KGDH	0.022 ± 0.001	0.026 ± 0.006	0.017 ± 0.003	0.030 ± 0.006
MDH	6.2 ± 0.7	8.3 ± 1.8	5.6 ± 0.5	6.3 ± 0.8
3-HADH	0.60 ± 0.05	1.06 ± 0.12*	0.53 ± 0.08	0.87 ± 0.13

Exercise training increased GAPDH activity in both ventricles. During ischemia, GAPDH is the primary rate controlling glycolytic reaction. Thus, increased GAPDH activity could support enhanced glycolysis in trained myocardium. Citrate synthase, which catalyzes carbon entry into the TCA cycle, and 3-HADH, a rate-controlling reaction in fatty acid β-oxidation, were also increased in trained LV; thus, training enhances myocardial oxidative capacity. (NIH support: HL 50441, HL 34172)

Abstract #19

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Ying Yu

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ELEVATED RIGHT ATRIAL PRESSURE DOES NOT REDUCE FLOW TO COLLATERAL-DEPENDENT CANINE MYOCARDIUM.

Ying Yu, Hong-Wei Wang, Masao Itoya, H. Fred Downey.
Department of Integrative Physiology, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX 76107.

Coronary venous pressure (CVP) may become substantially elevated during right ventricular failure, and the resulting decrease in the perfusion pressure gradient might impair coronary blood flow, especially to ischemic myocardium. The effects of elevated CVP on coronary collateral flow are controversial. Eng and Kirk (*Circ. Res.* 55:10-17,1984) described waterfalls in the coronary collateral circulation that would obviate increases in coronary venous pressure up to 20 mmHg. Manor et al. (*Am. J. Physiol.* 267:H1151-H1156, 1994) reported reduced collateral flow as right atrial pressure (RAP) was increased to 23 mmHg. Both findings were based on indirect estimates of collateral flow by the retrograde flow technique. We measured flow to normal and acutely ischemic myocardium directly with tracer microspheres during control (C, RAP=4.2±1.6(SE) mmHg) and elevated CVP (E, RAP=23.4±1.2 mmHg). RAP was elevated by constricting the pulmonary artery with pump controlled venous return to raise right heart pressures in 5 anesthetized dogs with acute LAD occlusion. Regional, transmural* blood flow (ml/min/g):

	Collateral-dependant Region			Normal Region		
	Epi	Mid	Endo	Epi	Mid	Endo
C	.21±.05	.12±.03	.16±.04	.82±.05	.92±.06	1.0±.1
E	.27±.04	.15±.01	.18±.04	1.0±.13	1.3±.3	1.3±.2

*Epi=Epicardial; Mid=Midmyocardial; Endo=Endocardial.

Raising RAP to 23 mmHg does not impair blood flow to acutely ischemic or normal canine myocardium. (Supported by NIH HL35027 and Tex. Adv. Res. Prog. 9768.)

Abstract #20

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Gerson Rocha, M.D., Ph.D.

Department: Department of Integrative Physiology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

HYPEROSMOLAR STRESS-INDUCED VASOMOTION IN SMALL ARTERIES

G.M. Rocha, P.A. Gwirtz and P.B. Raven, Department of Integrative Physiology, University of North Texas Health Science Center, Fort Worth, Texas 76107.

This study examined the hyperosmolar effect of impermeant and permeant osmolytes on vasomotion of mice tail arteries approximately 300µm in diameter. The mice tail arteries were isolated, cannulated and pressurized to 40 mmHg without intraluminal flow. *In vitro* measurements of the microarterial internal diameter were made with a video dimension analyzer system. Increases in osmolarity from 300 to 500 mOsm were produced by adding the impermeant osmolyte, D-mannitol or the permeant osmolyte, NaCl to the vessel bath. Increasing the hyperosmolar state with both NaCl and mannitol in a concentration-dependent manner induced significant constrictive vasomotion in endothelium-intact arteries. Hyperosmolarity induced by NaCl resulted in a lesser and later vasoconstrictive response in comparison to the response to mannitol. Therefore, we suggest that a Na+ and/or Cl- vascular smooth muscle cell transport mechanism exists and is affects the modulation of myogenic basal tone during hyperosmolar conditions.
(Supported by NIH HL-45547, HL-34172 and HL-29232)

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: J. Storm Shirley

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ACTIVATION OF CAM KINASE II ACTIVITY BY BETA ADRENORECEPTOR AGONIST IN CANINE AORTA FOLLOWING CHRONIC EXERCISE. J. S. Shirley, Y. Gong, W. W. Daniels, P. B. Raven and S.R. Grant, Departments of Integrative Physiology, and Biochemistry and Molecular Biology, UNTHSC at Fort Worth 76107-2699.

Recent studies in chronically exercised canines have shown that endurance training leads to increased vascular (arterial) sensitivity to alpha and beta adrenergic receptor agonist. In response to dynamic exercise, arterial smooth muscle cells apparently undergo extensive membrane remodeling. As a first step in identifying cellular mechanism(s) operative in the arterial myocyte activity, we have monitored changes in smooth muscle myocyte CaM kinase II activity. We have evaluated the effects of myocyte exposure to a dedicated beta-1 agonist, dobutamine (DOB) and its antagonist, metoprolol (MET) and correlated them to CaM kinase II activity in both cage-rested and endurance-trained canines. Similar studies have been performed for the beta-2 agonist/antagonist pair, isopreterenol (ISOP) and ICI-118551.

Results from this study indicate that β_1 agonists strongly activate and β_1 antagonist block CaM kinase II activation in aortic smooth muscle cells. The activation curves for cage-rested and endurance-trained animals were significantly different with respect to the activation and de-activation response. We have identified CaM kinase II as part on a nuclear signaling pathway which negatively controls growth regulated gene expression. We conclude that beta-1 adrenergic receptor signaling activates CaM kinase II in a calcium sensitive nuclear signaling pathway in vascular smooth muscle.

(The work was supported in part by Am. Heart TX. Affiliate Grant 95G-155 and an NIH Grant HL 45547.)

Abstract #22

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: MARIA ISABEL TALDO, MD

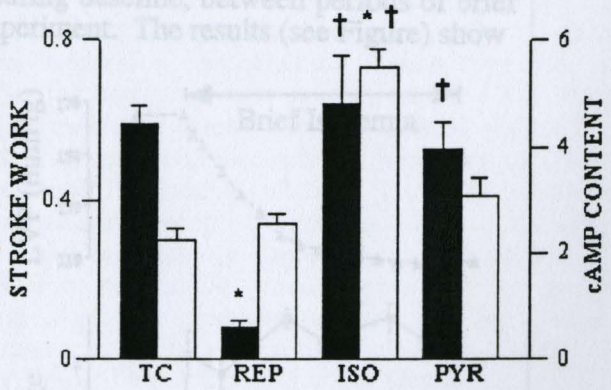
Department: INTEGRATIVE PHYSIOLOGY

Undergraduate or Medical Student___ Graduate Student__X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

PYRUVATE-ENHANCEMENT OF POST-ISCHEMIC FUNCTION IN ISOLATED WORKING GUINEA PIG HEARTS IS NOT MEDIATED BY CYCLIC AMP. Isabel Tejero-Taldo, Jie Sun, James L. Caffrey, Robert T. Mallet. Dept. Integrative Physiology, Univ. N. Tex. Hlth. Sci. Ctr., Ft. Worth, Texas 76107.

This study tested the hypothesis that pyruvate-enhancement of post-ischemic cardiac function, like that of catecholamines, is mediated by cyclic AMP (cAMP). Isolated working guinea-pig hearts, perfused with 10 mM glucose-fortified Krebs-Henseleit, were subjected to 45 min low flow ischemia (coronary flow 20% of baseline) , then reperfused for 35 min to produce reversible dysfunction (stunning). Four groups of 6 hearts were studied: 100 min nonischemic time control (TC); reperfusion without intervention (REP), or treatment with 50 nM isoproterenol (ISO) or 5 mM pyruvate (PYR) at 15-35 min reperfusion. cAMP was measured in frozen myocardium by radio-immunoassay. **Figure:** Cardiac function (left ventricular stroke work, mJ/g wet; filled bars) and cAMP content (nmol/g dry; open bars) were measured at 35 min reperfusion (*: P < 0.05 *vs.* TC; †: P < 0.05 *vs.* REP). In REP, cardiac function was severely impaired, but cAMP was unchanged. As expected, ISO stimulated function and increased cAMP content. PYR also restored function to TC level, but did not increase cAMP content. **Conclusions:** Cardiac stunning is not acompanied by decreased cAMP content. PYR enhancement of post-ischemic ventricular performance is independent of cAMP. (NIH support: HL 50441)



Abstract #23

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Miao-Xiang He, M.D.

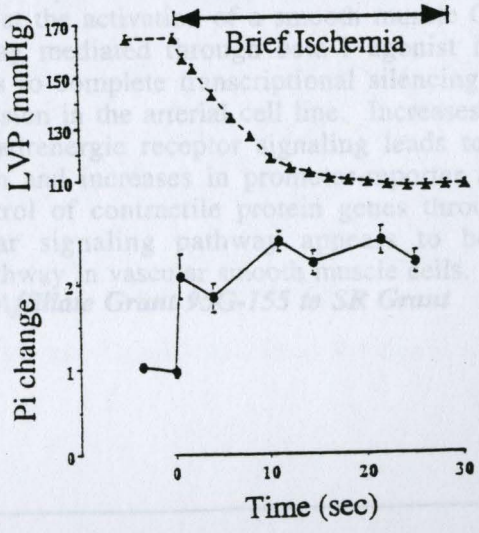
Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

RELATIONSHIP BETWEEN MYOCARDIAL CYTOSOLIC INORGANIC PHOSPHATE AND CONTRACTILE FUNCTION DURING ISCHEMIA IN RAT HEART. M.-X. He, S. Wang and H. F. Downey. Dept. Integrat. Physiol., Univ. N. Tex. Hlth. Sci. Ctr., Ft. Worth, TX 76107.

Myocardium deceases contractile function immediately at the onset of ischemia, to diminish further ischemic injury. This intrinsic protective mechanism which actively downregulates myocardial contractile function in the face of decreased coronary blood flow is poorly understood. Myocardial cytosolic inorganic phosphate (Pi) increases rapidly whenever energy demand exceeds energy supply, and increase in Pi depresses myocardial contractile force in vitro. To define whether Pi plays important roles in the downregulation of contractile function, the relationship between Pi and left ventricular pressure (LVP) of isolated rat hearts was determined during ischemia. ^{31}P-NMR spectroscopy was used to detect the rapid change of Pi, while LVP, an index of myocardial contractile force, was simultaneously recorded. High time resolution of NMR spectroscopy (0.5 sec) was achieved by averaging data collected during 40 repetitive periods of brief ischemia in each experiment. Each brief ischemia was induced by decreasing coronary flow to 30% of baseline abruptly for 30 sec followed by 3 min of reperfusion. The stability of the preparation was verified by unchanged hemodynamic and energetic indexes, which were measured during baseline, between periods of brief ischemia, and at the end of the experiment. The results (see Figure) show that Pi increased twofold within 0.5 sec at the onset of ischemia and reached an elevated plateau at 11 sec. LVP decreased rapidly as Pi increased and reached a lower steady level while Pi remained at its plateau. ATP did not change during brief ischemia. The results suggest that Pi may initiate the downregulation of myocardial contractile function at the onset of ischemia. (Supported by Faculty Research Grant, and NIH Grant HL35027)



Abstract #24

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Y. Gong

Department: Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff_X_

Read instructions and fit abstract inside the space given below:

A CALCIUM SENSITIVE NUCLEAR SIGNALING PATHWAY SILENCES SKELETAL AND CARDIAC ACTIN GENE EXPRESSION IN ARTERIAL PAC-1 CELLS. Y. Gong, H. Zeng, W. Daniels, R. Easom, & S.R. Grant, Dept of Biochem. & Mol. Biol., UNTHSC at Ft. Worth. 76107. The pulmonary arterial rat smooth muscle cell line, PAC-1, was used as a model to examine a potential role of calcium-sensitive protein kinases and phosphatases in regulating the induction of the contractile protein genes mediated through neural (adrenoreceptor) signaling. Pac-1 myocytes supplemented with phenylephrine (PE) following transfection (8-24 h) of skeletal and cardiac actin promoter-reporter constructs, showed elevated levels of promoter activity when compared to cells cultured in the absence of PE. Prazosin, a dedicated α1-antagonist, blocked the transcriptional induction mediated through PE. Exposure of PAC-1 cells to Dobutamine, a dedicated β1 agonist, resulted in the complete silencing of promoter-reporter activity for both of the actin promoter-reporter constructs. Over-expression of exogenous CaM kinase II isoforms co-transfected with the reporter vector constructs resulted in complete transcriptional silencing of PE-induced promoter reporter activity of both skeletal and cardiac actin constructs. Transfection of a constitutively active, mutant gene form of the calcium-dependent phosphatase 2B, calcineurin, increased the luciferase-based reporter activity for both of the actin genes. Exposure of PE-induced PAC-1 cells to either FK-506, a potent selective inhibitor of calcineurin, or KN-62, a selective inhibitor of CaM kinase II, resulted in greater skeletal and cardiac promoter reporter activity than observed by PE alone. Moreover, super-induction of the actin reporter activity was also observed in both KN-62 and FK-506-treated cells in the absence of PE exposure suggesting that promoter-reporter silencing may be mediated through a transcriptional repression mechanism. Taken together, results presented here suggest that the activation of a smooth muscle Ca^{2+}-sensitive nuclear signaling pathway mediated through beta-1 agonist induced CaM kinase II activation leads to complete transcriptional silencing of skeletal & cardiac actin gene expression in the arterial cell line. Increases in calcineurin activity through beta-2 adrenergic receptor signaling leads to inhibition of CaM kinase II activation and increases in promoter-reporter activity. Beta adrenergic receptor control of contractile protein genes through this novel calium sensitive nuclear signaling pathway appears to be a dominate transcriptional control pathway in vascular smooth muscle cells.

support: Am. Heart TX. Affiliate Grant 95G-155 to SR Grant

Abstract #25

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: H. Zeng

Department: Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff X

Read instructions and fit abstract inside the space given below:

A CALCIUM-SENSITIVE NUCLEAR SIGNALING PATHWAY SILENCES CARDIAC ATRIAL NATRIURETIC FACTOR GENE EXPRESSION. **H. Zeng, Y. Gong, W. Daniels, R. Easom, & and S.R. Grant, Dept. of Biochemistry & Mol. Biol. UNTHSC @ Ft. Worth**

A cultured myocardial cell model was used to examine a potential role of calcium-sensitive cardiac protein kinases and phosphatases in regulating the induction of the atrial natriuretic factor (ANF) gene mediated through adrenoreceptor signaling. In primary culture, rat neonate cardiomyocytes supplemented with phenylephrine (PE) following transfection (24 h) with ANF promoter-reporter constructs, showed elevated levels of promoter activity when compared to cardiomyocytes cultured in the absence of PE. Prazosin, a dedicated α1-antagonist, blocked the transcriptional induction mediated through PE. Exposure of neonate cardiomyocytes to Dobutamine, a dedicated β1 agonist, resulted in decreased ANF promoter reporter activity. Over-expression of an exogenous, constitutively active mutant gene form of CaM kinase II co-transfected with the ANF reporter gene resulted in complete silencing of PE-induced reporter activity for each of three nested deletion cardiac ANF promoter constructs. Transfection of a constitutively active, mutant gene form of the calcium-dependent phosphatase 2B, calcineurin, also transcriptionally activated ANF reporter activity. Exposure of cardiomyocytes to FK-506, a potent selective inhibitor of calcineurin, or KN-62, a selective inhibitor of CaM kinase II, resulted in greater ANF promoter reporter activity than observed by PE alone. Moreover, inhibitor induced super-induction of ANF promoter-reporter activity was also observed cultures treated in the absence of PE exposure. The results suggest that promoter-reporter silencing may be mediated through a transcriptional repression mechanism. This hypothesis is strengthened by Northern analysis in, KN-62, FK506 and DOB exposed cardiomyocytes cultures for changes in cardiac ANF message pools. Our results suggest that the activation of a cardiac Ca^{2+}-sensitive nuclear signaling pathway mediated through a beta-1 adrenergic receptor mediated CaM kinase II activation event results in complete ANF transcriptional silencing and that a calcineurin activation process leads to transcriptional induction probably through beta-2 adrenergic receptor signaling and inhibition of beta-1 induced CaM kinase II activation. This new model of beta adrenergic receptor mediated control of ANF transcription may play an important role in the transcriptional control of other cardiac genes induced during work overload, or physiological hypertrophy.

support: Am. Heart TX. Affiliate Grant 95G-155 to S.R.Grant

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Adnan Dibas

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow X Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

MECHANISM OF VASOPRESSIN-INDUCED INCREASE IN INTRACELLULAR Ca^{2+} ($[Ca^{2+}]_i$) IN LLC-PK_1 PORCINE KIDNEY CELLS.

Adnan Dibas and Thomas Yorio

Department of Pharmacology, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX. 76107.

