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Student Abstracts, Volume XIV, Summer 2002
Preface

The University of Texas Medical School at Houston Summer Research Program provides intensive, hands-on laboratory research training for medical and undergraduate students under the direct supervision of experienced faculty researchers and teachers. The success of our Summer Research Program depends primarily on the faculty who volunteer to mentor the trainees. These faculty members' enthusiasm for scientific discovery and commitment to teaching is vital for a successful training program. It is these dedicated scientists who organize the research projects to be performed by the MS-1 medical students and undergraduates.

To date, more than 1,200 students have gained research experience through the Medical School Summer Research Program. Past trainees have advanced to pursue research careers in the biomedical sciences, as well as gain an appreciation of the relationship between basic and clinical research and clinical practice.

First-Year Medical Student research training is supported by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and by the Dean of the Medical School. Funding for college undergraduates comes from the Dean and the departments and faculty of the Medical School as well as research faculty at the Dental School.

Sincere appreciation is expressed to L. Maximilian Buja, M.D., Dean, Medical School, and to Patricia M. Butler, M.D., Associate Dean, Office of Educational Programs, who have insured the continued success of the Summer Research Program.

This publication marks the completion of the eighteenth year of The University of Texas Medical School at Houston Summer Research Program.

Gary C. Rosenfeld, Ph.D.
Director, Summer Research Program
Assistant Dean for Educational Programs

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Medical Students
ABSTRACT

A Randomized Trial of Glucose-Insulin-Potassium to Protect the Heart in Cardiovascular Surgery

APRIL C. ALFORD                           U.T. at Houston Medical School           Graduation:  2006

Sponsored by:  Heinrich Taegtmeyer, MD, DPHIL, Department of Internal Medicine/Cardiology and
               Hazim J. Safi, MD, FACS, FRCS, Department of Cardiothoracic and Vascular Surgery

Supported by:  The University of Texas Health Science Center at Houston;  NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:  Glucose, Insulin, Potassium (GIK), myocardial preconditioning

The intravenous administration of Glucose, Insulin, and Potassium (GIK) increases the availability of carbohydrate substrate to the heart and corrects hypokalemia during periods of ischemic metabolic stress. In earlier studies myocardial preconditioning with GIK has been shown to improve cardiac protection in patients with myocardial infarction, low ejection fractions, and cardiogenic shock. Favorable results from small clinical trials suggest the utility of GIK as a pretreatment for myocardial protection of high-risk cardiac surgery patients. To assess the effect of GIK on cardiopulmonary function and the frequency of ventricular arrhythmias we are studying patients with hypertropic heart disease (valve surgery), ischemic heart disease (coronary bypass surgery), aortic aneurysm (thoracoabdominal aortic aneurysm repair surgery). In a single – blinded control trial GIK consisting of 50 % glucose, 80 IU/L insulin, and 100 mEq/L KCl is infused at a rate of 1ml/kg/hr for a minimum of 12 hours and a maximum of 24 hours prior to the scheduled operation time. We hope to enroll 50 patients in each group, with 25 per group randomized to GIK and 25 to placebo for a total of 150 patients. At the present time, the number of study participants is not sufficient as to yield results with statistical power. Further enrollment of participants will help to understand the efficacy of GIK as a pretreatment in cardiac surgery patients.
ABSTRACT

Treatment of the acutely injured adult rat spinal cord with the phosphodiesterase inhibitor Rolipram

ERIK ASKENASY                            U.T. at Houston Medical School      Graduation: 2005

Sponsored by: Raymond J. Grill, Ph.D., Department of Neurosurgery, The Vivian L. Smith Center for Neurologic Research

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676 and The Vivian L. Smith Foundation

Key words: glial scar, inflammation, astrogliosis, spinal cord injury

Astrocytes undergo rapid physiological alterations following spinal cord injury (SCI) in a process called astrogliosis. Shortly after SCI, astrocytes assume a “reactive” phenotype characterized by hypertrophy, and the upregulation of glial fibrillary acidic protein (GFAP), an intermediate filament unique to glial cells. These reactive astrocytes provide a long-term impediment to axonal regeneration by providing both mechanical and biochemical inhibitory signals. The onset of inflammation is thought to contribute to the initiation of astrogliosis following SCI. Rolipram, a phosphodiesterase inhibitor, has been shown to be a potent anti-inflammatory drug. We wished to determine whether rolipram, delivered to rats with acute SCI, could diminish astrogliosis by assessing tissue GFAP levels. Adult female Sprague Dawley rats received a moderate spinal contusion injury. Subjects were split into three groups (rolipram at 3 mg/kg, 0.3 mg/kg or saline-only lesioned controls dosed daily IP) and were sacrificed at 24 hr or 5 days post-injury (n=2 per condition/time point). An additional two non-lesion control animals were included. Animals were sacrificed and the cords removed, homogenized and processed for Western Blot analysis of GFAP protein levels. Animals dosed at 0.3 mg/kg demonstrated a decrease in GFAP compared to both non-lesion control- and saline-treated, lesioned animals at 24 hr post-SCI. This trend is diminished by 5 days. This pilot study provides interesting preliminary data to support future studies designed to enhance the effectiveness of phosphodiesterase-inhibitor class of drugs in treating SCI and to further explore their mechanism(s) of action.
ABSTRACT

A Comparison Study Between Two Cementing Techniques

CHRISTOPHER BLED SOE                  U.T. at Houston Medical School         Graduation: 2005

Sponsored by:    Terry Clyburn, M.D., Department of Orthopaedics

Supported by:    The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:          Hip replacements, cement, vacuum, trans-esophageal ultrasound

Objective: Assess the efficacy of a modified cementing technique (prototype cement injector), which removes blood, fluid and debris from the femoral canal during cement insertion.

Clinical Relevance: Cement insertion may generate embolic debris, hypotension and death. Fluid or fat in the bone-cement interface may lead to early failure.

Methods: Five sheep were used. After anesthesia, both hips were operated on using standard techniques of cement application (ream, canal plug, irrigation, suction, and pressurization of cement. The right hip was the control (standard cement injector) and the left hip the study (modified cement injector). Transesophageal ultrasound was used to quantify embolic debris in the right atrium during the procedure. Three blinded examiners, using a standard grading scale for the quality of the bone-cement interface, scored 4 sections from each femur. Each section was then placed on the MTS and the force required to “push out” the cement measured.