Vasopressin induces an increase in $[Ca^{2+}]_i$, however, the mechanism is not known. In this report, we provide evidence for the involvement of a mobilization of intracellular Ca^{2+} as well as the influx of extracellular Ca^{2+} in vasopressin-induced calcium effects. Nifedipine (20 μM), a potent inhibitor of L-type Ca^{2+}-channels abolished vasopressin-induced increase in $[Ca^{2+}]_i$. Thapsigargin (10 μM), an inhibitor of Ca^{2+}-ATPase to deplete intracellular Ca^{2+}-stores, also abolished vasopressin-induced increase in $[Ca^{2+}]_i$. A similar dose of vasopressin failed to generate inositol-1,4,5-trisphosphate (IP_3). By contrast, vasopressin increased the levels of cyclic adenosine monophosphate (cAMP). Surprisingly, the addition of dibutryl cAMP, a membrane-permeable analog of cAMP, induced an increase in $[Ca^{2+}]_i$ and the subsequent addition of vasopressin failed to induce an increase in $[Ca^{2+}]_i$. This result suggested that vasopressin-induced effects were mediated in part by cAMP and possibly the activation of cAMP-dependent protein kinase A (PKA). This was further confirmed by the ability of H-7, a potent inhibitor of PKA, to abolish both cAMP and vasopressin-induced increases in $[Ca^{2+}]_i$. In conclusion, the results suggest that vasopressin-induced increase in $[Ca^{2+}]_i$ is mediated in part by PKA and involves the activation of L-type Ca^{2+} channels which mediates the influx of extracellular Ca^{2+}, and a mobilization of intracellular Ca^{2+} through an IP_3-insensitive store.

Abstract #27

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: A. J. Mia, Ph.D.

Department: Jarvis Christian College

Undergraduate Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

ENDOCYTOSIS BY CAVEOLAE AND COATED PITS IN TOAD URINARY BLADDER GRANULAR CELLS. A. J. Mia[1], L. X. Oakford[2] and T. Yorio[2]. [1]Jarvis Christian College, Hawkins, TX 75765 and [2]UNT Health Science Center at Fort Worth, TX 76107.

Toad urinary bladder has been in use for many years as renal membrane model for experimental studies of transmembrane osmotic water flow mediated by vasopressin. Though many fine structural studies were made on granular cells, little if any was known about the presence of caveolae in these cells. During our previous investigation on the fine structure of toad urinary bladder epithelia involving water transport studies, we reported for the first time the presence of coated vesicles (Mia et al., 1994, Tissue & Cell, 26:189-201) in granular cells. During our current investigation, a large concentration of flask-shaped caveolae and coated pits and vesicles in toad urinary bladder granular cells were identified. Both caveolae and coated pits may originate from the same basal plasmalemma by inward invaginations. Many of the caveolae and clathrin coated pits may have been released into the cytosol as they are often seen deep into the cytosol. Caveolae appear to contain light coatings around the membrane component of the caveolar flask. Most commonly caveolae occur as single individual units but at times they may form clusters, which may very likely represent to be the sectional views of the caveolae in cells that occur beneath the level of the section. In addition to clathrin coated pits and vesicles and caveolae, multivesicular bodies within the cytoplasm of the granular cells are often encountered. The multivesicular bodies as seen in the ultrathin sections suggest that they also may contain a number of caveolae. The role of caveolae, multivesicular bodies and the clathrin coated pits and vesicles in toad urinary bladder epithelial tissues is uncertain. Additional experimental studies are needed in order to determine if these vesicles play any role in ADH receptor-mediated endocytosis in toad urinary bladder granular epithelia. (Supported by grants DAMD17-95-C-5086 and GM/DK48114.)

Abstract #28

CLINICAL

29.	Jill Peterson	FUNCTION, ELASTIC PROPERTIES, AND MICROSTRUCTURE OF HUMAN CIRCUMORBITAL BONE
30.	S. D. Dimitrijevich, Ph.D.	THE EFFECT OF MICROGRAVITY ON HUMAN TISSUE. I. ASSEMBLY OF THE HUMAN SKIN EQUIVALENT
31.	Ray D. Page	PRIMARY HEPATIC LYMPHOMA AND ASSOCIATION OF HEPATITIS C VIRAL INFECTION
32.	John M. Talent	ORAL INGESTION OF N-ACETYLGLUCOSAMINE AND POLY (N-ACETYLGLUCOSAMINE) FOLLOWED BY ANALYSES OF SERUM AND URINE
33.	M. Moshaddeque Hossain	ASSOCIATIONS BETWEEN LOW BIRTHWEIGHT (LBW) AND MATERNAL SOCIO-DEMOGRAPHIC AND REPRODUCTIVE CHARACTERISTICS IN AL AIN, UNITED ARAB EMIRATES (UAE)

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: JILL PETERSON

Department: GRADUATE SCHOOL OF BIOMEDICAL SCIENCES

Undergraduate or Medical Student___ Graduate Student XX Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

FUNCTION, ELASTIC PROPERTIES, AND MICROSTRUCTURE OF HUMAN CIRCUMORBITAL BONE. Jill Peterson and Paul C. Dechow, University of North Texas, Health Science Center, Fort Worth, Texas 76107, and Baylor College of Dentistry, Dallas, Texas 75246.

Research on elastic properties of cortical bone at glabella suggests that supraorbital bone is transversely isotropic, such that elastic moduli are similar in all directions parallel with the cortical surface. More recent studies on cranial vault bone show low variation in stiffness by direction, although directions of greatest stiffness vary considerably between individuals. This study examines elastic properties of bone from the circumorbit, including the frontal and zygoma, and tests the hypothesis that bone in the midface is more directional because of close proximity to masticatory muscles and occlusal loads, while bone from the upper face resembles cranial vault bone. Ultrasonic techniques were used to determine direction of greatest stiffness, and estimate elastic properties, in 9 frontal and 4 zygomatic sites of 10 fresh adult human crania. Statistical differences between sites and directions were determined by ANOVA. The results showed that the frontal strongly resembles the parietal in the pattern of elastic properties. Elastic properties differed little by direction, and directions of peak stiffness were not consistent between skulls or sites. However, the zygomatic bone showed larger and more consistent patterns of directional differences ($P<0.05$). Peak elastic moduli were similar at all sites (16.0GPa(SD=2.1) for the frontal, and 15.2GPa(SD=2.8) for the zygoma. However, elastic moduli in the least stiff direction, density, and shear moduli differed significantly between the two bones ($P<0.05$). These results suggest that the frontal bone, including the supraorbital region, is similar in structure to other bones of the cranial vault, while the zygomatic bone is adapted to occlusal and masticatory muscle loads.

(Support: 1995 AADR Student Research Fellowship sponsored by Johnson & Johnson, and NIH Grant DE07761.)

Abstract #29

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: S.D. Dimitrijevich

Department: Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff X

Read instructions and fit abstract inside the space given below:

THE EFFECT OF MICROGRAVITY ON HUMAN TISSUE. I. ASSEMBLY OF THE HUMAN SKIN EQUIVALENT

S. D. Dimitrijevich, T. J. Reese and J.G. Mills,
Departments of Biochemistry and Molecular Biology and Surgery; Wound Healing Research Institute. UNT HSC at Ft.Worth, Ft Worth,Texas.

Rotating Wall Vessel cell culture systems (RWVs) have been developed by NASA to simulate microgravitational (μg) environment on Earth. Utilizing "slow turning long vessel" (STLV) and "high aspect rotating vessel" (HARV), growth of anchorage dependent and independent cells was shown to be greatly improved. When compared to other methods of three dimensional cell growth, such as spinner culture bottles system, microgravitational environment greatly reduces the shear stress exerted on the cells. Also, there is a great improvement in mass transfer, thus optimizing nutrient supply and waste removal from the cells' immediate vicinity. Difficult to grow cells have shown a greatly improved growth in RWVs, and a profound tendency of cells to form aggregates ("organoids") has also been demonstrated.

In addition to understanding the effect of zero gravity on human physiology, simulated μg, may also be used to study carcinogenesis, pathogenesis and organogenesis of human tissues. We have developed several *in vitro* models of human tissue such as the skin and cornea based on the non-contracted connective tissue matrix composed of type I collagen and appropriate fibroblasts. Our interest in the μg environment is its effect on skin organogensis as it applies to various phases of tissue repair. Specifically we are interested in the contraction of the dermal equivalent (DE) its mechanical integrity, the attachment of of epidermal cells to the DE and the formation of the basement membrane, and differentiation of keratinocytes to form the fully stratified epidermis.

Our preliminary studies have resulted in two modifications of the RWV to specifically fit the needs of our experimental protocols. Using these new RWVs, assembly of the dermal equivalent proceeds without any specific orientation and migration of the normal human fibroblasts. Normal human keratinocytes attach, proliferate and differentiate on the DE under dynamic conditions.

We are gretaful for the support by NASA Biotechnology/Microgravity Program.

Abstract #30

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Ray D. Page

Department: Division of Medicine, Lymphoma Section, MDACC

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow X Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

PRIMARY HEPATIC LYMPHOMA AND ASSOCIATION OF HEPATITIS C VIRAL INFECTION. Ray D. Page, D.O. Ph.D. and Jorge Romaguera, M.D. Division of Medicine, Lymphoma Section, U.T. M.D. Anderson Cancer Center, Houston, Tx 77030.

Although involvement of lymphoma in the liver is not uncommon, primary hepatic lymphoma (PHL) is rare with less than 80 cases reported in the literature. Hepatitis C virus (HCV) is both a hepatotropic and lymphotropic virus, and has been implicated in sustaining clonal expansion of B cells. The purpose of this study was to characterize PHL and to determine its association with HCV. METHODS: Patients who had been evaluated at MDACC with a liver biopsy showing lymphoma were retrospectively reviewed btween 1974-1995. Over 400 charts were reviewed with 24 cases found that were determined to have PHL. Recent patients were tested for HCV. Archival serum specimens and tissue blocks of earlier cases of PHL are currently being evaluated for HCV RNA by PCR analysis. RESULTS: Twenty four cases were determined to be PHL. The mean age was 50 years (21-75), male sex (63%), white (88%), and hispanic (12%). Patients typically presented with RUQ pain (71%), with weight loss, fever and night sweats (38%). Physical exam revealed hepatomegaly (75%). Liver imaging showed multiple masses (50%), a solitary mass (42%), or diffuse involvement (8%). Liver function tests were elevated. Hypercalcemia (10.5-15.9 mg/dl) was found at presentation in 6 of 15 (40%). Normal tumor markers were seen with AFP (14 of 14) and CEA (15 of 16, outlier 6.6). The mean β_2-microglobulin (n=13) was 3.6 (1.7-6.4). Pathology revealed diffuse large cell lymphoma 23/24 (96%), with one case of low grade B-cell lymphoma. To date, HCV has been detected in 6 of 7 cases. One patient had a concurrent infection with HIV. HIV was found in 2 of 10 cases. Twelve cases were evaluate with a hepatitis B profile. One person showed chronic active hepatitis and one person had a prior infection. A variety of chemotherapy was given to all patients. A complete remission (CR) was achieved in 21 of 24 (88%). The 3-year disease free survival was 14 of 18 (78%). The presence of HCV does not appear to affect the ability to achieve CR 5 of 6 (83%). CONCLUSION: PHL is a rare disease which responds well to chemotherapy and has a favorable prognosis. Initial evaluation shows a close association of HCV and PHL, suggesting that HCV could be an etiologic factor of PHL.

Abstract #31

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: John M. Talent

Department: Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff X

Read instructions and fit abstract inside the space given below:

ORAL INGESTION OF N-ACETYLGLUCOSAMINE AND POLY(N-ACETYLGLUCOSAMINE) FOLLOWED BY ANALYSES OF SERUM AND URINE

J.M. Talent[1], M. Reyes[2], W. Tuntiwechapikul[1] and R. W. Gracy[1] [1]Molecular Aging Unit, Dept. of Biochemistry and Molecular Biology, UNTHSC at FT. WORTH, Ft. Worth, TX 76107, and [2]UNT, Denton, TX 76203.

Glucosamine, N-acetylglucosamine (NAG) and derivatives have been shown to be effective in tratment of osteoarthritis. N-acetylglucosamine has been effectively delivered by injection and by oral ingestion, however, the half life of the material in the blood is relatively short. Thus a sustained release form of the material is highly desirable. The polymeric form of NAG, chitin is readily available and might potentially provide a source of the material if delivered orally. The purpose of this study is to determine the appearance and disappearance of NAG and glucosamine in serum and urine from subjects who orally ingest NAG or polyNAG.

Ten normal healthy subjects (male and female; age 35-55) ingested 1 gram per day of encapsulated NAG or polyNAG for three consecutive days. Serum was collected at various intervals and 24 hour urines were collected. All samples were prepared and analyzed for carbohydrates by HPLC according to a protocol already developed in our laboratory. During the second week of the study subjects orignally ingesting NAG were switched to polyNAG and the polyNAG ingesters to NAG.

Whereas the chromatographic profiles of urine differed greatly among subjects the serum profiles were very consistent. Spiking samples with standards of NAG or Glucosamine confirmed the locations of glucose, glucosamine and NAG. A sustained elevation of glucosamine or NAG in serum was not observed.

Supported by Lescarden, Inc.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: **M. Moshaddeque Hossain and Muriel A. Marshall**

Department: **Department of Family Medicine**

Undergraduate or Medical Student ___ Graduate Student ___ Postdoctoral Fellow ___ Faculty _X_ Staff ___

Read instructions and fit abstract inside the space given below:

ASSOCIATIONS BETWEEN LOW BIRTHWEIGHT (LBW) AND MATERNAL SOCIO-DEMOGRAPHIC AND REPRODUCTIVE CHARACTERISTICS IN AL AIN, UNITED ARAB EMIRATES (UAE).

M. Moshaddeque Hossain and Muriel A. Marshall

To define the associations between LBW (<2.5 kg) and maternal socio-demographic and reproductive characteristics, obstetric records of 744 women who had given birth to single babies at the Oasis Hospital, Al Ain city, UAE, during January-December 1991 were randomly selected and reviewed. In 1991, 1945 (23.7%) of the 8193 babies born in Al Ain were born at the Oasis Hospital where prenatal and obstetric care is available for a nominal fee. Of the 744 neonates studied, 53 (7.1%) were LBW. Significant ($P<0.05$) univariate correlates of LBW in all women were nationality, age, and parity. In a multivariate logistic regression model including these three independent variables, only nationality (non-UAE *v* UAE: odd ration (OR) = 1.86) and age (<20 y: OR = 1.00; 20-29 y: OR = 0.38; ≥30 y: OR = .22) remained significantly associated with LBW. In mothers of parity ≥ 1, nationality, prior premature childbirths, and prior low weight childbirths were significantly associated with LBW in index neonates. After multivariate adjustment using a logistic regression model including all these three independent variables, only prior low weight childbirths (yes *v* no: OR = 6.58) remained significantly associated with LBW in index neonates delivered by this subgroup of mothers. These results indicate that nationality, age, and prior low weight childbirths may serve as risk indicators for LBW in women who choose to have childbirth at the Oasis Hospital in Al Ain. The reasons and remedies for the observed greater risk of low weight childbirths in non-UAE mothers need to be identified.

EDUCATION

34.	Richard B. Baldwin, D.O.	COMMUNITY-ORIENTED PRIMARY CARE: PROCESS AND PLANNING
35.	David P. Hill, D.O.	OSTEOPATHIC MANIPULATIVE THERAPY IN RESIDENCY
36.	S. L. MacCall, M.S.I.S.	WWW INSTRUCTION IN THE TEACHING CLINIC: TO BOOKMARK OR NOT TO BOOKMARK?
37.	Frank J. Papa, D.O., Ph.D.	THE USE OF COMPUTER ADAPTIVE TESTING IN THE RESEARCH AND IMPLEMENTATION OF THE VIRTUAL CLASSROOM VIA THE WORLD WIDE WEB
38.	I. D. Prather, D.O.	EDUCATING RURAL PHYSICIANS FOR THE 21ST CENTURY: AN INTEGRATED APPROACH BY THE UNTHSC FAMILY PRACTICE RESIDENCY PROGRAM
39.	Claudia S. Coggin, M.S.	DESIGN AND DEVELOPMENT OF A BROCHURE FOR PATIENT EDUCATION DEALING WITH HUMAN PAPILLOMAVIRUS
40.	Lauren Allen	EFFECT OF ENVIRONMENTAL FACTORS ON ORGANISMS IN AN ECOSYSTEM & HOW THESE FACTORS AFFECT THE WELLNESS OF HUMANS
41.	Jarreau James	LASERS - PAST, PRESENT, AND FUTURE
42.	Regina H. Lee, M.L.S.	LIBRARY

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Richard B. Baldwin, D.O.

Department: Family Medicine

Undergraduate or Medical Student__ Graduate Student__ Postdoctoral Fellow_ Faculty X__ Staff__ FP Resident_

COMMUNITY-ORIENTED PRIMARY CARE: PROCESS AND PLANNING, Richard B. Baldwin, Dept. of Family Medicine, University of North Texas Health Science Center, Fort Worth.

The Community-Oriented Primary Care (COPC) approach to health care delivery is receiving greater recognition and attention today due to its role in making health care more communally and socially responsive. This presentation will focus on the process of developing a COPC in a rural town in north Texas where the UNTHSC currently operates an ambulatory family medicine clinic. The first phase of this process is to generate a plan for community health assessment using a participatory model (to involve the community). The following issues are being used as guidelines during the initial phase: 1) How will the capacities of existing community associations/coalitions/networks be identified and used in problem-solving? 2) What mechanism will be used to clearly identify skills, abilities, capacities and assets that local residents will contribute to the problem-solving process? 3) How will local residents be enlisted to identify and address issues? 4) How will marginalized and other under-represented persons, such as the disabled and elderly, be involved? 5) How will local capacities be mobilized, and used in governance of the project? The planning team will predominately rely on, and be directly by, community members to develop the implementation plan for the program. Of particular interest is the participation of public health graduate students from the health science center in this process. The goal of the community health assessment is to guide local health providers in implementing community-based services identified as needed in the health assessment. The purpose of this presentation is to provide the audience with the issues, concerns and steps identified in developing a locally controlled ("grass-roots") COPC in a rural community.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: David P. Hill, D.O.

Department: Family Medicine

Undergraduate or Medical Student__ Graduate Student__ Postdoctoral Fellow_ Faculty__ Staff__ FP Resident X

OSTEOPATHIC MANIPULATIVE THERAPY IN RESIDENCY David. P. Hill, Department of Family Medicine, University of North Texas Health Science Center, Fort Worth.