Results: Ultrasound revealed less debris in the right atrium when utilizing the study cement injector. No significant difference was seen in the grading of the bone-cement interface. Mechanical testing looks very promising, but must be completed and sent for statistical analysis.

Conclusion: Although the subjective evaluation of the bone-cement interface was inconclusive, the reduction in embolic debris was impressive. We conclude that this technique may reduce the risk of hypotension and death as a result of cemented hip replacement. Histology evaluation will be performed to better evaluate the bone-cement interface.
Stabilization of the Foot and Ankle: A Comparison Study between Traditional Gracilis Tendon Transfer versus Fixation with Bioabsorbable Screws

CORBETT H. BOONE
University of Texas at Houston Medical School
Class of 2005

Sponsored by: Pablo C. Okhuysen, M.D., Department of Internal Medicine, Infectious Diseases

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Keywords: anterior talofibular ligament (ATFL), calcaneofibular ligament (CFL), gracilis tendon

Deformities of the ankle joint, as well as tendon ruptures and instabilities often require a tendon transfer. Studies of different graft site locations led to the choice of an approach using free tendon grafts. The use of free tendon grafts avoids weakening of evertors and length limiting split peroneus brevis grafts. However, instabilities found in studies using the semitendinosus tendon led to a choice of another graft. By the use of a free gracilis graft, the procedure used will be a modified Elmslie approach for the reconstruction of the CFL and ATFL. Not only will this avoid the peroneus brevis tendon, thus eliminating eversion weakness, but it will also emphasize the importance of the CFL. Another positive note is low graft site morbidity as well as significantly reduced anterolateral knee numbness with proper preoperative education. The technique proposed requires that the length of gracilis tendon used for the graft be such that it can be passed through three osseous tunnels and secured by suturing the ends of the tendon together. It has been demonstrated that the use of bioabsorbable screws as interference-fit screws provides adequate fixation in other foot and ankle transfers. The proposal is to test the fixation strength of bioabsorbable screws to the traditional method of suturing the tendon to itself for repair of subtalar instability. There is no current data due to the fact that the first procedure will be taking place on the 31st of July 2002.
ABSTRACT

Hospital Discharge Rate for Out of Hospital Cardiac Arrests in 2000

MARK BOYLE                  U.T. at Houston  Medical School                Graduation:2005

Sponsored by: Richard Bradley  M.D., Department of Emergency Medicine

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: cardiac arrest, EMS, hospital discharge

Out of hospital cardiac arrests are very common in a large urban environment. The EMS system that services this type of area has certain protocols in place to maximize patient care. One of the ways to evaluate these protocols is patient outcome such as hospital discharge following cardiac arrest. We gained authorization from the Houston (TX) Fire Department to review the EMS records for the year 2000. We also gained authorization from the hospitals that received these patients to review outcome data not found in the EMS records. Using a spreadsheet we entered the data into three columns: field termination, pronounced in the emergency department, and admitted to the hospital. Of those admitted to the hospital we looked at how many were discharged alive and how many expired in the hospital. In this study we did not separate patient populations by initial rhythm. Within the study period the units under study responded to 439 confirmed cardiac arrests. We were able to obtain outcome data on 327 (75%) cases. Of those 327 cases there were 56 (17%) that were field terminated, 215 (66%) of them were pronounced in the emergency department, and 66 (20%) were admitted to the hospital. Out of the 66 admitted to the hospital 14 (4%) patients were discharged alive. This study can be used as part of a larger study encompassing many years and other measurable variables to further evaluate EMS efficiency and protocol changes.
ABSTRACT

Retrospective Study of Hypothermia in Pediatric Trauma with regard to ISS and Outcome

JOSE A. CANTU  University of Texas at Houston Medical School  Class of 2005

Sponsored by: Kimberly A. Chambers, M.D., Department of Emergency Medicine

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Keywords: hypothermia, trauma, pediatrics, Injury Severity Score

Hypothermia, defined as body temperature below 37°C, is a significant factor to consider when evaluating a trauma case since it affects many physiologic processes in the body. The correlation between outcome and inability to maintain normothermia has not been well established in pediatric patients since the institution of measures to correct hypothermia have been implemented. A retrospective study of pediatric trauma patients transferred to the PICU from the emergency department was conducted. Injury severity score was used to compare normothermic control subjects with hypothermic patients. A total of 58 cases were reviewed, and 9 patients had a body temperature of less than 35.5°C at the time of admission to the PICU. Of the 58 cases, 8 patients expired in the PICU. 7 of the 8 patients that expired were found to be hypothermic, with an average body temperature of 33.6°C upon admission to the PICU and an average ISS of 25.4 determined post-expiration. The 2 surviving hypothermic patients had an average ISS of 16.5, body temperature of 35.1°C and hospital stay of 16.5 days. Compared with normothermic patients with a similar average ISS, the average hospital stay was 5.6 days. The dissimilarity is significant considering both patient groups have similarly rated injuries, differing only in body temperature. We conclude that hypothermia in pediatric trauma cases is a marker for poor outcome, and the exact breakdown of thermoregulation is an important topic that must be addressed.
ABSTRACT

Cell Culture and Cardiomyocyte Polarity; Effects of Matrix Composition

RACHEL A. DAVIS UT at Houston Medical School Class of 2005

Sponsored by: Roger J. Bick, PhD, Department of Pathology and Laboratory Medicine

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Keywords: adrenoreceptor polarity, cardiomyocyte cell culture, cytoskeleton

Cell and tissue culture techniques are becoming increasingly important for basic and applied life science research, yet studies in vitro do not always reflect a life-like cell environment. Methods currently employed in cardiomyocyte culture usually result in two-dimensional models, and often use simple adhesion proteins such as laminin. The objective of this study was to observe the effects of cell culture on cellular polarity in cardiomyocytes as influenced by cytoskeletal proteins. Cardiomyocytes from adult and neonatal rats were isolated and grown on two different extracellular matrices, laminin and a complex, fibroblast-derived extracellular matrix, cardiogel. The location of a number of proteins was visualized by means of Fluorescence Deconvolution Microscopy using fluorescent probes specific for alpha-adrenergic adrenoreceptors, beta-adrenergic adrenoreceptors, the sarcolemmal L-type calcium channel, and sodium potassium-ATPase protein. A probe (FITC-labeled secondary antibody) for actin filaments was also used to ensure that the particular cell being examined was in fact a cardiomyocyte and not a fibroblast, as determined by protein patterns. Migration of these proteins was followed over a culture period of four days, and images were reconstructed. From our experiments we conclude that a complex matrix leads to the appearance of more receptors, but does not seem to affect the number of ion channel proteins that develop. Definite patterns of adrenoreceptor localization occur during the development of cardiomyocytes in culture and, as we had hypothesized, there is a migration of constituent proteins and adrenoreceptors towards the complex matrix. From these observations we feel that cell culture models need to take into consideration i) type of culture matrix; ii) Polarity of the cultured cells in regard to relating results to in vivo occurrences; iii) simple v complex matrices with regard to localization of proteins, channels and receptors that are being investigated and iv) cell culture time. These cell culture techniques are excellent for investigating and understanding specific aspects of cell development and individual events in biochemical pathways but, it might be beneficial in certain instances to use gel sandwich techniques, or rotary chambers, to culture cells that exhibit minimal polarity and exhibit cell-cell interactions.
ABSTRACT

Do Matrix Metalloproteinases Play A Role In Lipopolysaccharide (LPS)-Induced Gastric Injury

ALIAN G. GARAY                UT at Houston Houston Medical School                             Graduation:  2005

Sponsored by:       David W. Mercer, M.D., Department of Surgery
                    Emily K. Robinson, M.D., Department of Surgery

Supported by:      The University of Texas Health Science Center at Houston;  NIDDK T35, National Institution Diabetes and Digestive and Kidney Diseases, T35DK07676-10 and Dr. D.W. Mercer's grant from the National Institute of General Medical Sciences NIGMS GM 38529

Key words:          matrix metalloproteinase, extracellular matrix, gastric mucosa, endotoxemia, LPS

Introduction: Matrix metalloproteinases (MMPs) are a family of Ca$^{2+}$ dependent endopeptidases that degrade components of the extracellular matrix. We have previously shown that LPS administration causes F-actin disruption and injury in rat gastric mucosa. Increased MMP activity during endotoxemia has been shown to cause tissue injury in other organ systems; however, the role of MMPs in the stomach during endotoxemia is unknown. Therefore, we hypothesized that MMP-2 and -9 would be up-regulated in the gastric mucosa during endotoxemia.

Methods: Rats were fasted overnight and given saline or LPS (20 mg/kg) intraperitoneally for 1, 5, 10, or 24 hours. Rats were sacrificed and gastric mucosa collected for determination of MMP activity using gelatin zymography. Histologic sections of glandular stomach were analyzed for morphologic injury by H&E and MMP activity by in situ zymography.

Results: LPS significantly increased MMP-9 activity compared to controls starting at 5 hours (p < 0.05; ANOVA, n = 5/group). MMP-2 and -9 activities were increased in a time dependent fashion at 10 and 24 hours (p < 0.01). In situ zymography revealed comparable increases in MMP activity in the gastric mucosa at 10 and 24 hours with LPS administration compared to controls. In addition, LPS time dependently increased gastric injury on histological assessment.

Conclusions: This study is the first to demonstrate that MMP-2 and -9 are up-regulated in the gastric mucosa during endotoxemia. These data suggest that MMPs may contribute to gastric injury during endotoxemia.
ABSTRACT

Differential Effects of Resuscitative Strategies on Gut Function

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Sponsored by:  
Rosemary A. Kozar, MD, PhD, Department of Surgery

Supported by:  
The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:  
gut Ischemia/reperfusion, lactated ringers

Background:  
Shock-induced gut ischemia/reperfusion (I/R) has been linked to multiple organ failure. In the lab, gut I/R primes circulating neutrophils to cause remote organ injury and hypertonic saline (HTS) abrogates these systemic events. We therefore hypothesized that HTS would lessen gut I/R induced local inflammation and improve gut function.

Methods:  
Rats underwent superior mesenteric artery occlusion (SMAO) for 60 minutes. Prior to restoring flow, animals were resuscitated with: HTS 4 cc/kg, LR 4 cc/kg (equal volume), LR 32 cc/kg (equal salt load), SMAO alone, or sham laparotomy. Six hours after reperfusion, transit was determined by quantitating the % of tracer in 10 segments of small intestine (mean geometric center). Ileum was harvested for histologic injury (Chiu score 0-5) or myeloperoxidase (MPO) activity. Results by ANOVA (means with different superscripts are significantly different, n=6/group).

Results:  
Intestinal transit was significantly improved with HTS (4.8 ± 0.3a, sham 4.6 ± 0.01a, SMAO 2.5 ± 0.01b, LR 32 cc/kg 3.1 ± 0.02c, LR 4 cc/kg 3.2 ± 0.02d) and morphologic injury lessened (HTS 1.3 ± 0.4a, Sham 0±0a, SMAO 4.6 ± 0.5b, LR 32 cc/kg 3.3±0.4c, LR 4 cc/kg 2.8±0.4d). There was also a significant reduction in MPO with HTS (1.0 ± 0.02a, Sham 2.3 ± 0.03b) compared to SMAO (2.3 ± 0.03b), LR 32 cc/kg (1.7±0.03c), or LR 4 cc/kg (1.5±0.03d).

Conclusions:  
HTS resuscitation lessens gut inflammation and improves transit after gut I/R compared to either equal volume or equal salt load LR.
ABSTRACT

Return of Spontaneous Circulation in a High Volume Urban EMS System

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Graduation: 2005

Sponsored by: Richard Bradley M.D., Department of Emergency Medicine

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: Cardiac Arrest, EMS, Return of Spontaneous Circulation (ROSC), Out of Hospital (OOH)

Out of Hospital Cardiac Arrest (OOHCA) is one of the most serious events encountered by Emergency Medical Service (EMS) personnel. Return of spontaneous circulation (ROSC) percentages from OOHCA may be used to determine the effectiveness of EMS system design and protocols. Many factors within an EMS system influence the rate of ROSC; therefore future EMS systems should be designed to maximize ROSC rates. We retrospectively reviewed all Houston (Texas) Fire Department EMS patient records from 2002 that resulted from patients with OOHCA. Using Microsoft Access the data was entered into spreadsheet format that could be easily queried using outcomes that we specified. Using only those patients with cardiac arrest of presumed cardiac origin within the study period, there were determined to be 833 total cardiac arrests. Of these patients, 304 (36%) had ROSC of any length or quality. Further data analysis shows the highest percentage of ROSC in ventricular fibrillation/ventricular tachycardia (VF/VT) patients (108/196, 55%) followed by pulseless electrical activity (PEA) or other rhythms not VF/VT (69/155, 44%) and asystole (127/482, 26%). ROSC data from other EMS systems has not been well reported in the past making comparison at this time difficult. By the effective reporting of these percentages in the future, EMS system design may be affected in the future, however further study of worldwide EMS systems is warranted.
Event-Related Functional Magnetic Resonance Imaging of Impulsivity in Methylene-dioxymethamphetamine (MDMA) Abuse