Osteopathic Residents in both Osteopathic and Allopathic programs were queried about: (1) their perceptions of the quality of their training in Osteopathic Manipulative Therapy (O.M.T.) that they have received as students, interns, and residents, (2) type and numbers of manipulative procedures used, (3) perceived results of O.M.T., (4) most common diagnoses for which O.M.T. is used, and (5) factors limiting the use of O.M.T. An evaluation instrument (survey) was sent to approximately 3000 Residents using addresses supplied by the American Osteopathic Association. The survey was designed to be completed in 5-7 minutes by using check-off questions for demographic and other objective data and ranking questions to obtain information about subjective topics. Ranking questions were presented in the "Strongly Disagree-Agree" format with choices ranging from 1-5. The entire instrument was one page front and back and was designed to be folded and stamped for easy return. Mailing was done in December 1995. Funds for copying and mailing supplied by grant from Osteopathic Medical Center of Texas.

Approximately 300 completed surveys have been received to date. Only 3-5% of surveys have been undeliverable.

Preliminary results indicate that Residents are not wholly satisfied with O.M.T. training in all aspects. Residents in Allopathic programs use much less O.M.T. than their Osteopathic counterparts. Most O.M.T. used is soft tissue, High Velocity Low Amplitude, and Muscle Energy. Very few Residents use Crania-Sacral therapy. Most report that patients experience some to great relief when O.M.T. is used. The most common diagnoses for which O.M.T. used are neck pain, back pain, headaches. Time, availability of suitable tables, and lack of preceptor support are the main limiters of O.M.T. use. A majority of Residents plan to use O.M.T. in their practice.

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: S.L. MacCall, M.S.I.S., Medical Informatics Coordinator

Department: Family Practice Residency Program

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

WWW INSTRUCTION IN THE TEACHING CLINIC: TO BOOKMARK OR NOT TO BOOKMARK?

S.L. MacCall, M.S.I.S., J.A. Whitham, D.O., H. McNulty, D.O.
Family Practice Residency Program
UNTHSC at Fort Worth

The advent of the World Wide Web (WWW) is creating new opportunities for information management in Family Medicine. At the same time, medical educators are facing the challenge of incorporating these networked information resources into the curriculum. The Family Practice Residency Program at UNTHSC is addressing this challenge by developing a teaching module concerning the use of the WWW in a clinical setting, with a particular emphasis on how to instruct residents about organizing information retrieved from the WWW. The goal of this module is to enable residents to become effective and autonomous users of the WWW. This effort is undertaken as a component of an overall strategy in the Residency Program to educated family medicine physicians for rural practice. The WWW is seen as an excellent means by which rural physicians can stay abreast of medical advances. The high level of connectivity that the WWW facilitates enables unprecedented opportunity for global interaction, collaboration, and resource sharing in medicine. However, there are persistent problems with the quality, reliability, and stability of WWW resources. In response to these problems, there has been recent emphasis on 1) creating WWW sites that are dedicated to certain types of practice; and 2) creating tailored networks, such as Physicians Online, that bypass the WWW entirely by setting up their own collection of resources using their own software. These approaches are compared to a strategy of self-selecting customized bookmark libraries, and we conclude that the creation of individually customized bookmark libraries, using standard sources from recognized content providers, is the best way to take full advantage of the networked information resources on the WWW.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: **Frank J. Papa, DO, PhD**

Department: **Dept of Family Medicine, Divison of Emergency Medicine**

Undergraduate or Medical Student ___ Graduate Student ___ Postdoctoral Fellow ___ Faculty _X_ Staff ___

Read instructions and fit abstract inside the space given below:

THE USE OF COMPUTER ADAPTIVE TESTING IN THE RESEARCH AND IMPLEMENTATION OF THE VIRTUAL CLASSROOM VIA THE WORLD WIDE WEB

Frank J Papa, Robert C Stone, David G Aldrich, Randall E Schumacker•

Clinically, evidence of diagnostic competency is demonstrated by the physician's ability to diagnose the presence of a given disease despite different combinations of signs and symptoms by which the disease manifests itself. From an assessment perspective, however, diagnostic performance on one case cannot be used to predict performance on another.

Given these two assumptions, the authors have argued that the assessment of diagnostic competency should be predicated upon a subject's performance against a number of different case presentations for any given disease. In order to produce logistically feasible assessments of disease-specific diagnostic capabilities, the authors have subsequently piloted the use of computer adaptive testing (CAT) procedures.

The CAT algorhythms and item bank needed to produce such measures have now been converted to HTML and are designed to work in conjunction with Netscape 2.02. Netscape is an interface tool which makes HTML-coded information functional on multiple paltforms including IBM compatible, Macintosh and UNIX-based machines. Netscape is the primary Internet interface in use in the United States.

The investigators will demonstrate how educators can now produce on-line assessments of disease-specific diagnostic capabilities wherever medical students or residents receive their training. Internet-based, disease-specific CAT assessment procedures make it possible to determine the strengths and weaknesses of both the learner and the training environment with a depth and immediacy that makes it possible for educators to create timely, in-training, learner-centered interventions.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: **I.D. Prather, D.O., Associate Professor and Director**

Department: **Family Practice Residency Program**

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

EDUCATING RURAL PHYSICIANS FOR THE 21ST CENTURY: AN INTEGRATED APPROACH BY THE UNTHSC FAMILY PRACTICE RESIDENCY PROGRAM I.D. Prather, D.O., H.F. Migala, M.S., L.S. Johnson, M.S.W., S.L. MacCall, M.S.I.S. Family Practice Residency Program, UNTHSC at Fort Worth

Although the supply of physicians in Texas has increased in recent years, rural shortages have not been eliminated. Of the 254 counties in Texas, 196 are considered rural and of those 196, 100 counties are recognized by the federal government as having a critical shortage of primary care physicians. Twenty-two rural counties have no primary care physicians. In response to this situation, the Family Practice Residency Program at UNTHSC has begun an integrated approach to educating rural physicians for the 21st Century. The principle objective of this new approach is to provide our residents with the training, skills, and knowledge necessary to practice medicine in rural Texas/America. The Residency Program selectively accepts applicants having the stated intention of returning to a rural area to practice. The Program provides for rural experience during the course of training and our desire is to optimize their clinical capabilities and psycho-social survival strategies needed for rural practice. This approach includes three integrated objectives: 1) *Medical Information Management*; providing instruction in the capabilities of available technology, information data systems, and their application to medicine. This has included purchasing required computer hardware, software and designing of the comprehensive medical informatics curriculum and teaching schedule. 2) *Clinical Decision Making*; instruction in decision-making and clinical reasoning using concepts from clinical epidemiology, educational psychology and medical informatics. Monthly conferences are held with the residents using an internal textbook in clinical reasoning written by Raymond Olson, D.O., as the foundation for the curriculum; 3) *Physician Well-Being*; strategies to reduces stress in personal, family and professional life and centers on the role of physicians as a professional, a family member, a parent and an individual who has emotional, psychological, physical and spiritual needs. This approach to educating rural physicians for the 21st Century focuses on the challenges of rural practice and is in step with the current efforts of UNTHSC to produce generalist physicians for the State of Texas.

Abstract #38

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Claudia S. Coggin, M.S.

Department: Public Health and Preventive Medicine and Public Health Program

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff x

Read instructions and fit abstract inside the space given below:

DESIGN AND DEVELOPMENT OF A BROCHURE FOR PATIENT EDUCATION DEALING WITH HUMAN PAPILLOMAVIRUS

Claudia S. Coggin, M.S.

Human Papillomavirus (HPV) infection is the fastest growing sexually transmitted disease in the United States. There is currently no cure, but there are measures which can be taken to prevent contracting the HPV. HPV has an associated risk with cervical cancer. In 1994, 4,600 women died of cervical cancer in the United States. Newly reported data indicate that black women over 50 years of age have the highest incidence of cervical cancer, with the next highest figures for white women over 50 years of age. Young white females as a group show an increase in cases, while new cases in other population groups are on the decrease.

The purpose of this project was to develop a brochure dealing with the risks, consequences, and preventive measures of HPV and was aimed at the young adult population. Development of this project began with research of the current literature. In comparison to other Sexually Transmitted Diseases (STD), there is relatively little written about this STD in the popular press. Education is needed to communicate preventive measures to the populations at risk. The author in consultation with a graphic artist designed a brochure dealing with HPV which answered these three questions: "What is HPV?"; "Do I Have It?"; and "What Can I Do About It?" The author wrote the text and used two formulae to measure the reading level. A pre-test/post-test evaluation of the brochure was conducted with target population. Two expert groups were used for evaluation of the brochure design and content. After the suggestions were incorporated into the final draft of the brochure, a focus group reviewed the brochure for the final evaluation.

Greater emphasis in patient education by the health professionals may help in raising the level of knowledge about HPV and the methods of prevention which may slow the incidence of this disease and its potentially severe consequences.

Abstract #39

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Lauren Allen

Department: Applied Learning Academy

Undergraduate or Medical Student ✓ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

EFFECT OF ENVIRONMENTAL FACTORS ON ORGANISMS IN AN ECOSYSTEM & HOW THESE FACTORS AFFECT THE WELLNESS OF HUMANS: Lauren Allen, Jennifer Hayes, Blake Holt, Jarreau James, Eric Walling: Applied Learning Academy: Fort Worth, Texas, 76109.

This project will provide opportunities for students to strengthen their understanding of science concepts while addressing a community need. Students and the professional staff at the Fort Worth Botanic Garden through a prior project have determined that because of the location of the gardens (close proximity to a major interstate highway and a large train yard) there is a need to determine the amount of pollinates in the area. Further, they have determined that there is a need to teach the many visitors to the area about the effect of pollinates on life in this popular area. Students also determined the need of scientifically sound investigation and the need to solicit help from graduate students from the University of North Texas Health Science Center. Through the project, students will (1) use the Botanic Garden as the primary environmental site to test air, land and water on a bimonthly basis for one year,May 1996-May 1997 (2) collect, record data, perform tests, and observe patterns of data with the help of UNTHSC graduate students (3) record all work, create databases and spread sheets, edit work for use on instructional videos, and publish a curriculum guide (4) plan and deliver presentations to middle school students and their teachers. Success of the project will be determined by the extent to which student work demonstratesan understanding of relevant scientific procedures and concepts and the extent to which students use this understanding to meet the expressed need of their clients, the Fort Worth Botanic Garden, the University of North Texas Health Science Center, and Fort Worth ISD. (This project is supported financially by UNTHSC and technically by the UNTHSC Graduate Student Association.)

Abstract #40

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Jarreau James

Department: Applied Learning Academy

Undergraduate or Medical Student ✓ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

LASERS - PAST, PRESENT, AND FUTURE: Jarreau James & Eric Walling: Applied Learning Academy: Fort Worth, TX 76109

Purpose: To determine the rotations per minute (RPM) and frequencies of both mirrors in our Lissajous figure. We will measure these RPM's by painting a white line one the back of both of our mirrors and adjusting a strobe light to the same frequency, causing the line to appear "frozen", or stationary. We believe that when shining a laser into these mirrors at exact frequencies, stationary shapes will appear on our screen. We will be able to tell the (RPM) by the number of blinks that the strobe light is set to. Are materials will include a laser lissajous figure apparatus with two rotating mirrors, a 0.8 mW unmodulated laser, a strobe light, a projector screen, and a TV/VCR Unit. Our most pertinent results include making shapes as stars with different frequencies we also are able to use the frequencies to rotate the shapes at different speeds and were able to change the shape at a more smoother pace it we could before. Our final result is that we will be able to compare frequencies and the shapes which they generate.

Abstract #41

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Regina H. Lee, M.L.S., Coordinator Public Access Service

Department: Gibson D. Lewis Health Science Library

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty XX Staff___

Read instructions and fit abstract inside the space given below:

The Gibson D. Lewis Health Science Library (Lewis Library) supports the teaching, research, patient care and service programs of the University of North Texas Health Science Center at Fort Worth, and the health care programs of North Texas through the provision of information services and access to the biomedical information collections fundamental to maintaining health and treating and preventing disease.

As a Resource Library in the National Network of Libraries of Medicine, the Lewis Library has access to the collections of medical libraries throughout the United States.

Faculty, staff and students in the Graduate School of Biomedical Sciences have access to the full services of the Library.

- Information Services -- location of factual information, computer searches from national and international online databases
- Electronic Resources -- Current Contents on disk, local MEDLINE database, Internet access, CDC Wonder
- Public Access Services -- a local collection of 2000 journals and 130,000 volumes, document delivery, interlibrary loan
- Learning Resource Center -- 5000 audiovisual titles, anatomical models, three microcomputer labs,

The Lewis Library Exhibit--Tradition, Transition, Technology--includes fact sheets from:

- the National Library of Medicine
- the National Center for Biotechnology Information
- the Lewis Library highlighting information resources specific to the seven research centers of excellence

Abstract #42

MOLECULAR BIOLOGY AND CELLULAR BIOCHEMISTRY

43.	Paramjit Kaur Bhogal	DETERMINATION OF CYCLIC ADP-RIBOSE LEVELS IN CULTURED HUMAN CELLS
44.	Jean Rawling	EUKARYOTIC TRANSCRIPTION FACTORS AS SUBSTRATES FOR POLY (ADP-RIBOSYL)ATION
45.	Hilda Mendoza	ENZYMATIC CHARACTERIZATION OF THE 40 kDa CARBOXY-TERMINAL CATALYTIC DOMAIN OF HUMAN POLY (ADP-RIBOSE) POLYMERASE
46.	Raghu Krishnamoorthy	IDENTIFICATION OF A POTENTIAL ALTERNATE START OF TRANSCRIPTION OF HUMAN APOLIPOPROTEIN B mRNA
47.	Harshika Bhatt	RE-EVALUATION OF THE ROLE OF CaM KINASE II IN INSULIN SECRETION FROM PANCREATIC β-CELLS
48.	Jimmy L. Tarpley	DEPHOSPHORYLATION AND INACTIVATION OF CaM KINASE II IN PERMEABILIZED βTC3 CELLS IS MEDIATED BY PROTEIN PHOSPHATASE 2C
49.	Jimmy L. Tarpley	CARBACHOL ACTIVATES THE MULTIFUNCTIONAL Ca^{2+}/CALMODULIN-DEPENDENT PROTEIN KINASE II IN ISOLATED RAT PANCREATIC ISLETS
50.	Wirote Tuntiwechapikul	DEGRADATION PATHWAY OF TRIOSEPHOSPHATE ISOMERASE IN FIBROBLASTS
51.	P. John Kamthong	REGULATION OF M-CSF GENE EXPRESSION
52.	Debra White	PHYLOGENETIC DISTRIBUTION OF THE CARBON STORAGE REGULATOR GENE, *csr*A, AMONG EUBACTERIA
53.	Michael Murphy	MONONUCLEAR CELL INFILTRATION AND β-CHEMOKINE PRODUCTION IN MYCOPLASMA LUNG DISEASE IN MICE

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Paramjit Kaur Bhogal

Department: Microbiology and Immunology

Undergraduate or Medical Student____ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

DETERMINATION OF CYCLIC ADP-RIBOSE LEVELS IN CULTURED HUMAN CELLS. P. BHOGAL and R. ALVAREZ-GONZALEZ. Department of Microbiology and Immunology, University of North Texas Health Science Center at Fort Worth, TX 76107-2699

Mobilization of intracellular Ca^{++} is a signaling mechanism that is of fundamental importance to cellular physiology. Cyclic adenosine diphosphoribose (cADPR) is a recently discovered metabolite of nicotinamide adenine dinucleotide (NAD) that appears to play a role in the Ca^{++} - induced Ca^{++} -release from intracellular stores. Previous research has allowed the determination of intracellular cADPR levels indirectly, through the quantification of calcium concentrations. However, cADPR in human cells has never been directly measured. We have used the method of Kim *et al.* (Science, 261:1330-1333, 1993) to separate purified cADPR from other adenine nucleotide containing compounds associated with NAD metabolism following phosphodiesterase treatment and dihydroxyboronyl-Bio-Rex affinity chromatography. We propose to convert cADPR to ADPR, using NAD glycohydrolase isolated from *Bungarus fasciatus*. Following derivitization of ADPR to Σ-ADPR, HPLC - fluorescence detection of this compound will allow the quantification of cADPR. This method will allow the accurate measurement of endogenous levels of cADPR in both normal and transformed human cells.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: JEAN RAWLING

Department: MICROBIOLOGY AND IMMUNOLOGY

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow X Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

EUKARYOTIC TRANSCRIPTION FACTORS AS SUBSTRATES FOR POLY(ADP-RIBOSYL)ATION.

Jean M. Rawling and Rafael Alvarez-Gonzalez Dept of Microbiology and Immunology, University of North Texas Health Science Center, 3500 Camp Bowie Boulevard, Fort Worth, Texas 76107-2699.