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Sponsored by: Joel L. Steinberg, M.D., Department of Psychiatry and Behavioral Sciences

Supported by: Bernard Saltzberg Summer Research Fellowship

Keywords: Methylene-dioxymethamphetamine (MDMA), Functional Magnetic Resonance Imaging (FMRI), Immediate Memory Task/Delayed Memory Task (IMT/DMT), Event Related Design, HDR (hemodynamic response)

Statistics indicate the percentage of high school students that have reported MDMA use is on the rise, possibly because of the general perception that MDMA is a “safe” drug. While the effects of MDMA on the brain can be seen in a number of areas, we chose the prefrontal cortex as the main area of interest for this study because previous studies found effects of MDMA on the frontal cortex, and the prefrontal cortex is critical in impulse control. This project used FMRI data from both healthy control subjects and MDMA abusing subjects to identify the brain neuronal pathways underlying human impulsive behavior.

The behavioral protocol during each session was a rapid-presentation, stochastic, event-related design consisting of the following trials: DMT, IMT, and a Null trial (rest, 2s) over a period of 10 minutes per session, and a 5 minute rest between the 2 sessions. The first stimulus (target) of each trial (TARG), the probe stimulus (PR), and motor response (M) of each trial were regarded as separate events. The data was analyzed using Statistical Parametric Mapping software to contrast the FMRI response from the TARG and false-alarm PR events within each group. Following the false alarm probe, control subjects had a significant increased HDR in visual association areas and the hippocampus after correction as compared to MDMA abusers. In addition, controls had marked increases in HDR throughout the entire brain, including the prefrontal cortex during the working memory trials.
ABSTRACT

Stem Cell Research in the United States and the United Kingdom: Two Nations, Two Bioethical Standards

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                  Piers Benn, PhD, Medical Ethics Unit, Imperial College School of Medicine, London, U.K.

Supported by:    The University of Texas Health Science Center at Houston;  NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Keywords:            stem cell research, bioethics, United Kingdom

Embryonic stem cell research has been placed at the forefront of the scientific and medical community in recent years with the potential to lead to therapies for a wide range of illnesses. Such research has come under critical fire, especially in the United States. This criticism reached a head in August of 2002 when President George W. Bush announced that no federal funding would be given to stem cell research in which embryos were destroyed. In the United Kingdom, such research is allowed and funded heavily by their government. This paper outlines an understanding of both the US and UK approaches to stem cell research in which embryos are used. By an elucidation of the regulatory guidelines instituted in each of these countries, a clarification of the differing assessment of the value and rights of the early embryo is achieved. First an empirical section, outlining the relevant regulations for such research, is included. This is followed by an analysis of the specific arguments of potentiality and identity, and how these questions are evaluated in each country. After an assessment of these differing values has been approached, the status of stem cell research in the US is critically evaluated, noting inconsistencies within the US framework. In conclusion, a suggestion is made that the US should reevaluate its stance on stem cell research allowing such research to take place using excess in vitro fertilization embryos.
ABSTRACT

Lymphocyte Activation in Microgravity Models

DAVID MARETH UT at Houston Medical School Class of 2005

Sponsored by: Anil D. Kulkarni, M.Sc., Ph.D, Department of Surgery

Supported by: The University of Texas-Houston Summer Research Program; National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676

Keywords: microgravity, AOS, Lymphocytes

Research by both NASA and the Russian space program indicates that stressors associated with space flight induce immunosuppression in Astronauts. A ground based simulated microgravity model called Anti-orthostatic suspension (AOS) has a documented immunosuppressive effect on mice. Previous experiments indicate that diets fortified with RNA and Uracil can counteract the immune weakening effects of simulated microgravity. To further explore the effects of microgravity on T lymphocyte activation a mixed leukocyte culture (MLC) assay and immunofluorescent staining of leukocytes was performed. Seven to eight week old Balb/C mice were placed in the following housing groups: 1) group housing, 2) isolation housing and 3) AOS housing. Mice in each of these groups were fed either standard chow or a RNA or Uracil supplemented chow. On day seven of the experiment, spleens were harvested and splenocyte cell suspensions prepared. Initial data show increased lymphocyte stimulation in mice in supplemented groups, particularly in the Uracil supplemented group as compared to the control chow group. Immunofluorescence staining experiments currently underway identify and evaluate the T3 and IL2 cell surface receptors. Primary analysis of T lymphocyte surface receptors such as the ones tested, will help understand better the mechanisms by which supplemental nucleotides modulate lymphocyte proliferation.
Arthroscopic Tenodesis Comparing Suture Anchors versus Bioabsorbable Interference Screws: A Biomechanical Study

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Graduation: 2005

Sponsored by:  Gary M. Gartsman, M.D., Department of Orthopaedic Surgery  
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Supported by:  The University of Texas Health Science Center at Houston;  NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:  biceps tendon, arthroscopic Tenodesis, biomechanics

Biceps tenodesis is a surgical procedure used to restore flexion and supination function of the biceps brachii muscle.  Proximal biceps tenodesis is primarily indicated in young active patients with complete ruptures, partial tears greater then fifty percent, or severe degenerative disease of the biceps brachii tendon.  Recently, two arthroscopic methods have been developed using either suture anchors or bioabsorbable interference screw fixation to reattach the tendon insertion site.

The goal of this study is to evaluate and compare the fixation strength of these two techniques.  The long-term goals are to determine which method will provide better fixation, and thus lead to a reduction in recovery time and fewer post-operative complications, such as re-rupture.

Ten fresh frozen cadaver shoulders were thawed and disarticulated with the biceps tendons dissected.  Each specimen underwent dexta scanning prior to testing to account for bone mineral density.  Half the specimens underwent the suture anchor technique while the other half had the interference screw procedure as described in the literature.  To measure pull out strength the humerus with the biceps tendon attached was placed in the mechanical testing system machine and displaced at a constant rate until failure.  The peak load to failure was recorded.