We have examined the susceptibility of eukaryotic transcription factors to covalent poly(ADP-ribosyl)ation. Human recombinant TBP, TFIIB and TFIIF (RAP30/74) were incubated with calf thymus poly(ADP-ribose) polymerase (PARP) and [^{32}P]-labeled NAD$^+$ at 37^{o}C. Upon LDS-PAGE and autoradiography, two bands of radioactivity, coincident with RAP30 and RAP74, were observed. No radioactivity co-migrated with TBP or TFIIB. The phenomenon was dependent on the presence of nicked DNA, which is essential for PARP activity. Covalent modification of TFIIF increased in a time-dependent manner between 30 seconds and 5 minutes of incubation. During the time course, the RAP74 subunit was labeled preferentially to RAP30. The level of poly(ADP-ribosyl)ation also increased with TFIIF concentration, as well as with NAD$^+$ concentration. Furthermore, the association of [^{32}P] with the TFIIF subunits was not merely due to the ionic interaction between pre-formed ADP-ribose polymers and TFIIF subunits. High-resolution PAGE confirmed the radioactive species associated with RAP30 and RAP74 were ADP-ribose polymers. From these observations, we conclude that both TFIIF subunits are highly specific substrates for covalent poly(ADP-ribosyl)ation in a pure enzyme system. [Funded by grants from the Texas Advanced Research program (# 009768-14) and NIH (# GM45451)]

Abstract #44

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: **Hilda Mendoza**

Department: **Microbiology and Immunology**

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff **X**

Read instructions and fit abstract inside the space given below:

ENZYMATIC CHARACTERIZATION OF THE 40 kDa CARBOXY-TERMINAL CATALYTIC DOMAIN OF HUMAN POLY(ADP-RIBOSE)POLYMERASE. *H. Mendoza-Alvarez, λG. deMurcia, and *R. Alvarez-Gonzalez. λ Ecole Superieure de Biotechnologie de Strasbourg, UPR 9003 du CNRS, Strasburg, France and *Department of Microbiology and Immunology, University of North Texas Health Science Center at Fort Worth, Fort Worth, Texas 76107-2699.

The carboxyl-terminal 40-kDa catalytic domain (CD) of human Poly(ADP-ribose)polymerase (PARP) was cloned, expressed, and purified to homogeneity as described elsewhere [J. Biol. Chem. 268, 13454-13461, (1993)]. This peptide catalyzes the synthesis of protein bound poly(ADP-ribose) in the absence of DNA with a 500-fold lower efficiency than native enzyme. An analysis of the polymer size distribution of the ADP-ribose chains synthesized by CD by high resolution-PAGE shows that this peptide catalyzes the initiation, elongation and branching reactions. Kinetic studies indicate that the reaction occurs in a: i) time-dependent; ii) NAD-concentration-dependent; and iii) peptide-concentration dependent manner. Surprisingly, the initial rates of the reaction show second order kinetics as a function of CD concentration from 100 to 600 nM levels indicating that a CD-dimer can also be formed in the absence of DNA. Therefore, the carboxy-terminal domain of PARP must contain amino acid residues that contribute to protein-protein interactions during automodification. However, the binding affinity in the CD-dimer must be lower than the affinity of the DNA-dependent dimerization of PARP promoted by peptides present in the 74 kDa amino-terminal fragment which contains the DNA-binding and automodification domains. CD also utilized [^{32}P] 3'-deoxyNAD as a substrate for the ADP-ribose chain initiation reaction. However, due to the lower efficiency of this reaction in the absence of DNA, we could not fully characterize it. (This project was supported by grant GM45451 from the NIH.)

Abstract #45

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Raghu Krishnamoorthy

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow__X__ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

IDENTIFICATION OF A POTENTIAL ALTERNATE START OF TRANSCRIPTION OF HUMAN APOLIPOPROTEIN B mRNA

Raghu Krishnamoorthy, Samuel S. Chuang and Dr. Hriday K. Das
University of North Texas- Health Science Center
Fort Worth, Texas, 76116

Apolipoprotein B-100, the only protein component of low density lipoprotein, is produced primarily in the human liver and serves as a ligand for the LDL receptor. High levels of plasma LDL and apoB have been directly linked with the risk of coronary heart disease. Hepatic cell-specific expression of the human apoB gene is controlled by at least four *cis*-acting elements located within the gene fragment spanning -128 to +122. The positive elements (-104 to -85), (-84 to -60) and (+43 to +53) are the binding sites for transcription factors BRF-2, BRF-1 and BRF-4 respectively. The negative element (+20 to +40) interacts with the factor BRF-3. This study establishes the roles of *cis*-acting elements in *in vitro* transcription of the apoB gene. Addition of competitive double-stranded oligonucleotides corresponding to the downstream element (+43 to +53), in *in vitro* transcription assays produced truncated RNA transcripts. Mutation analysis of downstream promoter sequences revealed the sequence +50 to +56 as important to alternate transcription initiation site of the human apolipoprotein B gene. These results suggest that protein factor BRF-4 may act as a repressor for this alternate transcription initiation of apoB mRNA.

Abstract #46

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Harshika Bhatt

Department: Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff X

Read instructions and fit abstract inside the space given below:

RE-EVALUATION OF THE ROLE OF CaM KINASE II IN INSULIN SECRETION FROM PANCREATIC β-CELLS. H. Bhatt, J. Tarpley and R.A. Easom, UNTHSC at Fort Worth, Fort Worth TX 76107.

Current evidence addressing the role of CaM kinase II in insulin secretion is conflicting. We have previously demonstrated that glucose activates the multifunctional Ca^{2+}/calmodulin-dependent protein kinase II (CaM Kinase II) in a concentration-dependent manner that correlates with insulin secretion. Others have demonstrated that the CaM kinase II inhibitor, KN-62 (1 μM), failed to inhibit Ca^{2+}-induced insulin secretion from streptolysin O-permeabilized HIT cells, leading to the implication that this enzyme has no role in the secretory process. In this study, however, KN-62 at concentrations up to 100 μM did not inhibit CaM Kinase II activity in cellular extracts of βTC3 cells in the presence of exogenous calmodulin, and only modestly in the absence of the cofactor. In α-toxin-permeabilized βTC3 cells, Ca^{2+} induced the rapid activation of CaM kinase II in a concentration-dependent manner that was maintained for at least 30 min. This activation was not prevented by KN-62 (0-100 μM) negating the suggestion that CaM kinase II is not involved in Ca^{2+}-induced insulin secretion. The kinase inhibitor, K252a and a selective peptide inhibitor, [Ala^{286}] CaMK 281-302 strongly inhibited CaM kinase II activity in βTC3 cells and conditions have been established to permit the evaluation of the effects of these compounds on Ca^{2+}-induced insulin secretion. A more stringent correlation of the extent of inhibition of CaM Kinase II and insulin secretion by these compounds will permit a better assessment of the role of this enzyme in insulin secretion. (Supported by NIH 47925).

Abstract #47

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Jimmy L. Tarpley

Department: Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student ✓ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

DEPHOSPHORYLATION AND INACTIVATION OF CaM KINASE II IN PERMEABILIZED βTC3 CELLS IS MEDIATED BY PROTEIN PHOSPHATASE 2C. Jimmy L. Tarpley, Harshika Bhatt and Richard A. Easom, University of North Texas Health Science Center, Fort Worth, TX 76107-2699.

The activation and induction of autonomous CaM kinase II by glucose in pancreatic β–cells has implicated this enzyme in the regulation of insulin secretion. This autonomy is mediated by the autophosphorylation of a threonine 286/287 in its regulatory domain and persists as long as this residue remains phosphorylated. In order to delineate the regulatory mechanism responsible for kinase deactivation, we studied the involvement of protein phosphatases in α-toxin-permeabilized βTC3 cells. In these cells, Ca^{2+} induced the dose-dependent activation of CaM kinase II such that the proportion of the enzyme in autonomous form was 0.67 ± 0.25 % and 39.39 ± 1.90 % in the presence of 50 nM and 10 μM Ca^{2+}, respectively. Following activation, the return of Ca^{2+} to pre-stimulatory levels (50 nM) resulted in the rapid decline in autonomous kinase activity such that basal activation levels were achieved by 2.0 min. The rate of this reverse was not affected by okadaic acid (100 nM) or cyclosporin A (20 nM) eliminating the involvement of protein phosphatases 1, 2A or 2B. However, the chelation of Mg^{2+} by the inclusion of EDTA prolonged autonomy levels in the absence of stimulatory concentrations of Ca^{2+}. These data suggest a primary function of a Mg^{2+}-dependent protein phosphatase in the reversal of CaM kinase II activation in the pancreatic β–cell and is consistent with a function previously ascribed to protein phosphatase 2C. (Supported by NIH, DK 47925)

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Jimmy L. Tarpley

Department: Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student_✓_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

CARBACHOL ACTIVATES THE MULTIFUNCTIONAL Ca^{2+}/ CALMODULIN-DEPENDENT PROTEIN KINASE II IN ISOLATED RAT PANCREATIC ISLETS. Jimmy L. Tarpley, Eric l. Babb and Richard A. Easom, University of North Texas Health Science Center, Fort Worth, TX 76107-2699.

A previous demonstration that glucose activates the multifunctional Ca^{2+}/calmodulin-dependent protein kinase II (CaM Kinase II) has implicated this enzyme in the regulation of insulin secretion from the pancreatic β–cell. The current study demonstrated that the muscarinic agonist, carbachol (500 μM), induced the rapid, transient activation of CaM kinase II that was maximal by 15 s and had returned to basal levels by 1 min. This activation was not influenced by verapamil (20 μM) which completely prevented that induced by glucose suggesting that it was mediated by the mobilization of intracellular Ca^{2+}. Surprisingly, the exposure of islets to carbachol, either simultaneously with, or prior to, glucose prevented the activation of CaM kinase II by the nutrient secretagogue. This effect was mimicked by cholecystokinin (CCK-8) and thapsigargin suggesting that it was mediated by the activation of phospholipase C and the mobilization of intracellular Ca^{2+}. In contrast to enzyme activation, glucose-induced insulin secretion was markedly potentiated by CCh, CCK-8 and thapsigargin. These data demonstrate that CaM kinase II can be activated by Ca^{2+} released from both extracellular and intracellular stores. While enzyme activation may not temporally correlate with insulin secretion, these data do not exclude an important positive role of CaM kinase II in this process. (Supported by NIH, DK47925).

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Wirote Tuntiwechapikul

Department: Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

DEGRADATION PATHWAY OF TRIOSEPHOSPHATE ISOMERASE IN FIBROBLASTS. Tuntiwechapikul W., Dimitrijevich D., Gracy R.W., Department of Biochemistry and Molecular Biology, University of North Texas Health Science Center at Fort Worth, Fort Worth, Texas 76107.

Modified proteins accumulate in aging cells and tissues, and are implicated in the mechanism of age-associated deterioration of physiological functions of tissues. Most of these modified proteins result from post-synthetic, covalent modifications such as deamidation and oxidation and label proteins for degradation. The accumulation of modified proteins appears to be due to age related alterations of their degradation system(s) rather than abnormal synthesis. In order to elucidate the mechanisms of protein degradation, we employ the best characterized of all housekeeping enzymes, triosephosphate isomerase (TPI), as a specific probe. Deamidated or oxidized isoforms of TPI have been found to occur in both young and old cells, however, they are accumulated only in aging cells. It has been proposed that the accumulation of the modified isoforms of TPI is due to an impaired degradation system(s) in aging cells, but the degradation pathway has not yet been established. In this study, we are determining the degradation pathway of TPI in young and old human fibroblast cells by specifically and covalently radiolabeling TPI with the substrate analogue 3-chloroacetal phosphate (CAP). CAP-TPI is then introduced into fibroblasts by mild osmotic lysis of pinocytic vesicles. This will allow us to tract the degradation of the protein. For example, the specific inhibition of the lysosomal or proteasomal pathways can be directly assessed to determine the normal pathway of degradation of this housekeeping enzyme. The site(s) of the age-related defect in degradation can also be determined.

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: P. John Kamthong

Department: Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

REGULATION OF M-CSF GENE EXPRESSION P. John Kamthong, Georgia Gray, Fu-mei Wu and Ming-chi Wu Department of Biochemistry and Molecular Biology UNT-HSC, Fort Worth, TX 76107.

Macrophage colony-stimulating factor (M-CSF) is a growth factor required for the production of macrophages/monocytes. The expression of M-CSF gene can be regulated by either chemicals or cytokimes. Using a human pancreatic carcinoma cell line MIA Pa Ca-2 as M-CSF producing cells, we have previously reported that M-CSF expression can be stimulated by interleukin 1 or phorbol esters. The expression can be inhibited by cyclic AMP or cAMP elevating agent such as foskolin. However, the molecular mechanism involved in the regulation by 1L-1 or cAMP is not clear. Examing the 5' flanking region of M-CSF gene revelaed potential cis-acting sites for the binding of AP-1, NF-kB Egr-1 etc. Gel shift experiments were carried out to identify the possible transcriptional factor regulating M-CSF gene expression. We have identified the involvement of NF-kB in IL-1 stimulated M-CSF expression. Under the same experimental condition, however, TPA has no effect on NF-kB activation suggesting a different mechanism for TPA-induced M-CSF expression. This is consistant with our previous results that inhibition of Pk-C did not inhibit IL-1-induced M-CSF production. Treatment of IL-1 and cAMP did not show any decrease in NF-kB activity as compared to IL-1 treatment suggesting inhibition of M-CSF expression by cAMP is not involved in blocking NF-kB activation. The signal transduction pathway of IL-1 induced M-CSF gene expression is currently under investigation.

Abstract #51

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Debra White

Department: Microbiology and Immunology

Undergraduate or Medical Student___ Graduate Student_x_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

PHYLOGENETIC DISTRIBUTION OF THE CARBON STORAGE REGULATOR GENE, *csr*A, AMONG EUBACTERIA

D. White , M. Hart and T. Romeo

University of North Texas Health Science Center, Fort Worth, TX. 76116

The gene *csrA* (carbon storage regulator) encodes a global regulator of carbon metabolism in *Escherichia coli*, and it is known to control expression of genes which encode virulence factors in *Erwinia carotovora.* In order to evaluate the phylogenetic distribution of *csrA*, genomic DNA was collected from species representing four major branches of the domain Bacteria; Flavobacteria, Cyanobacteria, Purple and Gram positive bacteria. The DNA was digested with the restriction endonuclease *Eco*RI and separated by agarose gel electrophoresis. A probe consisting of the coding region of the *Escherichia coli* K-12 *csr*A gene was labeled with digoxigenin using random primed DNA synthesis. Chemiluminescent detection was conducted using Anti-Digoxigenin alkaline phosphatase antibody and Lumingen PPD chemiluminescent substrate. Apparent *csr*A homologs were detected in *Agrobacterium tumefaciens*, *Salmonella typhimurium*, *Erwinia chrysanthemi*, *Vibrio furnissi*, *Vibrio vulnificus* O and *Escherichia coli* B. DNA from other species did not hybridize specifically with the probe, either because these species lacked a *csr*A homolog or because of species divergency. (National Science Foundation).

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Michael Murphy

Department: Microbiology and Immunology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

MONONUCLEAR CELL INFILTRATION AND ß-CHEMOKINE PRODUCTION IN MYCOPLASMA LUNG DISEASE IN MICE.
Michael R. Murphy and Jerry W. Simecka, Dept. of Microbiology and Immunology, UNTHSC, Ft. Worth, TX 76107-2699.

The infiltration of lymphocytes and macrophages into the respiratory submucosa contributes to the histopathology of many pulmonary diseases. A family of chemotactic cytokines, the ß-chemokines, are thought to mediate the infiltration of mononuclear cells to inflammatory sites. The ß-chemokines consists of a number of cytokines including macrophage chemoattractant factor (MCP-1), macrophage inflammatory peptides (MIP-1α & MIP-1ß), and RANTES. Although the ß chemokines are implicated in the infiltration of lymphocytes and macrophages to inflammatory sites, their role in pulmonary diseases are not well understood. The purpose of ongoing studies is to characterize the production of ß-chemokines in a murine model of pulmonary inflammation. *Mycoplasma pulmonis* infection of mice causes a respiratory inflammatory disease in mice with similar histopathologic features to *Mycoplasma pneumoniae* disease in man. To examine the expression of ß-intercrine mRNA, we have designed and tested PCR primers specific for MCP-1, MIP-1α, MIP-1ß and RANTES. Using these primers, we demonstrated that there is an increase in the expression of mRNA encoding MCP-1, MIP-1α, and MIP-1ß in *M. pulmonis* infected C3H/HeN mice. RANTES mRNA expression was not increased. In addition, lung homogenates from mice were tested for MCP-1 by capture ELISA. MCP-1 was found to be much higher in lung homogenates from *M. pulmonis* infected mice 14d post-infection than in uninfected mice. However, we have yet to determine if MIP-1α or MIP-1ß are indeed produced in these mice. Overall, our results indicate MCP-1, MIP-1α, and MIP-1ß may have a major influence on mononuclear cell infiltration in *M. pulmonis* disease, but there was no apparent relationship between RANTES expression and inflammatory response. Future studies will take advantage of two mouse strains, DBA/2N and C3H/HeN mice, which differ in the severity of pulmonary mononuclear cell infiltration. By comparing these two mouse strains, we will determine the relationship between the histopathologic features of disease and ß-chemokine mRNA expression and production.

Abstract #53

NEUROSCIENCE AND BEHAVIOR

54.	Stephen A. Stoffel	BLOCKADE OF KETAMINE-INDUCED DOPAMINE FLUX IN NUCLEUS ACCUMBENS
55.	Robert R. Luedtke, Ph.D.	IMMUNOBLOT CHARACTERIZATION OF A MONOCLONAL ANTI-(RAT D1b DOPAMINE RECEPTOR) ANTIBODY
56.	Beatriz de A. Rocha, M.D., Ph.D.	COCAINE I.V. SELF-ADMINISTRATION IN 5-HT1B KNOCKNOUT MICE
57.	Rachel Peltier	CHRONIC HIGH-DOSE COCAINE TREATMENT DOES NOT EFFECT COCAINE METABOLISM IN RATS
58.	Donghang Li	KETAMINE BLOCKS TOLERANCE TO THE REINFORCING EFFECTS OF COCAINE
59.	Kevin J. Blanton	LOCALIZATION OF PHOSPHOINOSITIDE SECOND MESSENGER RESPONSE IN THE SPINAL CORD DURING HYPERALGESIA
60.	Jennifer A. Jenkins	ETHANOL SUBSTITUTES FULLY FOR A DIAZEPAMKETAMINE MIXTURE
61.	Nicolle R. M. Conway	CRANIECTOMY ACTIVATES DURAL MAST CELLS, INCREASES CEREBRAL CORTICAL HISTAMINE AND ALTERS PIAL VASCULAR PERMEABILITY

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: STEPHEN A. STOFFEL

Department: PHARMACOLOGY

Undergraduate or Medical Student X Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

BLOCKADE OF KETAMINE-INDUCED DOPAMINE FLUX IN NUCLEUS ACCUMBENS. Stephen A. Stoffel and Cleatus Wallis. University of North Texas Health Science Center and S.A.I.N.T., Fort Worth,TX 76107.