A paired t-test showed no significant difference in pull out strength between the two techniques, nor any correlation between bone mineral density and pull out strength.  Based on this data, we conclude that both biceps tenodesis procedures provide adequate fixation strength.
ABSTRACT

Diagnostic performance of computed tomography (CT) the aorta in detecting acute traumatic aortic injury (ATAI)

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Supported by:  The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:  Aorta; Tomography, X-ray computed; Wounds and Injuries; Diagnostic Tests, Routine; Outcome Assessment

Trauma involving rapid deceleration carries a substantial risk of ATAI, requiring immediate detection and surgical repair. Catheter angiography (CA) has been the gold standard for diagnosis. Since 1996, UT-Houston has increasingly used aorta CT as a definitive test for ATAI.

This retrospective analysis of trauma patients imaged on the multi-slice CT scanner in MHH Emergency Center evaluates the diagnostic performance of CT for detecting ATAI.

From 9/15/00 – 6/30/02, 1458 CT scans of the chest were performed in Emergency Center. Of these, 939 were performed for evaluation of potential aortic injury due to decelerating blunt trauma which forms the study population. 52 (5.5%) had mediastinal hematoma without evidence of aortic injury (Class 3). 11 (1.2%) had mediastinal hematoma and the CT was suspicious but not diagnostic of aortic injury (equivocal, Class 4). 2 had aortic injury confirmed by CA (true-positive). 9 had no injury by CA or had no confirmatory test (false-positive). 16 (1.7%) had a definitive CT diagnosis of aortic injury (Class 5). 15 had ATAI confirmed by surgery (10), angiography (4) or clinical outcome (1) (true-positive). 1 had definitive CT for minor aortic injury that could not be confirmed by angiography or trans-esophageal echocardiography (false-positive). If classes 4 and 5 are considered positive: sensitivity 100%, specificity 98.9 %, PPV 63%, NPV 100%. If only class 5 is considered positive: 88.2%, 99.9%, 93.8%, 99.8%.

When supplemented by CA in equivocal cases, CT is an excellent diagnostic test for detecting ATAI.
ABSTRACT

Third Place, 2002 Frank Webber Prize for Student Research

Gastric Emptying Following Traumatic Shock

CRAIG ALAN MESSICK                      UT at Houston Medical School                                      Class 2005

Sponsored by:    Rosemary A. Kozar, M.D., PhD, Department of Surgery
                    Christine S. Cocanour, M.D., Department of Surgery

Supported by:    The University of Texas Health Science Center at Houston;  NIDDK T35, National
                    Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:         gastric emptying, nutrient meal, enterogastric reflex

Background:  Controversy exists whether the stomach or small bowel is the optimal site to administer enteral feeds in critically injured patients. However, there have been no prior studies investigating gastric motility in this patient population. The purpose of the present study was to assess gastric emptying in trauma patients requiring shock resuscitation.

Methods:  Patients admitted to a Level 1 trauma center that met criteria for shock resuscitation (major torso trauma, base deficit on admission >6 meq/L, and transfusion requirement >6 units in the first 12 hours) underwent gastric emptying analysis using a non-nutrient (saline) and nutrient (Impact, a polymeric enteral feed) meal. Either 500cc of saline or Impact was instilled into the stomach with serial withdrawals every 15 minutes over 1 hour on the 2nd and 4th post-injury day (PID). The t ½ for emptying was calculated for each time-point. Results:  Five patients met inclusion criteria, 4 males and 2 females, age 34 ±2. Following shock resuscitation, the stomach was capable of emptying a non-nutrient meal, with t ½ for saline = 12 minutes at PID 2 and 17 minutes at PID 4. There was an unexpectedly high rate of emptying a nutrient meal on PID 2 (t ½ = 15 minutes), which slowed toward normal (t ½ = 60 minutes) by PID 4.

Conclusions:  Severely injured trauma patients appear to have intact non-nutrient emptying and enhanced early nutrient emptying, suggestive that the enterogastric feedback mechanism is inhibited by trauma.
ABSTRACT

Second Place, 2002 Frank Webber Prize for Student Research

Geometrical Analysis of Fracture Patterns in Intra-Articular Distal Tibia (Pilon) Fractures

JOHN W. MUNZ  The University of Texas at Houston Medical School  Class of 2005

Sponsored by: Dhiren S. Sheth, MD, Department of Orthopaedic Surgery

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: Pilon Fracture, Fracture geometry, CT scan

Surgical reconstruction of distal tibia fractures is a challenging task due to the complexity of fracture geometry. These fractures result from axial compression forces causing a severe degree of fragmentation of the articular surface. The purpose of this study was to define the geometry of articular surface loss following pilon fractures. Twenty-nine fractures (AO-type-C3) were selected for the study and were evaluated using post-traction CT scan. The CT scans were examined for anatomical zone of involvement (medial malleolar, posterior, anterior-lateral and central), number of articular fragments, fragment size and zone of comminution. An assessment was made based on axial and reformatted images on whether the articular surface in the zone of comminution was surgically reconstructable. The mechanism of injury was MVA in 20 patients and fall in 9 patients. In 75.8% of patients there was associated fibular fracture. The average number of fracture fragments per patient was 3.72 (range 3-6). The average size of the largest fragment was 3.64cm and that of the smallest fragment was 1cm. In 37.9% of cases the largest fragment was posterior, which was the most consistent pattern recognized. The area of comminution was central (48%), anterior-lateral/central (24.1%) and anterior-lateral (17.2%). In 58.6% of patients the articular surface was deemed non-reconstructable due to the severe degree of comminution. This analysis indicates that in the majority of high velocity pilon fractures, the articular surface is non-reconstructable. Most severe comminution involves the central and anterolateral zones. A consistently present large posterior fragment can be used as a stable fragment to aid the reconstruction.
ABSTRACT

Development of a Counterselection System for Bacillus anthracis

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Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: Bacillus anthracis, counterselection, trimethoprim, thyA gene deletion,

Traditional genetic selections can be used to select mutants that have acquired a new gene. In contrast, “counterselection” methods can be used to isolate mutants that have lost a particular gene. We hypothesize that the thyA gene of B. anthracis will function as a counterselectable marker in this species. In the highly conserved thymine synthetic pathway of bacteria, uracil is converted to thymine by thymidylate synthetase. dUMP is converted to dTMP in the presence of the methyl donor tetrahydrofolate. Tetrahydrofolate is oxidized to dihydrofolate (FH2) in the process. Dihydrofolate reductase reduces FH2 back to FH4 so it can accept a methyl group again. Trimethoprim inhibits the dihydrofolate reductase and disrupts the pathway. In previous work, a thyA-null mutant in B. anthracis strain 7702 was created by replacing the thyA with an Ω-spectinomycin resistance cassette. We determined the minimum inhibitory concentration of trimethoprim (TMP) for 7702 was 750 µg per mL. The ΔthyA mutant required at least 150 µg of thymine per mL for growth on a minimal medium. We also determined that the thyA-null mutation did not confer resistance to TMP. Moreover, the mutant grew poorly in minimal media even with the addition of thymine. We hypothesize that these phenotypes are due to one of the following: the thymine biosynthetic pathway of B. anthracis is different from that of the other closely related species, or the thyA mutation caused a polar effect on downstream genes. Future experiments will address these possibilities.
Transfusion of ABO-Compatible/Nonidentical RBCs and Platelets Is Not Associated with Hemolysis

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Sponsored by:       Elizabeth A.  Hartwell, MD, Department of Pathology and Laboratory Medicine
Supported by:        The University of Texas Health Science Center at Houston
Key words:            transfusion, hemolysis, lactase dehydrogenase, bilirubin, haptoglobin

The practice of transfusing ABO-compatible/nonidentical red blood cells (RBCs) and platelets is used daily in many hospitals; however, some hospitals are reluctant to implement this practice due to the risk for hemolysis. There are two reasons why transfusing patients with ABO-compatible/nonidentical RBCs and platelets is important. The first is that there is a limited supply of products, and the second is in trauma patients requiring emergency transfusion. This study was designed to show that there is no significant hemolysis associated with ABO-compatible/nonidentical RBC and platelet transfusions.

A study was conducted on forty-six patients receiving ABO-compatible/nonidentical RBCs and/or platelets at a university teaching hospital between May 29, 2002 and July 19, 2002. There were fifty-eight transfusions that qualified. Blood samples from before the transfusion and from each day after, up to the third day when possible, were collected and tested for the following: direct anti-globulin test (DAT), lactase dehydrogenase (LDH), total bilirubin (TBIL), and haptoglobin (HPT).

Of the transfusions reviewed, only one patient developed a positive DAT post-transfusion; this was not associated with a significant increase in LDH, TBIL, or HPT. Of the other transfusions, there was no development of a positive DAT and no significant increase or decrease between the average pre-transfusion and post-transfusion levels of LDH, TBIL, and HPT. Therefore, transfusions with ABO-compatible/nonidentical RBCs and platelets are not associated with any significant hemolysis and should be conducted without concern.
ABSTRACT

Does Obesity Increase Complications in Patients Sustaining Significant Trauma?

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Robert M. Pousman, D.O., Department of Anesthesiology

Supported by:  The University of Texas Health Science Center at Houston;  NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:  trauma patients, obesity, morbidity and mortality

Background:  Obesity is an increasingly common healthcare problem.  We therefore hypothesized that obese patients would have an increased morbidity and mortality following significant trauma.

Methods:  A retrospective chart review of all trauma patients admitted between January and July 2000 to the Intensive Care Unit (ICU) of a Level I Trauma Center was performed.  Data was collected on admission height and weight, age, gender, Injury Severity Score (ISS), co-morbidities, length of stay (LOS), morbidity and mortality.  Body Mass Index (BMI) was calculated and patients divided into either normal weight (BMI < 25 kg/m²), overweight (BMI 25-30 kg/m²) or obese (BMI > 30 kg/m²).  Results:  Of 180 charts reviewed, 141 had admission height and weight:  59 (42%) patients were normal weight, 52 (37%) overweight, and 30 (21%) obese.  There was no difference in ISS (normal 25 ± 1, overweight 25 ± 1, and obese 22 ± 1) nor pre-injury co-morbid diseases (cardiac, pulmonary, endocrine or neurologic) though age was greater in patients with BMI > 25 (normal 32 ± 2, overweight 42 ± 3 and obese 36 ± 3).  There was no significant difference in LOS, pulmonary, renal, urinary or infectious morbidity nor overall mortality.

Conclusions:  Despite a 58% incidence of obesity in trauma patients requiring admission to the ICU, there was no associated increase in morbidity and mortality.  This may be due to heightened awareness of potential problems unique to obesity and improved ICU care.
ABSTRACT

Assessment of CWW and Redbridge PCTs According to National Service Framework for Diabetes: Standards

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Class: 2005

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Supported by:  
The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Keywords:  
Diabetes, U.K. National Service Framework

Diabetes is becoming more common as the number of cases is steadily on the rise. Diabetes can have devastating impacts on an individual as its many complications can lead to blindness, renal failure, and amputation. Diabetics must become accustomed to strictly controlling their blood sugar, eating a well balanced diet, exercising and receiving regular visits with general practitioners, chiropodists, and optometrists for surveillance of complications. The Department of Health released the National Service Framework for Diabetes: Standards last year and the medical community is awaiting the arrival of the delivery strategy. In preparation, a baseline assessment was needed to ascertain areas of strengths and weakness in Chingford, Wanstead, and Woodford PCT and Redbridge PCT. Interviews were conducted with general practitioners, practice nurses, diabetic nurse specialists, podiatrists, optometrists, and dieticians. The assessment will be used to determine what steps will be taken to assure quality health care provision to diabetics.
ABSTRACT

Endovascular versus Open Repair of Infrarenal Abdominal Aortic Aneurysm: Risks and Benefits

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Sponsored by: Tam Huynh, M.D., Department of Cardiothoracic & Vascular Surgery

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: endoluminal, Infra-renal, abdominal, aortic, aneurysms, ancure

Purpose: Endovascular repair has increasingly become a popular treatment for patients with infrarenal abdominal aortic aneurysm (AAA). We reviewed our recent results of conventional versus endovascular AAA repair.

Methods: From September 1999 to May 2002, 83 patients had AAA repair. Thirty patients underwent endovascular repair (Endo) using the bifurcated Ancure graft (Guidant, CA) and 53 had conventional repair (Open). Multivariable linear regression and unpaired student's t-test were used for comparison between the 2 groups when appropriate. 16/83 (19%) were women and 3/30(10%) had Endo repair.