Phencylidine (PCP) and it's derivative, ketamine are dissociative anaesthetics that have proven to have high abuse liability. These drugs bind to a variety of receptor sites including n-methyl-d-aspartate (NMDA)-type glutamate receptors, sigma receptors, and potentially acetylcholine receptors. The abuse liability of these drugs is believed to be due to their ability to stimulate dopamine release in the nucleus accumbens, an area of the brain involved in reward. The mechanism by which these drugs change dopamine is complex. The response appears to be biphasic: stimulation at low doses and potential inhibition at high doses. In the present experiments, we measured *in vivo* dopamine (DA) release by chronoamperometry with stearate-modified graphite-paste electrodes (SGEs) implanted bilaterally into the nucleus accumbens. Ketamine produced an inverted U-shaped dose-response curve to single injections (IP). The maximal response occurs at 8 mg/kg with an average increase above baseline of 1.9 ± 0.3 nA. Administration of saline ($n = 3$) did not produce a significant increase in dopamine oxidation current. The sigma antagonist, rimcazole, which has little direct effect on DA release, and the competitive NMDA antagonist, AP-7, were used to block ketamine induced DA release. Our findings support the hypothesis that ketamine stimulated mesolimbic DA release is sufficient to contribute to the abuse potential of ketamine. Supported by NIDA grant DA04137-09.

Abstract #54

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Robert R. Luedtke, Ph.D.

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

Immunoblot Characterization of a Monoclonal Anti-(Rat D1b Dopamine Receptor) Antibody.

Robert R. Luedtke, Suzy Griffin, Susan Summers and Xiaolan Jin. Department of Pharmacology University of North Texas Health Science Center at Fort Worth

A murine monoclonal antibody, SG4-D1b, was prepared by immunizing with a recombinant protein which corresponds to the carboxy terminus of the rat D1b dopamine receptor (rD1b-COOH). The carboxy terminus was selected as the immunogen because of the low level of primary sequence homology between the rat D1a and D1b dopamine receptor subtypes within this region. The immunoreactivity of SG4-D1b with rat D1b dopamine receptors was established using an immunoblot protocol in conjunction with a chemiluminescence detection format. Rat D1a and D1b dopamine receptors were expressed in Sf9 cells using the baculovirus expression system. Membrane extracts from these two homogeneous preparations of receptor subtypes were used to verify that SG4-D1b binds to the rat D1b dopamine receptor subtype, but is not immunoreactive with rat D1a receptors. Immunoreactive components with apparent molecular weights of 121,200 daltons (n = 3), 64,100 daltons (n = 3) and 52,600 daltons (n = 3) were consistently observed. The temporal expression of D1b dopamine receptors in Sf9 cells infected with a recombinant virus was monitored using a membrane homogenate radioligand binding technique and an immunoblot protocol. The temporal expression of D1b receptors was found to be similar for both techniques. In addition, preparations of rat D1b receptors expressed in Sf9 cells were solubilized with digitonin and chromatographed using an ion exchange resin. The elution profile of D1b receptors was monitored using a charcoal adsorption radioligand binding assay and an immunoblot protocol. The elution profile was found to be similar for both techniques. These studies indicate that SG4-D1b binds rat D1b receptors and provides an important immunologic reagent that can be used to study the dynamics of the expression and regulation of rat D1b receptors expressed in tissue cultured cell lines. *This work has been supported in part by grants from the Scottish Rite Schizophrenia Research Program, the National Alliance for Research on Schizophrenia and Depression (NARSAD) and from the NINDS (NS 30507).*

Abstract #55

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Beatriz de A. Rocha M.D., Ph.D.

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty_x_ Staff___

Read instructions and fit abstract inside the space given below:

COCAINE I.V. SELF-ADMINISTRATION IN 5-HT1B KNOCKNOUT MICE

Beatriz de A. Rocha[1], Robert Ator[1], Michael Emmett-Oglesby[1] and Rene Hen[2]; [1]Depart. of Pharmacology, UNTHSC/FW, Fort Worth TX 76107-2699; [2]Depart. of Pharmacology, College of Physicians & Surgeons of Columbia University, New York, NY 10032.

Previous studies have generally ascribed cocaine's reinforcing effects to the inhibition of dopamine re-uptake and the associated enhancement of dopaminergic neurotransmission. However, other studies have examined the ability of serotonergic systems to modulate cocaine's reinforcing effects. Global manipulations of this system have shown that enhancement of serotonin (5-HT) neurotransmission decreases cocaine self-administration; while depletion of 5-HT increases it. More recently, a series of experiments point toward a role of the 5-HT1B receptors modulating the activity of dopaminergic neurones. Further, compounds displaying affinity for the 5-HT1B receptors show substitution for cocaine in rats trained to discriminate cocaine. The present experiments tested the hypothesis that 5-HT1B receptors are involved in the reinforcing effects of cocaine. For testing this hypothesis transgenic mice lacking the 5-HT1B receptors were used as subjects and compared to the wild-type in the acquisition and maintenance of cocaine i.v. self-administration. Male 129/Sv-ter and 5-HT1B-minus 129/Sv-ter inbred mice (Columbia University, NY) were initially trained to press a lever under fixed ratio 1-2 (FR1, FR2) schedule for sweetened condensed milk as reinforcer; after responding was stable on both levers, each subject was implanted with a permanent indwelling jugular catheter. Two days following catheter implantation, mice started cocaine self-administration (2.0 mg/kg/inj under FR1schedule). Once they met acquisition criteria (at least 75% of active lever pressings and at least 16/20 injections within 3 h for three consecutive days), they were switched to FR2 schedule, and dose-response curves were determined. Each dose of cocaine (1.0, 2.0 and 4.0 mg/kg) was tested separately, during three consecutive days; the number of reinforcers per hour was the dependent variable. Both strains equally and dose-dependently responded to cocaine. However, the mutant mice were faster than the wild-type on acquiring cocaine self-administration, suggesting that the 5-HT1B receptors are mainly implicated in the acquisition of cocaine self-administration. Supported by RO1 DA 4137.

Abstract #56

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Rachel Peltier

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

CHRONIC HIGH-DOSE COCAINE TREATMENT DOES NOT EFFECT COCAINE METABOLISM IN RATS. Rachel L. Peltier[1], Angela Springfield[1,2] and Cleatus Wallis[1]. [1]UNT Health Science Center, Dept. of Pharmacology, 3500 Camp Bowie Blvd. Fort Worth TX 76110 and S.A.I.N.T. [2]Tarrant County Medical Examiners Office, Dept. of Toxicology, 200 Feliks Gwozdz Pl Fort Worth TX 76104.

We have previously demonstrated that chronic high-dose treatment with cocaine (20 mg / kg /8 hr X 7 days) produces tolerance to the reinforcing effects of cocaine in rats trained to self-administer cocaine (Emmett-Oglesby *et al.*,1992). In that study, chronic cocaine treatment produced a 2-fold shift to the right of the dose response curve for cocaine self-administration. The aim of the present experiment was to determine if the same protocol of chronic cocaine treatment decreased the reinforcing efficacy of cocaine by causing an increase in the rate of cocaine metabolism. Nineteen male, Fisher F-344 rats, were implanted with intravenous (i.v.) jugular catheters. After 1 week of recovery, the pre-chronic time-course of cocaine clearance was determined. The first blood sample was taken 15 min prior to an i.v. injection of 2.0 mg/kg of cocaine. Samples were taken through the jugular catheter from each subject at 15, 30, 60 and 120 min following the cocaine injection. Subjects were then assigned to one of two groups; Group 1 received chronic cocaine (20 mg/kg/8 hr/7 days; i.p.) and Group 2 received chronic saline. Twenty four hours after the last chronic injection, the post-chronic time-course of cocaine clearance was determined. All blood samples were then analyzed for cocaine and benzoylecgonine, a cocaine metabolite, content using Gas Chromatography Mass Spectroscopy (GCMS). The GCMS analysis showed no significant differences in the pre- and post-chronic levels of benzoylecgonine indicating that the chronic cocaine treatment did not alter the metabolism of cocaine. These results demonstrate that chronic cocaine treatment does not decrease the reinforcing efficacy of cocaine by increasing the rate at which cocaine is metabolized. (NIDA RO1 4137)

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: DONGHANG Li

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

KETAMINE BLOCKS TOLERANCE TO THE REINFORCING EFFECTS OF COCAINE. D.-H. Li and M. W. Emmett-Oglesby*. Dept. of Pharmacol., University of North Texas HSC, 3500 Camp Bowie Blvd., Fort Worth, TX 76107-2699.

This experiment tested the hypothesis that an NMDA antagonist can be used to prevent the occurrence of tolerance to the reinforcing effects of cocaine. The effect of the uncompetitive NMDA antagonist ketamine on tolerance to cocaine self-administration was determined under both a progressive-ratio schedule (PR) and a fixed-ratio schedule (FR 2). Rats were implanted with chronic indwelling jugular catheters. Following implantation, they were trained to self-administer cocaine, 0.25 mg/infusion, under either a PR schedule or a FR 2 schedule. After each subject was stable for at least three consecutive days, they were tested with various doses of cocaine. Subsequently, subjects in the PR and the FR 2 groups were assigned into two subgroups. One group was treated chronically with cocaine (20mg/kg/8hr) for 7 days; the other group received this same cocaine regimen, but each injection was accompanied by an injection of ketamine (25 mg/kg/8hr). Rats treated chronically with cocaine alone showed a significant decrease in breaking points under the PR schedule, and showed a significant increase in the rate of cocaine self-administration under the FR 2 schedule. however, results from the groups treated with the cocaine/ketamine combination are also significantly different from control data. These data failed to support the hypothesis that NMDA antagonists can prevent tolerance to the reinforcing effect of cocaine. Supported by RO1 DA 4137.

Abstract #58

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Kevin J. Blanton

Department: Biological Sciences

Undergraduate or Medical Student XX Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

LOCALIZATION OF PHOSPHOINOSITIDE SECOND MESSENGER RESPONSE IN THE SPINAL CORD DURING HYPERALGESIA. K.J. Blanton, J.L. Fuchs, H.D. Schwark
Dept. Biological Sciences, University of North Texas, Denton, TX 76203

Hyperalgesia develops during prolonged nociceptive stimulation (such as inflammation), and is thought to arise from changes in the spinal cord. At the same time that hyperalgesia develops, there is an increase in the number of substance P receptors in the spinal cord dorsal horn. However, the nature of the resulting functional change is not known. To begin to address this issue, we have measured the response of a substance P-linked second messenger system in the dorsal horn during hyperalgesia. Substance P binding to NK1 receptors initiates hydrolysis of phosphatidylinositol 4,5-bisphosphate to generate the second messengers, inositol 1,4,5-trisphosphate and diacylglycerol (DAG). Slices of spinal cord were incubated in [^{3}H]cytidine as precursor to membrane-bound [^{3}H]CDP-DAG, and LiCl was added to prevent recycling of the intermediates. Substance P or carbachol (a muscarinic cholinergic agonist) was added to initiate the phosphoinositide (PI) response. After 45 min, slices were frozen and sectioned, and film autoradiographs were prepared. For both agonists, labeling was densest in the upper layers (I-III) of the dorsal horn. Preliminary results suggest that, during hyperalgesia, substance P-stimulated PI turnover decreased (approximately 30% relative to the contralateral dorsal horn). In contrast, carbachol-stimulated PI activity increased. Thus, hyperalgesia results in increased numbers of substance P receptors but decreased substance P-stimulated PI turnover. This difference might reflect receptor internalization or a change in linkage between substance P receptors and PI responses.

Supported by NSF IBN9221956 to H.D.S.

Abstract #59

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Jennifer A. Jenkins

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ETHANOL SUBSTITUTES FULLY FOR A DIAZEPAM-KETAMINE MIXTURE.

J. Jenkins, Y. Egilmez, B. Rocha and M. Emmett-Oglesby. Dept. Pharmacology, University of North Texas Health Science Center, Fort Worth, TX 76107

The present study tested the hypothesis that in rats trained to discriminate a mixture of diazepam (DZP, 5.6 mg/kg) and ketamine (KET, 10 mg/kg) from saline, ethanol (EtOH) would substitute fully for this training mixture. The mixture was trained using a two-lever choice procedure in which food served as a reinforcer under a fixed-ratio 10 schedule. After the discrimination was acquired, dose-effect testing showed full substitution with: the mixture, DZP alone, KET alone, pentobarbital, chlordiazepoxide and dizocilpine. In the initial experiment, EtOH fully substituted for the mixture. However, preliminary substitution tests revealed a more potent contribution of the DZP component in the mixture compared to the KET component. Thus using the same protocol, a second set of experiments involved rats trained to discriminate a mixture of a lower dose of DZP (3.2 mg/kg) with KET (10 mg/kg). In addition, substitution tests with a CNS stimulant (cocaine) and an opiate (morphine) were performed. As with the initial experiment, full substitution was seen with: the mixture, DZP alone, KET alone, pentobarbital, chlordiazepoxide and dizocilpine. However, cocaine and morphine did not substitute and EtOH partially substituted for the mixture. These data, therefore, partially support the hypothesis that simultaneous activation of GABAergic neurotransmission and blockade of glutamate neurotransmission are critical in producing an EtOH like stimulus. (Supported by R01 AA9378.)

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Nicolle R.M. Conway

Department: Department of Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

CRANIECTOMY ACTIVATES DURAL MAST CELLS, INCREASES CEREBRAL CORTICAL HISTAMINE AND ALTERS PIAL VASCULAR PERMEABILITY. Nicolle R.M. Conway, Martha E. Stokely and Edward L. Orr. Department of Anatomy and Cell Biology, U.N.T. Health Science Center at Fort Worth, Fort Worth, TX.

The dura mater contains numerous mast cells which are degranulated in response to various types of head trauma such as cryogenic lesions (Orr, 1988, *Neurochem. Pathol.* **8:**43-51) or a simple craniectomy (Olesen 1987, *Acta Physiol. Scand.* **130**:63-68. Since degranulated mast cells release large quantities of histamine (HA) and, since exogenous HA can alter the diameter and permeability of pial blood vessels (Yong, et al., 1994, *J. Neurotrauma* **11**:161-171), the possibility exists that histamine from dural mast cells may cross the meninges to enter the subarachnoid space and affect adjacent brain tissue and pial blood vessels. To test this possibility, anesthetized adult female Lewis rats were subjected to unilateral craniectomies, then killed 10 min. later. Samples of cerebral cortex and meninges subjacent and contralateral to the craniectomies were assayed for HA using a specific radioenzymatic assay. Compared to contralateral tissues, the meningeal HA concentration was 62.7 ± 11.8% (mean ± SEM, n=5) of control, while the subjacent cerebral cortical HA concentration was 452.5 ± 165.3% (mean ± SEM, n=5) of control. Since the concentration of HA in the meninges (2.13 ng/mg wet weight) is 140-fold higher than the concentration in the cerebral cortex (0.015 ng/mg wet weight), the decrease in dural HA can easily account for the increased cortical HA observed on the lesioned side of the head. The changes in histamine content were accompanied by hyperemia and increased permeability of the pial blood vessels subjacent to the craniectomy. These results suggest that HA, and possibly other products of dural mast cells, cross the arachnoid barrier and enter the subarachnoid space to affect the underlying brain and cerebral vasculature. (Supported by a grant from the National Multiple Sclerosis Society.)

Abstract #61

OCULAR

62.	T. J. Reese	AN *IN VITRO* MODEL OF THE HUMAN CORNEA
63.	Robert J. Wordinger, Ph.D.	EXPRESSION OF EGF, HGF, KGF, BASIC FGF, TGFβ1 AND THEIR RECEPTOR mRNAs IN CULTURED HUMAN TRABECULAR MESHWORK (HTM) CELLS
64.	Karen A. White	ENDOTHELIN STIMULATION OF PLC AND PLA_2 ACTIVITY IN CULTURED HUMAN CILIARY MUSCLE CELLS
65.	Bhalchandra J. Kudchodkar	EYE AQUEOUS HUMOR CONTAINS THE ENZYMES PARAOXONASE AND LECITHIN: CHOLESTEROL ACYLTRANSFERASE
66.	Yongli Kong, Ph.D.	IMMUNOCYTOCHEMICAL LOCALIZATION OF NA, K-ATPASE CATALYTIC SUBUNITS IN THE BOVINE LENS
67.	I. Kovacs	POTASSIUM DEPENDENT CONFORMATION CHANGES IN NaK-ATPASE
68.	Alberta Davis, Ph.D.	EXPRESSION OF INTEGRINS BY HUMAND MULLER CELLS IN TISSUE CULTURE IS SIMILAR TO EXPRESSION IN VIVO
69.	Scott Krueger	MECHANISM OF RETINAL CELL DEATH BY PHOTO-OXIDATIVE INSULT TO SPRAGUE DAWLEY RAT
70.	Dr. Ning Lin	AGE-RELATED PHOTORECEPTOR CELL DEGENERATION IN THE FISCHER 344 RAT IS DELAYED BY VITREAL INJECTION OF BASIC FIBROBLAST GROWTH FACTOR (bFGF)
71.	Dr. Harold J. Sheedlo	AN ANTISERUM RAISED AGAINST RPE CELL SECRETED PROTEINS IN VITRO: AN IMMUNOCYTOCHEMICAL CHARACTERIZATION IN RETINA AND RPE
72.	Dr. James E. Turner	EFFECTS OF FACTORS SECRETED BY TRANSFORMED NEONATAL RAT RPE CELLS IN RETINAL EXPLANT CULTURES AND NEONATE RETINAS
73.	Stephen Moorman	PERTUSSIS TOXIN BLOCKS THE EFFECTS OF CONTACT BETWEEN OLIGODENDROCYTES FROM THE NEONATAL RAT OPTIC NERVE *IN VITRO*

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: T.J. Reese

Department: Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff X

Read instructions and fit abstract inside the space given below:

AN *IN VITRO* MODEL OF THE HUMAN CORNEA

T.J. Reese, T. Yorio, R.W. Gracy and S.D. Dimitrijevich,

Departments of Biochemistry and Molecular Biology, Pharmacology and Surgery and North Texas Eye Research Institute. UNTHSC at Ft. Worth.