Results: 2/30 (6.7%) patients in the Endo group had to be converted to Open and both were women. One patient in the Endo group (1/30; 3.3%) and none in the Open group died during hospitalization. 14/30 (46.7%) Endo patients had to have additional procedures done including balloon angioplasty, stenting, placement of cuff, coiling, and/or arterial repair. There was one major limb amputation in the Endo group and none in Open. The average time for repair was significantly longer for Endo versus Open (183 vs. 100 minutes, respectively, p<0.001). The average aortic clamp time for Open was 27 minutes. Post-operative length of stay was shorter after Endo compared to Open (6.3 vs. 10.3 days, respectively, p<0.0001)

Conclusion: Our initial experience shows that endovascular repair of AAA requires prolonged operative time and may be associated with higher morbidity and mortality than conventional open repair.
ABSTRACT

The Efficiency of a 90-second Triage Evaluation

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Sponsored by:      Brent King, M.D., Department of Emergency Medicine

Supported by:      The University of Texas Health Science Center at Houston;  NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:         triage, physician triage, abdominal pain

A triage instrument was tested on 27 patients who presented with a chief complaint of abdominal pain. Using the instrument, patients were given an acuity score of 3, 2, or 1. A nurse and physician (blinded to the triage instrument score) independently evaluated the patients and ranked them in terms of acuity after a history and physical had been performed. They were asked to rank patients as a 3 if they were felt to be quite sick and very likely to be admitted to the hospital. A 2 was to be given to patients who were equally likely to be admitted or sent home and a 1 was given to patients who were very likely to be sent home. All rankings data were collected prospectively as were final dispositions. The results were then analyzed and revealed that the triage acuity matched the disposition in 24 of the 27 cases. In 18/27 cases, the doctor’s first assessment was in agreement with the triage device. In 13/27 cases, the nurse’s first assessment was in agreement with the triage device. In the three cases in which the triage device made errors with respect to patient disposition, it occurred by assigning patients a higher acuity than was necessary. Results showed that the triage instrument predicted the disposition of the majority of patients and when not accurate, the patient would not suffer any delay in care since it predicted higher levels of acuity. Further evaluations of time course and increased numbers of patients will be done before adopting the device.
Observation of Physician – Adolescent Visits for High Risk Behavior Modification

ERIN R. SCOTT  University of Texas at Houston Medical School  Graduation: 2005

Sponsored by:  Michelle S. Barratt, M.D., MPH, Department of Pediatrics

Supported by:  The University of Texas Health Science Center at Houston;  NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:  abstinence, confidentiality, risk behaviors

My study analyzed and augmented previously collected data pertaining to the frequency that health care providers in the Harris County and surrounding counties address high-risk behaviors with their adolescent patients. The observational study allowed observation of health care providers in East Texas. Forty-two health care providers were contacted and an n=9 were directly observed. The Research Assistant attended patient interviews and recorded data utilizing the Davis Observation Code. Data analysis showed that the history comprised 49 % of the interview. Further analysis of percent time elapsed per topic during the history showed: 11% sex, 5% cigarettes, 6% drugs, 6% alcohol, 7% dating, 12%STDs, 9% pregnancy, 16% contraception, 4%abstinence, 2% abstinence until marriage, 5% confidentiality. Of 56 providers 22 discussed sex, 17 discussed cigarettes, 18 discussed drugs, 11 discussed alcohol, 17 discussed dating, 10 discussed STDs, 5 discussed pregnancy, 19 discussed contraception, 2 discussed abstinence, 2 discussed abstinence until marriage, and 5 discussed confidentiality. Further analysis of time allocation of the patient interview yielded the following: 11%counseling, 1% compliance, 26%health education, and 3% health promotion. With a plurality of the interview involving history taking, insufficient time was given to health promotion, compliance and counseling. These areas allow physicians to know their adolescent patients more in depth and thereby promote better healthcare. A disparity exists in the time spent providing high-risk behavior modification; lack of such intervention results in insufficient care to the adolescent patient population.
ABSTRACT

Biomechanical Comparison of One-Third Tubular vs. Periarticular Plate for Distal Fibular Fixation

MICHAEL D. SPEARS                University of Texas at Houston Medical School                Class of 2005

Sponsored by: Kevin J. Coupe M.D., Department of Orthopaedics

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: fibula, lateral malleolus, one-third tubular plate, periarticular plate, torsional testing

Ankle fractures involving the distal fibula are typically treated by open reduction and internal plate fixation. Traditionally, the one-third tubular plate is used most often to stabilize such fractures, however recently a new periarticular plate design was approved for use by the FDA. The one-third tubular plate must be contoured at the time of application to fit the lateral malleolus. The periarticular plate, on the other hand, was designed using the average dimensions of the distal fibula and has a pre-contoured shape which does not need adjustment prior to application. The purpose of this study was to determine the efficacy of each plate design utilizing biomechanical stress testing. Ten cadaveric human fibulas were harvested, five were plated with the one-third tubular plate and five received the periarticular plate. Gap osteotomies were made in the plated fibulas to create an unstable fracture in which to test the plates. The unstable plated fibulas were then torsionally tested using the mechanical testing system (MTS). An axial load was applied to the bone while torsional stress was applied to the distal end. The load and torque at which each plate failed were then measured and recorded for comparison of plate performance.
ABSTRACT

Biochemical Characterization of Multiple Sclerosis Lesions through Magnetic Resonance Spectroscopy

MICHAEL J. STEPHEN           University of Texas at Houston Medical School           Graduation:   2005

Sponsored by:  Ponnada A. Narayana, Ph.D., Department of Radiology

Supported by:  The University of Texas Health Science Center at Houston;  NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:        MRS, multiple sclerosis, NAA, choline

Magnetic resonance spectroscopy(MRS) is a noninvasive approach used to characterize biochemical variations within multiple sclerosis(MS) lesions and so-called normal appearing neural tissues.  The objective of this work is to better understand the pathology of MS by quantifying proton MRS-observed metabolites evident in brain tissue.

All subjects previously diagnosed with MS were scanned on a GE 1.5T Sigma echospeed clinical scanner.  The raw SI(spectroscopic imaging) data was then processed using Automated Proton Spectroscopic Image Processing(APSIP) and an image interface display(Viewer).  APSIP, an in-house developed software, allows various functions to be performed including baseline correction and filtration.  The spectral peaks are then normalized to an internal reference, the total unsuppressed water concentration, within the cerebral tissue.  A line shape fitting is then performed to determine the area of each peak in each voxel.  Finally, the metabolic maps were created allowing for visual representation of the data.