Cornea is subjected to a variety of injuries, some of which are difficult to repair and require corneal graft transplantation. We have been interested for some time in generating a model of the human cornea, which would be suitable for wound healing studies, and as a possible source for tissue/cell replacement therapy.

Human corneal endothelial and epithelial cells were harvested from donor corneas as described previously. Early passage cells were plated on the opposing surfaces of the "Stroma Equivalents" (SE), composed of collagen type I, human vitreous, and human keratocytes. These were cultured in semipermeable membrane inserts, and were sandwiched by acellular overlays of type I collagen. On these SEs were plated first the endothelial cells, and then the epithelial cells. While the endothelial surface was always submerged, epithelial differentiation took place at the air-liquid interface. The Corneal Equivalent was characterized by electron microscopy (EM) and immunofluorescence.

The corneal epithelial and endothelial cells proliferated and differentiated on the stroma equivalents. The presence of the components of the vitreous greatly improved the mechanical integrity of the model. Scanning and transmission EM demonstrated the cellular characteristics and ultrastructural features found in the human donor tissue. The expression of cytokeratin markers characteristic of the epithelium (1,3,5), and the endothelium (18,19), *in vivo* was observed.

We previously reported the construction of partial tissue equivalents of the human cornea, modeling the epithelium and the endothelium. In this presentation we discuss the parameters involved in the construction of the entire corneal model and some of its characteristics.

Supported by NIH (AG10274), and the Texas Adv. Tech. Prog. (09768-008). Supply of eye tissue by Dr. W. E. Howe (Alcon Laboratories, Inc.) and of transfected corneal endothelial cells by Dr. S.E. Wilson, (Dept. of Ophthalmol., UT Southwestern Med. Center at Dallas), is gratefully acknowledged.

Abstract #62

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Robert J. Wordinger, Ph.D.

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty_X_ Staff___

Read instructions and fit abstract inside the space given below:

EXPRESSION OF EGF, HGF, KGF, BASIC FGF, TGFβ1 AND THEIR RECEPTOR mRNAs IN CULTURED HUMAN TRABECULAR MESHWORK (HTM) CELLS. R. J. Wordinger[1], A. F. Clark[1,2], and S. E. Wilson[3] Department of Anatomy and Cell Biology and the North Texas Eye Research Institute, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX.[1]., Glaucoma Research, Alcon Laboratories, Fort Worth, TX.[2]., Eye Institute, The Cleveland Clinic Foundation, Cleveland, OH.[3]

Purpose: Elevated intraocular pressure is often associated with primary open angle glaucoma and is due to impaired aqueous humor outflow through the trabecular meshwork. Defects in the structure, function, or number of human trabecular meshwork cells (HTM) may underlie the pathophysiology of this disease. Growth factors are known to control a diverse number of biological functions. However, the role growth factors and their receptors play in the normal structure and function of HTM cells has not been extensively studied. The purpose of this study was to begin to establish which growth factors and growth factor receptors are expressed in normal, cultured HTM cells. **Methods:** Total cellular RNA isolation, cDNA synthesis, reverse transcriptase-polymerase chain reaction (RT-PCR) and agarose gel electrophoresis were performed using well characterized HTM cell lines obtained from a 48 day and a 54 year old donor. The PCR primers for specific growth factors or growth factor receptors were established using Entrez (NCBI, Bethesda, MD.) and Oligo 4.0 (National Biosciences, Inc., Plymouth, MN.). Nucleic acid sequencing was performed by cloning PCR products in the TA Cloning Vector (Invitrogen, San Diego, CA.) and sequencing with Sequenase 2.0 (United States Biochemical, Cleveland, OH.). **Results:** We detected mRNA's for hepatocyte growth factor (HGF), keratinocyte growth factor (KGF; FGF-7), epidermal growth factor (EGF), transforming growth factor β1 (TGFβ1), and basic fibroblast growth factor (FGF-2) in both cell lines. These cell lines express message for the following growth factor receptors: HGFR, KGFR, EGFR, TGFβR-1, TGFβR-2, and FGFR-1(flg). Message for an alternatively spliced form of HGFR and TGFβR-2 was detected. In addition, HGF (5 ng/ml), and EGF (10 ng/ml) were found to stimulate HTM cell proliferation in low serum media but there was no significant proliferative effect with KGF. **Conclusions:** These results indicate that HTM cells express message for several growth factors and growth factor receptors that may be important for the structure and function of the trabecular meshwork. We also show that HGF and EGF stimulate proliferation of HTM cells.

Abstract #63

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Karen A. White

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ENDOTHELIN STIMULATION OF PLC AND PLA_2 ACTIVITY IN CULTURED HUMAN CILIARY MUSCLE CELLS K. White[1], P. Magnino[2], I.-H. Pang[1,2] and T. Yorio[1] Department of Pharmacology, North Texas Eye Research Institute, University of North Texas Health Science Center at Fort Worth[1], Fort Worth, TX; Alcon Laboratories, Inc.[2], Fort Worth, TX.

Purpose: To determine if the effects of endothelin (ET) on PLC and PLA_2 activity in cultured human ciliary muscle (HCM) cells are mediated through independent ET_A receptor-coupled events.

Methods: PLC activity was measured as changes in $[Ca^{2+}]_i$ determined by single cell dynamic fluorescence ratio imaging in cells preloaded with fura-2/AM. PLA_2 activity was determined by measuring PGE_2 production by RIA.

Results: In the HCM cells, endothelin-1 (ET-1) and endothelin-2 (ET-2) increased $[Ca^{2+}]_i$. Endothelin-3 (ET-3) had no effect on $[Ca^{2+}]_i$. BQ610, an ET_A receptor subtype-selective antagonist, blocked the ET-1 and ET-2 increase in $[Ca^{2+}]_i$. IRL-1620, an ET_B receptor subtype-selective agonist, had no effect on $[Ca^{2+}]_i$ and IRL-1038, an ET_B receptor subtype-selective antagonist did not block Ca^{2+} mobilization. U73122, a phospholipase C (PLC) inhibitor, abolished the ET-1 stimulated calcium mobilization, where as the phospholipase A_2 inhibitor, AACOCF3 (at 1μM) had no effect. Manoalide, but not AACOCF3, decreased ET-1 mediated PGE_2 production and decreased $[Ca^{2+}]_i$.

Conclusions: ET-1 and ET-2 stimulate $[Ca^{2+}]_i$ in HCM cells via an ET_A receptor subtype. The increase in $[Ca^{2+}]_i$ mediated by ET-1 appears to be mediated through the phospholipase C signalling pathway, whereas the effects of ET-1 on PGE_2 production appears to be the result of an ET_A receptor coupled to PLA_2.

Abstract #64

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Bhalchandra J. Kudchodkar

Department: Biochemistry and Molecular Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

EYE AQUEOUS HUMOR CONTAINS THE ENZYMES PARAOXONASE AND LECITHIN:CHOLESTEROL ACYLTRANSFERASE. **Bhalchandra J. Kudchodkar, Pamela Brett*, Walter J. McConathy* and Andras G. Lacko. Departments of Biochemistry and Molecular Biology and Medicine*, UNTHSC, Fort Worth, Texas 76107.**

Paraoxonase (POX) and Lecithin Cholesterol Acyltransferase (LCAT) are synthesized in liver and transported in the blood, bound to high density lipoproteins (HDL), specifically to a very high density lipoprotein fraction (VHDL; d > 1.15 g/ml). Whereas LCAT is known to participate in reverse cholesterol transport (transport of cholesterol from peripheral tissue membranes to the liver for catabolism), the physiological role of POX is presently not well understood. Recent evidence suggests that POX may be involved in hydrolyzing oxidized lipids and thus protecting endothelial membranes from tissue damage. Recently, lower serum POX activity has also been found in diabetics, especially in patients whose disease advanced to neuropathy. Since diabetes may also lead to retinopathy, it was of interest to determine if POX and other HDL associated enzymes were present in eye tissue fluid. Aqueous humor from rabbits was obtained at necropsy and POX and LCAT activities were determined. Both enzymes were found to be present in the aqueous humor at a concentration between 2-7% of the plasma activities. Immunoblotting for HDL associated apolipoproteins (apos) showed the presence of apo AIV and apo E. These findings suggest that the aqueous humor of the eye contains VHDL with the associated POX and LCAT enzymes. It is hypothesized that in addition to the well known function of VHDL in reverse cholesterol transport, it may also be involved in protecting the eye tissue membrane(s) from oxidative damage.

Abstract #65

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Yongli Kong, Ph.D.

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff X

Read instructions and fit abstract inside the space given below:

IMMUNOCYTOCHEMICAL LOCALIZATION OF NA, K-ATPASE CATALYTIC SUBUNITS IN THE BOVINE LENS.

Y. Kong and M. H. Garner, Department of Anatomy and Cell Biology and North Texas Eye Research Institute, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX, 76107

Purpose. The Na, K-ATPases are plasma membrane bound enzymes which maintain the lens Na^+ and K^+ gradients. Since Na, K-ATPase destruction would appear to the common in cataract, the studies of the distribution and localization of Na, K-ATPases should be an essential step to resolve the mechanism of cataract formation. **Methods.** Cultured central lens epithelial cells (CLE) and cryosections of adult bovine lens were used as materials. Rabbit antibodies for α1, α2, α3 N-terminus (α1NT, α2NT, α3NT) and α1, α2, α3 ouabain site (α1OS, α2OS, α3OS) were incubated with cultured cells or cryosections. Normal rabbit serum was used as a control. They were incubated again with FITC-goat anti-rabbit IgG and observed with an immunofluorescence microscope. **Results.** In the cultured cells, the positive immunofluorescence was found for α1NT and α3OS antisera but negative for α1OS and α3NT antisera. In the cryosections, the positive immunofluorescence was located in the epithelial cells of anterior and equatorial parts with α1NT, α2NT, α1OS, α2OS, α3OS. The specific positives were detected in the apical and lateral membrane of epithelial cells for α1OS but lateral membrane for α3OS antisera. The lens fiber cells (LFC) specifically stained with α2OS antibody. **Conclusions.** The results of cultured LEC suggested that Na, K-ATPases catalytic subunits presented quite different immunoreactivities between N-terminus and ouabain site. In the cryosections, different membrane binding of CLE suggested a polarization of the CLE. Specific binding of α2OS to LFC confirm the importance of the LFC Na, K-ATPases in lens monovalent cation homeostasis.

Abstract #66

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: I. KOVÁCS

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

POTASSIUM DEPENDENT CONFORMATION CHANGES IN NaK-ATPASE I. Kovacs, M. H. Garner, Dept. of Anatomy and Cell Biology, Univ. of North Texas Health Science Center, Fort Worth, Texas 76107

The potassium induced pNPPase activity of NaK-ATPase from rabbit kidney was studied at different sodium and potassium concentrations. The temperature dependence of the kinetics also was measured in the temperature range from 278°K to 313°K by applying a fast linear temperature scan. The potassium occlusion was monitored with the potential-sensitive membrane probe RH421. Without Na the pNPPase activity increases with increasing K concentration and saturates at about 8 mM [K]. There is an intermediate plateau from 8 to 80 mM [K]. At higher potassium concentration the activity gradually drops. Beyond 300°K the temperature dependence of the kinetics could be described by the Arrhenius relationship. Below the saturation potassium concentration both the activation enthalpies and the relative entropies are small. Beyond the saturating potassium concentration the entropy increases considerably. The drop of the activity at high potassium concentration is associated with an increase of the activation enthalpy.

Abstract #67

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Alberta Davis, Ph.D.

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

EXPRESSION OF INTEGRINS BY HUMAN MULLER CELLS IN TISSUE CULTURE IS SIMILAR TO EXPRESSION IN VIVO.

A.A. Davis, S.E. Brady, J.E. Turner and M.H. Chaitin. Dept. of Anatomy and Cell Biology and North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, TX 76107

In proliferative vitreoretinopathy (PVR) Muller cells migrate into the vitreous where they participate in the formation of membranes which cause traction detachment of the retina. Integrins are involved in cell-cell contact and cell substratum adhesion. We wished to determine if human Muller cells express different integrins *in vitro* than in *vivo* since they adopt a migratory function during this pathology. For sections, eyes from human donors (Ft. Worth Lions Eye Bank) were fixed in Bouins. The tissue was dissected and embedded in paraffin. Sections were deparaffinized, rehydrated in alcohols, blocked and reacted with a dilution of one of the following anti-integrin antibodies: $\beta_{1,2,3}$, and $\alpha_{1,2,3,4,5,6,v}$, followed by a biotinylated second antibody conjugated to HRP. Muller cells in tissue culture were isolated from Eye Bank donors. Neural retinae were washed several times in HBSS, cut in small pieces (~ 3mm) and triturated in a 1.0ml pasteur pipet and seeded in laminin, fibronectin, collagen-coated six well plates. Cells were seeded on glass coverslips, fixed in either acetone/methanol (50:50) or 2% paraformaldehyde, blocked and reacted with the above anti-integrin antibodies and the appropriate FITC-conjugated second antibody. Human Muller cells in vitro express: $\beta_{1,2,3,}$ and $\alpha_{1,2,v}$. Although staining of tissue sections does not allow unequivocal identification of Muller cell staining only, human retina sections stained positive for $\beta_{1,2,3}$ and $\alpha_{1,2,5,v}$. There does not appear to be any difference in the expression of integrins by human Muller cells in normal human eyes from that seen in Muller cells grown in tissue culture. Staining for α_5 on sections gave a specific staining pattern in the photoreceptor cell body which indicates it is not likely expressed on Muller cells *in vivo*. Interestingly, on retinal sections, β_2 integrin was detected on Muller cell apical microvilli at the OLM and on processes in the nerve fiber layer.
Supported by NIH Grants EY04337 awarded to JET and EY06590 awarded to MHC.

Abstract #68

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Scott Krueger

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

MECHANISM OF RETINAL CELL DEATH BY PHOTO-OXIDATIVE INSULT TO SPRAGUE DAWLEY RAT. DS Krueger[1,2], N Agarwal[1], E Martin[2], MJ Rooney[1], RJ Wordinger, and RJ Collier[1,2]
University of North Texas Health Sciences Center[1], Fort Worth, TX 76107; Alcon Laboratories[2], Fort Worth, TX 76134.

Purpose. Photo-oxidative insult has been well established as inducing apoptosis in retinal tissue. The purpose of these experiments was to elucidate mechanism(s) of apoptosis by measuring changes in retinal structure and proto-oncogene expression resulting from photo-oxidative stress. **Methods**. Albino Sprague Dawley rats were dark adapted for 24-hours and then exposed to continuous broad-band white light (900 ft.cd.) for 48-hour (h). Animals were then permitted to recover in dark for up to 14 days prior to sacrifice. Six animals from each group were sacrificed at 12, 24, and 48 hours of exposure (E) and at days 1, 2, 7 and 14 post-exposure in dark recovery (R). Retinal tissues were prepared for morphological, immunocytochemical (clusterin, arrestin) or Bcl-2 and Bax (RT-PCR) evaluation. **Results**. Histologic evaluation demonstrated a significant increase in pyknotic photoreceptor cell number after 12hE. Significant decreases on ONL and RPE thickness, IS+OS length, and a significant increase in macrophages in the subretinal space occurred at 48hE. Bax/Bcl-2 ratio peaked at 12hE which coincided with the appearance of pyknotic photoreceptor nuclei. Clusterin expression was observed to be associated initially (2hE) with the IS of the photoreceptor and moved into the ONL at later time points. Arrestin was localized in the OS and synaptic regions in Controls and in the ONL in light damaged animals. **Conclusions**. Changes in Bcl-2 and Bax gene expression in the retina resulted from photo-oxidative stress. Arrestin expression in the synaptic region was lost as a result of light exposure. Changes in clusterin expression occurred early in response to photo-oxidative stress and preceeded pyknotic photoreceptor changes. (Supported by Alcon Laboratories, Inc.).

Abstract #69

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Dr. Ning Lin

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow_X_ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

AGE-RELATED PHOTORECEPTOR CELL DEGENERATION IN THE FISCHER 344 RAT IS DELAYED BY VITREAL INJECTION OF BASIC FIBROBLAST GROWTH FACTOR (bFGF). N. Lin, W. Fan, H.J. Sheedlo and J.E. Turner. Department of Anatomy and Cell Biology, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas 76107.

Basic fibroblast growth factor (bFGF) was injected into the vitreous of adult Fischer 344 rats, which exhibit an age-related photoreceptor cell loss, and retinas were analyzed by light microscopy. Sixteen male Fischer rats aged 16 months were injected intraviteally with 2.0µg bFGF in right eyes, while vehicle was injected into left eyes. Eight rats were sacrificed two months post-injection. The remaining eight rats were injected again two months later, then sacrificed 2 months later. After enucleation, eyes were fixed for light microscopic and morphometric analyses. The distance from the ora serrata to the region of an intact photoreceptor layer, called the die-back zone, in superior retinas of 20-month-old rats with two-bFGF injections was significantly shorter than that in respective sham-injected retinas ($p < 0.01$). However, there was no significant difference in this region when comparing the single-bFGF injected retinas with their sham-control retinas ($P > 0.05$). In addition, the thickness of the outer nuclear layer in retinas at a distance of 2 and 3 mm from the ora serrata in the two-bFGF injected eyes was significantly thicker than that in sham-injected eyes ($p < 0.05$), but not in the single-bFGF injected eyes ($P > 0.05$). These findings reveal that bFGF administration to eyes of aged Fischer rats significantly delayed the progress of the age-related peripheral retinal degeneration, which suggests that bFGF acted as a survival-promoting and/or neurotrophic factor in the aged retina. (Supported by NIH grant EY04337).

Abstract #70

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Dr. Harold J. Sheedlo

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty_X_ Staff___

Read instructions and fit abstract inside the space given below:

AN ANTISERUM RAISED AGAINST RPE CELL SECRETED PROTEINS IN VITRO: AN IMMUNOCYTOCHEMICAL CHARACTERIZATION IN RETINA AND RPE. H.J. Sheedlo, A.A. Davis and J.E. Turner. Department of Anatomy and Cell Biology, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas 76107.

An antiserum was generated against proteins secreted by transformed neonatal rat (tnr) retinal pigment epithelial (RPE) cells and we determined its specificity, cellular distribution and nullification effects in retinal explant cultures and *in vivo*. The antigen consisted of proteins from conditioned media (CM) of tnrRPE-cell cultures. Western blot determined the specificity of the antiserum, we call RPE-SP, in rat and human RPE-CM and its distribution was shown by immunocytochemistry in rat and human RPE and normal and Royal College of Surgeons (RCS) dystrophic rat retinas. The antiserum alone and when mixed with the tnrRPE-CM was tested in explant cultures and injected into the vitreous of rat neonates. Probing CM from normal and transformed rat and human RPE with the antiserum revealed primarily one band which migrated to 67kDa. Cytoplasmic vesicles surrounding nuclei and within processes of cultured normal and transformed rat and human RPE cells were immunolabelled by this antiserum. In retinas of adult rats and humans, this antiserum densely immunostained RPE and ganglion cells, while neonate retinas had light diffuse immunoreactivity. In retinas of 2-month-old RCS rats, intense immunolabelling was observed in the outer retina, determined to be photoreceptors, as well as in RPE and ganglion cells. The number of immunolabelled ganglion cells decreased in retinas of older RCS rats. The antiserum eliminated the stimulatory effects of tnrRPE-CM on retinal explants and caused retinal degeneration after only 7 days, when injected into the vitreous of rat neonates. The RPE-SP antiserum described here eliminated the *in vitro* and *in vivo* biological activity of tnrRPE-CM and indicates that an RPE-derived retina trophic factor (RPE-RTF) may be essential for retina development and survival. (Supported by NIH grant EY04337).

Abstract #71

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Dr. James E. Turner

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

EFFECTS OF FACTORS SECRETED BY TRANSFORMED NEONATAL RAT RPE CELLS IN RETINAL EXPLANT CULTURES AND NEONATE RETINAS. J.E. Turner and H.J. Sheedlo. Department of Anatomy and Cell Biology, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas 76107.

Factors secreted by transformed neonatal rat (tnr) retinal pigment epithelial (RPE) cells were studied in retinal cell cultures and explants and in neonatal rat eyes and were fractionated by high pressure liquid chromatography (HPLC). Retinal explants and dissociated retinal cells from postnatal day 2 (PN2) rats were supplemented with conditioned media (CM) from tnrRPE-cell cultures. Explants grown in RPE-CM were dissociated into single cells, then studied by opsin immunocytochemistry. Vitreal RPE-CM injections were performed in PN7 rats and eyes were analyzed by light microscopy. RPE-CM was also fractionated using HPLC. Retinal explants grown in RPE-CM showed neurite outgrowth and progenitor cells within 2-3 days. About 90% of cells dissociated from explants grown in RPE-CM immunostained for opsin, while only 20% of cells isolated from explants grown in 10% serum and defined media were opsin positive. Cells isolated from PN2 rat retinas proliferated 3-6 fold after 3 days in the presence of RPE-CM. In addition, eyes of 14-day-old rats injected with RPE-CM at day 7 showed accelerated differentiation as shown by hyperplasia within the outer and inner nuclear layers and an increased number of ganglion cells. Fractionation of RPE-CM by HPLC revealed a fraction that contained a 67kDa band that had biological activity. Retinal progenitor cells from PN2 explants were also caused to proliferate in the presence of RPE-CM. The tnrRPE cells secrete a factor(s) that caused proliferation of retinal cells, neuroepithelial cells, and progenitor cells within 3 days. The RPE-CM has a factor that affected the development of neonate retinas and explant cells. We call this putative factor the RPE-derived retinal trophic factor (RPE-RTF). (Supported by NIH grant EY04337).

Abstract #72

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: STEPHEN MOORMAN

Department: ANATOMY

Undergraduate or Medical Student___ Graduate Student___ Postdoctoral Fellow___ Faculty X Staff___

Read instructions and fit abstract inside the space given below:

PERTUSSIS TOXIN BLOCKS THE EFFECTS OF CONTACT BETWEEN OLIGODENDROCYTES FROM THE NEONATAL RAT OPTIC NERVE *IN VITRO*.

Stephen J. Moorman, Department of Anatomy and Cell Biology.

When an extract of CNS myelin is placed in contact with an oligodendrocyte, the oligodendrocyte's growth cones (oligo-GCs) collapse and retract. This morphological change is accompanied by an increase in internal free calcium concentration ([Ca]i) in the oligo-GC. Since myelin is a product of differentiated oligodendrocytes, those results suggested that oligodendrocytes might be able to recognize and react to specific molecules on the surface of other oligodendrocytes. However, it remained possible that the initial observation was relevant only to contact between an oligodendrocyte and myelin-extract, possibly even contact with molecules that are inaccessible to oligodendrocytes *in vivo*. Therefore, the *in vitro* interactions between neonatal-rat oligodendrocytes from the optic nerve were examined. Spontaneous and manipulated contact between oligodendrocytes resulted in collapse of the fine structure of the oligo-GC *in vitro*. This inhibition of oligodendrocyte motility was preceded by a substantial (approximately threefold) increase in intracellular free calcium concentration. The calcium concentration increase was due, at least in part, to a release of calcium from internal stores, since it persisted when extracellular calcium was removed by chelation by EGTA. The contact-induced calcium increase was blocked by the combination of EGTA and thapsigargin. In addition, the calcium increase and the coincident morphological change were blocked by pertussis toxin. The increase in calcium concentration and the coincident morphological change suggest that oligodendrocytes are able to recognize and react to specific molecules on the surface of other oligodendrocytes. These types of inhibitory responses on the part of oligodendrocytes could be limiting remyelination in the optic nerve. Moreover, the similarity of this response to the response of oligodendrocytes to contact with myelin supports the idea that molecules present in myelin might be used in intercellular communication between oligodendrocytes.

Abstract #73

STUDENT ORAL PRESENTATION COMPETITION

(1:30)	Matthew Crawford	ARRESTIN EXPRESSION RESULTS IN CELL DEATH OF CULTURED PHOTORECEPTOR CELLS
(1:45)	Cheng Zhou	CHARACTERIZATION OF THE HYPERTONIC-SENSITIVE PROMOTER THAT MEDIATES ENHANCED TRANSCRIPTION OF THE Na^+/MYO-INOSITOL COTRANSPORTER GENE IN RESPONSE TO HYPEROSMOTIC STRESS
(2:00)	Karla R. Davis	DEVELOPMENT OF A NON-INVASIVE MOLECULAR DIAGNOSTIC TEST FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)
(2:15)	Gustavo Pacheco	DISTRIBUTION OF POLY (ADP-RIBOSE) GLYCOHYDROLASE IN DIFFERENT SUBNUCLEAR FRACTIONS
(2:30)	Kimberly Krueger	CALCIUM-STIMULATED PHOSPHORYLATION OF MAP-2 IN PANCREATIC β-CELLS IS MEDIATED BY CaM KINASE II
(2:45)	Johnathan D. Tune	INCREASED GLUCOSE UPTAKE IS NOT RESPONSIBLE FOR INCREASED OXYGEN UTILIZATION EFFICIENCY DURING MODERATE CORONARY HYPOPERFUSION IN CANINE MYOCARDIUM
(3:00)	Wayne W. Loney	THE EFFECTS OF GEMFIBROZIL TREATMENT ON LOW AND HIGH DENSITY LIPOPROTEINS AND PREDICTIVE RESPONSE WITH LIPOPROTEIN SUBFRACTIONS
(3:15)	Kyle P. May	INTERACTIVE EFFECTS OF HYPOXIA AND HYPERCAPNIA ON SYMPATHETIC NERVE ACTIVITY IN HUMANS
(3:30)	Rob D. Dickerman	EXTRAHYPOTHALAMIC REGULATION OF VASOPRESSIN BY STEROIDS
(3:45)	Linda Odom	CLASSICAL CONDITIONING AND SENSITIZATION TO COCAINE IN MICE
(4:00)	Marianna E. Jung	SEX DIFFERENCES IN THE ANXIOGENIC STIMULI INDUCED BY GABAERGIC AND SEROTONERGIC DRUGS
(4:15)	Alayne D. Kulvicki	EVALUATING NURSING HOME RESIDENTS' ABILITY TO SELF-REPORT THE OCCURRENCE OF DAILY EVENTS

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Matthew Crawford

Department: Department of Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

ARRESTIN EXPRESSION RESULTS IN CELL DEATH OF CULTURED PHOTORECEPTOR CELLS ((M. Crawford, V. L. Rudick, R. J. Wordinger, Harold Sheedlo, M. Rooney, N. Agarwal, and M. R. Al-Ubaidi*.)) Department of Anatomy and Cell Biology, North Texas Eye Res. Inst., UNT Health Science Center, Fort Worth, TX, and *Department of Ophthalmology and Visual Sciences, Univ. of Illinois, Chicago, IL.

Purpose. The photoreceptors in the *rds* model of retinal dystrophy undergo apoptosis. However, the primary gene defect in retinal dystrophies is not sufficient to warrant the ultimate end-point, i.e., death. Therefore, to explain a possible mechanism of photoreceptor cell death, we are investigating other genes whose activities may be altered in the *rds* mouse as a result of the primary mutation. We have previously reported a loss of arrestin diurnal rhythm in *rds* mutant retinas. High levels of arrestin were present in the mutant retina throughout the light/dark (L/D) cycle (Agarwal et al., Exp. Eye Res., 1994). **Methods.** To study the effect of elevated levels of arrestin, we transfected cultured photoreceptor cells (661W) with a mini gene composed of the mouse cDNA under the CMV promoter by the calcium-phosphate DNA precipitation method. The 661W cells express opsin and were immortalized by the expression of SV40 T-antigen driven by an IRBP promoter in a transgenic mouse model. The plasmid DNA without arrestin cDNA was used as a control. Cells were fixed in 4% paraformaldehyde 72 hr after transfection and subjected to (a) TUNEL staining for apoptosis, (b) immunocytochemistry for arrestin or (c) co-localization for TUNEL and arrestin. RT-PCR for Bcl-2 and Bax. **Results.** The cells transfected with mouse arrestin or Drosophila arrestin gene undergo cell death and arrestin could be detected with TUNEL positive cells. They also had lower levels of Bcl-2 with no change in Bax mRNA levels. **Conclusions.** Transfection of arrestin in cultured photoreceptor cells results in lowering of Bcl-2 and apoptosis of 661W cells. And thus high arrestin expression throughout the L/D cycle in *rds* mutant retinas may indeed be one of the factors driving the cells toward death via apoptosis. None

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Cheng Zhou

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

CHARACTERIZATION OF THE HYPERTONIC-SENSITIVE PROMOTER THAT MEDIATES ENHANCED TRANSCRIPTION OF THE Na^+/MYO-INOSITOL COTRANSPORTER GENE IN RESPONSE TO HYPEROSMOTIC STRESS C. Zhou and P.R. Cammarata. Department of Anatomy and Cell Biology, University of North Texas Health Science Center/North Texas Eye Research Institute, Fort Worth, TX 76107.

The hypertonic-induced enhancement of myo-inositol (MI) uptake activity is preceded by augmentation of transcription and abundance of the Na^+/MI cotransporter mRNA. We previously identified multiple transcription start sites for the Na^+/MI cotransporter mRNA in cultured bovine lens epithelial cells (BLECs) based on 5'-RACE analysis. Besides two isotonic transcription start sites, hypertonicity causes preferential utilization of a third transcription start site further upstream. To analyze the mechanism of transcriptional regulation by tonicity, the bovine Na^+/MI cotransporter gene was cloned and the 5'-flanking region of the gene was characterized. A bovine genomic library was screened using a 5'-untranslated region (UTR) specific probe and a cDNA probe encoding the 3'-end of the open reading frame (ORF). Nucleic acid sequence of the gene was determined using the dideoxynucleotide method. Sequence analysis of the cloned bovine Na^+/MI cotransporter gene revealed an intron in the 5'-UTR but the ORF was intron-free. Various fragments of the 5'-flanking regions upstream of the individual transcription start sites were fused upstream of the luciferase reporter gene. Transient transfection assays in cultured BLECs maintained in isotonicity or hypertonicity were used to determine the promoter activities of these 5'-flanking regions. The 5'-flanking regions upstream of the hypertonic transcription start site displayed four fold induction of promoter activity upon osmotic insult. The results of various length of the 5'-flanking regions upstream of the hypertonic transcription start site indicated the existence of multiple cis elements. However, osmotic stress showed little effect on the promoter activities of the 5'-flanking regions upstream of the isotonic transcription start sites (hs/iso=1.3). This is the first report of the cloning of a Na^+/MI cotransporter gene. Transient transfection analysis identified a tonicity-responsive promoter whose selective utilization contributes to the induction of the Na^+/MI cotransporter mRNA by hypertonicity. (EY05570 PRC)

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Karla R. Davis

Department: Anatomy and Cell Biology

Undergraduate or Medical Student___ Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

DEVELOPMENT OF A NON-INVASIVE MOLECULAR DIAGNOSTIC TEST FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)

K.R. Davis[1] , J.M. Sherman[2] , A.J. Eisenberg[2]

[1] Department of Anatomy and Cell Biology, University of North Texas Health Science Center-Fort Worth, Texas 76107
[2] Department of Pathology, University of North Texas Health Science Center-Fort Worth, Texas 76107

Attention Deficit Hyperactivity Disorder (ADHD) has been presented in research literature as a polygenic, or multiple gene disorder. Currently, three genes have been associated with ADHD, dopamine receptor D_2 (DRD_2), dopamine transporter (DAT_1), and dopamine beta hydroxylase (DBH). The primary objective of this study is to analyze the DRD_2, DAT_1, and DBH genes to determine if a positive correlation exists between certain allelic variations of these three genes and the clinical psychological diagnosis of ADHD. Approximately 3000 subjects will be enrolled in this study from a combination of schools in the San Antonio ISD and the ADHD department of the Child Study Center located in Fort Worth. We have developed an assay for the DRD_2, DAT_1, and DBH genes, utilizing polymerase chain reaction (PCR) technology. Within the DRD_2 gene, two allelic variants have been identified, the A_1 and A_2 alleles. The A_1 allele consists of a 310 bp fragment in which the Taq I restriction site has been deleted. The A_2 allele consists of a 180 bp fragment and a 130 bp fragment of the original 310 bp fragment. The presence of the A_1 allele after enzyme digestion has shown a strong correlation with ADHD. With respect to the DAT_1 gene, previous studies have shown that the presence of a 480 bp fragment following amplification by PCR is positively correlated with a clinical diagnosis of ADHD. Analysis of the DBH gene consists of a determination of the presence or absence of a Taq I polymorphism within the gene. The presence of the allelic form with the Taq I site has been noted in ADHD as well as Tourette Syndrome and a spectrum of other neuropsychiatric disorders. Currently data is continuing to be collected and analyzed with respect to the dopamine family of genes. Preliminary results strongly indicate a positive correlation between the DAT_1 allele and ADHD, with approximately 95% of subjects exhibiting the 480 bp allele. DRD_2 is also suggestive of a positive correlation with 51% of subjects presenting with the A_1 allele, indicating a deletion of the Taq I restriction site. Studies and results for the DBH gene are still pending as are further studies on both the DAT_1 and DRD_2 genes.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Gustavo Pacheco

Department: Microbiology and Immunology

Undergraduate or Medical Student___ Graduate Student__X__ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

DISTRIBUTION OF POLY(ADP-RIBOSE) GLYCOHYDROLASE IN DIFFERENT SUBNUCLEAR FRACTIONS. [λ]G. PACHECO-RODRIGUEZ, and *R. ALVAREZ-GONZALEZ. *Depts. of [λ]Biochem. & Mol. Biol. and *Microbiol. and Immunol., University of North Texas Health Science Center at Fort Worth, Fort Worth, Texas 76107-2699.

The poly(ADP--ribosyl)ation of DNA-binding proteins is a reversible post-translational pathway that is elicited in the cell nucleus by genotoxic agents that lead to the formation of breaks on DNA. Protein-bound ADP-ribose polymers are synthesized by poly(ADP-ribose) polymerase (PARP) [E.C. 2.4.2.30] and degraded by poly(ADP-ribose) glycohydrolase (PARG) *in vivo*. Here, we have determined the distribution of PARG activity in distinct functional domains of the cell nucleus. Nuclei were isolated from rat liver tissue and fractionated into separate chromatin, nuclear envelope, and nuclear matrix structures by: i) endogenous endonuclease digestion (to eliminate most of the chromosomal DNA); ii) low salt and high salt treatments (to extract histone and non-histone proteins); and iii) a Triton X-100 detergent extraction (to separate the nuclear envelope from the nuclear matrix fraction). The identity of these structures was confirmed by the biochemical analysis of their protein components following SDS-polyacrylamide gel electrophoresis (PAGE) and Coomassie blue staining. The total amount of PARG activity associated with each fraction was determined by high resolution PAGE, autoradiography and densitometric analysis of the [^{32}P]radiolabeled ADP-ribose formed utilizing protein-free ADP-ribose polymers of 2-70 residues in size as a substrate. Our assay was highly specific and sensitive to the femtomole level. Excellent reproducibility was observed with both, crude extracts of eucaryotic nuclei and purified PARG. Our results show that roughly equivalent amounts (35-45%) of the total PARG activity were associated with chromatin and the nuclear envelope. By contrast, a smaller portion of the enzyme (10-20%) was obtained with the nuclear matrix fraction. We also observed that pure histones and nuclear matrix proteins inhibited the activity of purified PARG. Therefore, this phenomenon has to be taken into consideration for the accurate measurement of PARG activity in both chromatin and the nuclear matrix. (This project was supported by grants GM45451 from NIH and 9678-014 from the Texas Advanced Research Program.)

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Kimberly Krueger

Department: Biochemistry & Molecular Biology

Undergraduate or Medical Student___ Graduate Student__X__ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

CALCIUM-STIMULATED PHOSPHORYLATION OF MAP-2 IN PANCREATIC β-CELLS IS MEDIATED BY CaM KINASE II. K.A. Krueger, H. Bhatt, M. Landt and R.A. Easom, University of North Texas Health Science Center, Fort Worth, TX 76107 and Washington University School of Medicine, St. Louis, MO 63110.

An elevation of intracellular Ca^{2+} is a critical signal in the initiation of insulin secretion from the pancreatic β-cell but the mechanism involved is not understood. Previously, we have demonstrated that the multifunctional Ca^{2+}/calmodulin-dependent protein kinase II (CaM kinase II) is activated by glucose implicating this enzyme in the secretory process, but its cellular targets are unidentified. One of the best substrates of CaM kinase II *in vitro* that could function in secretory events, is the microtubule-associated protein, MAP-2. The current study represents an evaluation, *in situ*, of MAP-2 as a substrate of CaM kinase II using a permeabilized β-cell model. By immunoblot analysis, the presence of MAP-2 in the βTC3 cell was established. In α-toxin-permeabilized βTC3 cells, Ca^{2+} induced the concentration-dependent activation of CaM kinase II. In parallel and by immunoprecipitation, Ca^{2+} also induced the phosphorylation of MAP-2 that closely correlated with CaM Kinase II activation. Ca^{2+}-induced phosphorylation of MAP-2 was not inhibited by an inhibitor of protein kinase A (H89) at concentrations that prevented phosphorylation induced by forskolin. These data provide evidence that MAP-2 is phosphorylated by CaM kinase II in the pancreatic β-cell *in situ*, and that this event may provide an important link in the mediation of Ca^{2+}-dependent insulin secretion. (Supported by NIH grant DK-47925).

Submit to Laura Barber, Graduate School of Biomedical Sciences DEADLINE: March 1, 1996

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Johnathan D. Tune

Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

INCREASED GLUCOSE UPTAKE IS NOT RESPONSIBLE FOR INCREASED OXYGEN UTILIZATION EFFICIENCY DURING MODERATE CORONARY HYPOPERFUSION IN CANINE MYOCARDIUM

Johnathan D. Tune, Masao Itoya, Robert T. Mallet, H. Fred Downey. Department of Integrative Physiology, University of North Texas Health. Science Center, Fort Worth, TX. 76107

A mismatch in myocardial O_2 supply and demand may be restored by decreasing myocardial power or by increasing O_2 utilization efficiency. This study tested the hypothesis that O_2 utilization efficiency is improved by increased glucose uptake during reductions in coronary perfusion pressure, since oxidation of glucose requires 12% less O_2 than fatty acids. Coronary perfusion pressure was lowered from 100 to 60 and to 40 mmHg in the left anterior descending coronary artery of 10 anesthetized open chest dogs. Glucose uptake, power index (PI: heart rate x left ventricular systolic pressure x regional segment shortening), and O_2 utilization efficiency (PI / MVO_2) were determined during control (n = 6) and intracoronary insulin (4 U / min, n = 6). MVO_2 significantly decreased ($p < 0.001$) as coronary perfusion pressure was reduced in both groups. Without insulin, O_2 utilization efficiency increased 11% ($p < 0.35$) at coronary perfusion pressure = 60 mmHg, but decreased 260% with considerable dyskinesia at coronary perfusion pressure = 40 mmHg. With insulin, O_2 utilization efficiency was not significantly altered when coronary perfusion pressure was reduced to 60 or 40 mmHg. ($p = 0.71$). Glucose uptake was increased by insulin at all perfusion pressures ($p < 0.001$), and PI was substantially higher at coronary perfusion pressure = 40 mmHg in insulin treated hearts. Glucose uptake was not significantly changed by reduced coronary perfusion pressure in either condition ($p > 0.1$). Thus, insulin stimulates myocardial glucose uptake at all coronary perfusion pressures and attenuates decreases in O_2 utilization efficiency and PI at more severe reductions in coronary perfusion pressure. However, oxygen utilization efficiency in not enchanced by increased myocardial glucose uptake during moderate coronary hypoperfusion. (Supported by NIH HL35027, HL50441 and Tex. Ad. Res. Prog. 9768).

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: WAYNE W. LONEY

Department: BIOMEDICAL SCIENCE

Undergraduate or Medical Student___ Graduate Student ✓ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

THE EFFECTS OF GEMFIBROZIL TREATMENT ON LOW AND HIGH DENSITY LIPOPROTEINS AND PREDICTIVE RESPONSE WITH LIPOPROTEIN SUBFRACTIONS.

Wayne W. Loney, Bhalchandra J. Kudchodkar, Stephen Weis, Michael B. Clearfield, Jay Shores and Andras G. Lacko. Department of Biomedical Science, University of North Texas Health. Science Center, Fort Worth, TX. 76107

Subjects with high density lipoprotein cholesterol (HDL-C) values less than 47 mg/dl (mean 35 ± 5.5 mg/dl) were selected for this study to determine those metabolic factors that influence the efficacy of gemfibrozil therapy for raising HDL. Changes in plasma low (LDL) and high density lipoprotein subfractions were examined to better understand the variability of the responses seen previously (S. Weis et al. Artery 19:353-367 [1992]) and to gain a better understanding of the metabolic events during gemfibrozil therapy. Serum samples were analyzed at the outset and following the conclusion of twelve weeks of gemfibrozil therapy. Because the HDL-C response was highly variable, the data from patients were assigned into two subgroups: designated as responders (> 20% increase in HDL-C) and non-responders (< 20% increase in HDL-C). In the responder group, there was a significant correlation between the changes in HDL-C and the lowering of triglycerides (TG) ($r = 0.61$; $p = 0.03$) while the non-responder group showed no such correlation ($r = 0.17$; $p = 0.52$). Multiple regression analysis was used to descriminantly predict the group classification with 78% accuracy using specific lipoprotein subfractions to estimate an individuals percent change in HDL-C. Differences in the changes in lipoprotein lipids suggest that the non-responder group had a higher potential for hepatic triglyceride lipase (HTGL) activity that resulted in the lower or negative response to gemfibrozil therapy. (Support provided by the Research Bureau of the American Osteopathic Association Grant# 89-11-299, Warner-Lambert/Park-Davis and the Office of Research at UNTHSC).

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Kyle P. May

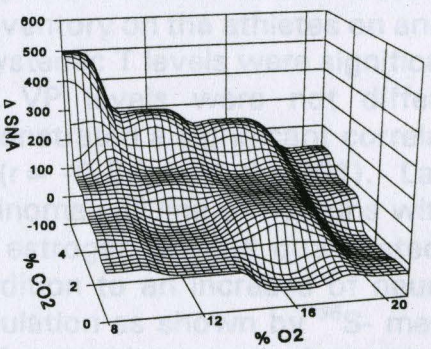
Department: Integrative Physiology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

Interactive Effects of Hypoxia and Hypercapnia on Sympathetic Nerve Activity in Humans. May, K.P., *M.E. Dibner-Dunlap, M.L. Smith, Dept. of Integrative Physiology, UNTHSC at Fort Worth, TX and *Dept. of Medicine, Case Western Reserve University, Cleveland, OH 44106.

Hypoxia and hypercapnia can provoke chemoreflex-mediated vasopressor effects. Previous studies have shown that hypoxia and hypercapnia produce facilitatory interactive effects on carotid body afferent nerve activity; however, it is not known whether similar interactions are manifest in the control of efferent sympathetic nerve activity and vascular resistance. The combined effects of hypoxia and hypercapnia on the sympathetic nervous system were investigated in nine healthy subjects by having them breathe a four by four matrix of hypoxic (21%, 16%, 12%, 8%) and hypercapnic (0%, 2%, 4%, 6%) gas mixtures. **Methods**: Sympathetic nerve activity (SNA microneurography), oxygen saturation (pulse oximetry), arterial pressure (photoplethysmography), end tidal CO_2 (capnometer), and tidal volume (integrated pneumotach) were measured continuously before and while breathing each gas mixture for 90 seconds. Changes in SNA over a prior baseline period for each gas mixture were determined. SNA also was segmented into low lung volume phases and high lung volume phases to investigate the modulation of SNA by respiratory phase. **Results**: Main effects were significant for hypoxia ($p<0.05$) and hypercapnia ($p<0.01$), and the between group interaction was significant. This facilitory interaction is apparent from the data shown in the figure. **Conclusions**: These data support the hypothesis that combining low levels of hypoxia and hypercapnia facilitate a greater increase in SNA than their separate combined effects. This interaction is even more striking during periods of low lung volumes due to both the lack of lung inflation receptor inhibition and hemodynamic effects.



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UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Rob D. Dickerman

Department: Biochemistry and Medicine

Undergraduate or Medical Student X Graduate Student X Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

EXTRAHYPOTHALAMIC REGULATION OF VASOPRESSIN BY STEROIDS. R. Dickerman, N. Zachariah, P. Brett, T. Fungwe, R. Pertusi, and W. McConathy. Departments of Biochemistry and Medicine, UNTHSC, Ft. Worth, TX, 76107.

Aging of the brain has been associated with cellular atrophy and cell death. Sex differences in aging brain have been documented by magnetic resonance imaging, suggesting age-related changes in neuronal systems may be due in part to changes in the hormonal milieu. Age-related decline of systemic sex hormones is one of the most consistent findings in aging. The objective of this study was to relate sex hormones levels to neuronal function and behavior. It has been demonstrated in the rat that hypothalamic vasopressinergic neurons are responsible for many of the behaviors that are impaired in aging, including social memory, temperature regulation and conditioned avoidance behavior. Vasopressin (VP) content and VP mRNA in rat neurons all show a marked decline in senescence. Testosterone (T) can reverse this decline in extrahypothalamic VP mRNA in rats. VP nerve fiber density is reduced by castration and restored with T replacement therapy. Thus, we measured systemic VP and T by RIA in elderly males, athletes with elevated T levels and an age-matched control group with normal T levels. Secondly, we performed Beck depression inventory on the athletes on and off testosterone treatment. While systemic T levels were significantly different between the groups, VP levels were not different. Athletes on/off T treatment demonstrated a significant correlation with the Beck depression score ($r = -0.85$, $p < 0.0001$). Lastly, we incubated a human tetracarcinoma cell line of neurons with T, dihydrotestosterone (DHT), and estrogen (E) and quantitated VP secretion into the media. In addition to an increase of neuronal protein synthesis with DHT stimulation as shown by ^{35}S- methionine labeling, both T and DHT treated neurons demonstrated elevations in vasopressin secretion, while VP secretion in E treated neurons paralleled controls. Thus androgens regulate VP secretion at the neuronal level. VP regulation by androgens could be associated with subsequent behavioral alterations.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: LINDA ODOM

Department: PHARMACOLOGY

Undergraduate or Medical Student___ Graduate Student ✓ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

CLASSICAL CONDITIONING AND SENSITIZATION TO COCAINE IN MICE,

Odom, L. A. and Forster, M. J., UNTHSC, Fort Worth, TX 76107

In order to test the hypothesis that mice would show context-dependent (classical conditioning) sensitization to the behavioral effects of cocaine and that increased pairings of drug with environment would result in greater conditioning, one (N=6), two(N=6) and four(N=15) pairing experiments were conducted. In these experiments Swiss Webster mice were divided into three groups. The paired group received a pairing injection of cocaine (40 mg/kg) prior to being placed into a locomotor activity cage for 30 min. Following this the animals were returned to their home cages in the animal care facility. An hour later they received an injection of saline. The unpaired group received saline prior to placement in the activity cage and cocaine (40 mg/kg) in their home cages. The control group received saline for both injections. This schedule was followed for one, two or four days. On the day after the last pairing injection, challenge injections of cocaine doses (0, 1, 2.5, 5, 10, 20, 40, and 60 mg/kg) were given to all three groups prior to placement in the activity cage for 30 min.

The locomotor activity cages were acrylic with dimensions of 40.5 x 40.5 x 30.5 cm. They were surrounded by 2 arrays of 16-infrared photocell beams arranged to detect movements in the horizontal plane and an additional array arranged at a fixed height of 7.7 cm above the floor to detect vertical movement.

One pairing was sufficient to classically condition and sensitize the paired group (left shift of the dose response curves of horizontal activity and stereotypy). This was also seen after four pairings with an increase in maximal stereotypy and a reduction in maximal horizontal activity in the paired group. The unpaired group showed a decline in basal activity and maximal effect that was significantly different from that of the control group. Therefore, context-dependent sensitization was seen using this model but there was no enhancement of sensitization seen with increased pairings. Rather, tolerance began to effect the behavior of the mice with repeated exposure to cocaine.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Marianna E. Jung

Department: Pharmacology

Undergraduate or Medical Student___ Graduate Student_X_ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

SEX DIFFERENCES IN THE ANXIOGENIC STIMULI INDUCED BY GABAERGIC AND SEROTONERGIC DRUGS.

Marianna E. Jung and Cleatus J. Wallis, University of North Texas Health Science Center, Fort Worth, TX 76107

A number of studies have established animal models of anxiety, but few studies have systematically characterized sex differences in these models. In the present study, we investigated sex specific responses associated with anxiogenic stimuli. Two typical anxiogenic drugs were employed to induce a discrimination cue: a GABA-A antagonist, pentylenetetrazol (PTZ) and a 5-$HT_{2a/2c}$ agonist, m-chlorophenylpiperazine (mCPP). In the PTZ discrimination paradigm, a baseline dose-response of animals was not different between sexes. However when treated with diazepam (IP) prior to PTZ (IP, 16 mg/kg), females required 50% less drug to block the PTZ stimulus. In the mCPP discrimination paradigm, sex differences were observed throughout training and testing. In the acquisition stage, 80 % of male rats vs 40 % of female rats acquired the task. In dose response tests, the ED50 for females (0.88 mg/kg) was greater than that for male rats (0.36 mg/kg). In a manner comparable to the PTZ discrimination paradigm, DZP (5 mg/kg) blocked the mCPP (1.2 mg/kg) cue at a lower dose in females than in male rats. Therefore, 1) Baseline GABAergic and serotonergic-induced anxiogenic stimuli differ with regard to the sex-related factors; 2) Male rats are more responsive to the baseline mCPP cue than females; 3) Female rats are more sensitive to the GABA-A agonistic system than males. Supported by NIAAA # #AA09567 and #AA10545.

UNIVERSITY OF NORTH TEXAS HEALTH SCIENCE CENTER AT FORT WORTH

Research Appreciation Day 1996

ABSTRACT FORM

First Author: Alayne D. Kulvicki

Department: (not at this institution)

Undergraduate or Medical Student X Graduate Student___ Postdoctoral Fellow___ Faculty___ Staff___

Read instructions and fit abstract inside the space given below:

EVALUATING NURSING HOME RESIDENTS' ABILITY TO SELF-REPORT THE OCCURRENCE OF DAILY EVENTS Alayne D. Kulvicki, BS; Sandra F. Simmons, MA; John F. Schnelle, PhD; Gwen Uman, PhD; Patrice Cruise, PhD; and Joseph A. Ouslander, MD; UCLA Dept. of Medicine, JHA, 7150 Tampa Ave, Reseda, CA 91335

Purpose: The objective of this study was to validate a screening algorithm that will identify nursing home (NH) residents capable of accurately reporting care activities.

Methods: Residents were first observed to confirm the occurrence of incontinence and mobility care activities done from 7:00a-3:00p. Residents were then interviewed at 3 pm and asked if the care activities occurred. Resident accuracy during the interviews was predicted with descriptive data described from the Minimum Data Set (MDS).

Subjects and Setting: Convenience sample of 84 NH residents with an average age of 90 years and an average length of stay of 2.7 years (32 months).

Summary and Results: The best predictor of resident accuracy was a measure of cognitive function (CPS score) derived from the MDS. Residents in CPS categories 0-1 and 2 scored 93% to 94% (±10.8 and 9.4, respectively); those in category 3 scored 77% (±21.6), and those in category 4-6 scored 46% (±29.2). On interview questions, 89% of the NH residents with a CPS of 0 - 1, 90% of the residents with a score of 2, 53% with a score of 3, and 17% of residents with a score of 4-6 fell above the chance level of response (80% accuracy).

Conclusions: A CPS score of 0 - 2 can predict the accuracy of NH residents' self-reporting the occurrence of daily events. When evaluating NH residents with CPS scores of 3 - 6, CPS and additional measures must be developed to predict the accuracy of self-report.

FIRST AUTHOR INDEX