The three main compounds studied are choline, creatine, and N-acetyl aspartate(NAA); each metabolite exhibits a characteristic peak with a particular chemical shift in a proton spectrum whose concentration is dependent on the pathology of the disease.  As a result of degeneration of axons from MS, certain compounds particularly NAA, found in cerebral matter show significant decreased levels.  Moreover, choline, a compound in membranes, has been known to be present in elevated concentration levels within certain regions of the brain prior to visual lesion formation.  Therefore, quantifying metabolites is another avenue used in the pursuit of evaluating the progression of the disease, MS.
ABSTRACT

The Efficacy of Using Extensive Patient Education and Functional Exercise Guidelines in Regard to Improving Quality of Life and Adherence to Lifestyle Changes Post-operatively with TAAA Patients

CHRIS STUTZ                                      UT at Houston Medical School                          Graduation:  2005

Sponsored by:      Hazim J. Safi, M.D., F.A.C.S., F.R.C.S., Department of Surgery
                   Charles C. Miller, III  Ph.D., Department of Cardiothoracic & Vascular Surgery

Supported by:      The University of Texas Health Science Center at Houston;  NIDDK T35, National
                   Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:           thoracoabdominal aortic aneurysm, rehabilitation, quality of life

The study is intended to determine whether patient education and moderate, functional exercise prescription will improve quality of life and exercise adherence measures following repair of a thoracoabdominal aortic aneurysm (TAAA). Currently there are no well-delineated functional exercise guidelines for TAAA patients and no data describing quality of life and adherence to lifestyle changes with these patients. There is a need for methodical, scientific approach to helping these patients return to life more quickly and with less hindrance. Proper exercise prescription has been shown to positively affect the outcomes of patients after undergoing coronary artery bypass graft surgery and proves most beneficial with thorough patient education regarding lifestyle changes. Whether such changes are efficacious for TAAA patients is unknown. With this in mind, this study draws generally from the cardiac rehabilitation model of exercise prescription while incorporating current motivational/educational techniques to modify the lifestyle and behavior of the TAAA patient post-operatively. A randomized clinical trial of a structured exercise and educational/motivational intervention compared to usual care is being used to determine the efficacy of the intervention. Currently 40 patients are enrolled in the study. Only 10 have reached the first follow-up, so no analyzable efficacy data are available at this time. The intervention appears to be well tolerated and readily understandable by the patients. In conclusion, it has been possible to develop functional exercise guidelines for use following TAAA repair and to apply these guidelines in the context of a clinical trial. Whether the guidelines are efficacious with respect to outcome will have to await the results of the clinical trial.
ABSTRACT

The Role of AlphaVbeta6 in Corneal Scarring

BILUE A. THOMAS            University of Texas at Houston Medical School            Class of 2005

Sponsored by: Richard W. Yee, M.D., Department of Ophthalmology

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: corneal healing, AlphaVbeta6, integrins

The integrin, AlphaVbeta6, is a dimerized single transmembrane protein that is expressed in wounded epithelium. AlphaVbeta6 mediates the healing process by activating latent TGFβ, a key mediator of inflammatory cell function, growth inhibition and differentiation, and extracellular matrix production. In epithelial tissue, down-regulation of AlphaVbeta6 leads to decreased fibrosis. AlphaVbeta6 expression has been observed in pathological corneal conditions. To determine if alphaVbeta6 expression occurs in corneal epithelium following laser surgery, corneal tissue that had previously undergone LASIK surgery was stained for the presence of alphaVbeta6.

Methods: Paraffin embedded human corneal tissue was sliced into 5µm sections and stained for alphaVbeta6 using a horseradish peroxidase (HRP) detection method. A cell line transfected with beta6, SW480B+6, served as a positive control and a similar cell line, SW480B-6, not expressing beta6, served as a negative control. Results of the staining technique were observed using light microscopy.

Results: Paraffin embedded corneal tissue that had previously undergone LASIK surgery did not express alphaVbeta6. Both positive and negative controls were positive and negative respectively for alphaVbeta6 expression.

Conclusion: Alphavbeta6 expression has been previously observed in wounded human cornea. One reason for a lack of AlphaVbeta6 expression in our laser-wounded sample could be due the fact that the cornea was cadaveric and the length of time between the procedure and the staining was too long. Further studies done in vivo might better ascertain the role of AlphaVbeta6 in corneal scarring.
Local Immune Responses to Bacterial Vaginosis in Pregnancy

LATRICIA M. THOMPSON University of Texas at Houston Medical School Graduation: 2005

Sponsored by: Lisa M. Hollier, M.D., MPH, Department of Obstetrics and Gynecology

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10 (3-5) Key

Key words: bacterial vaginosis, inflammatory cytokines, pregnancy, pre-term delivery

Objective: Our goal was to evaluate the predominant local cytokine response to bacterial vaginosis in pregnancy.

Methods: Pregnant women were offered enrollment in this case-control study when they presented for prenatal care or were found to have bacterial vaginosis at a prenatal care visit. All women received screening for chlamydia and gonorrhea, testing of vaginal pH, and a slide of vaginal discharge was prepared for gram stain. A sample of cervicovaginal secretions was obtained by saturating filter paper strips. These were frozen immediately at –70°C for later evaluation. Women with bacterial vaginosis diagnosed by their providers received standard antimicrobial therapy with metronidazole. All women were asked to return for reevaluation 7-28 days after their study entry visit. The gram stain was repeated and the cervicovaginal specimen collected again. The women were followed in their prenatal clinic throughout their pregnancy.

A single blinded microbiologist performed gram stains of the vaginal discharge on all enrolled patients. Bacterial vaginosis was defined as a Nugent’s score of ≥7 with a vaginal pH >4.5. The frozen vaginal fluid samples will be tested for cytokine profiles including type-1 (IL-2, IL-12, IFNγ) and type-2 (IL-4, IL-10, IL-13) and lactoferrin. All markers will be measured using ELISA assays, except lactoferrin which will be measured using a latex agglutination assay. The median values of each of the cytokines will be compared in cases and controls using the Mann-Whitney U test. Cytokine profiles will then be collapsed into dichotomous variables: Th1 predominant or Th2 predominant. The proportion of women with Th1 predominance among the cases will be compared to the proportion among the controls with Fisher’s Exact test or Chi square as appropriate.

Results: 82 women have been enrolled from 6/13/02 until the present. A total of 24 (29%) of the women were diagnosed with bacterial vaginosis and an additional 7 (8%) had intermediate gram stain scores. Of the patients diagnosed with bacterial vaginosis on blinded gram stain, only 4 (16%) were also diagnosed with BV by their providers.

All cytokine studies are pending at this time as the enrollment period continues to complete the necessary sample size.

Discussion: BV is a common complication of pregnancy which is frequently misdiagnosed.
ABSTRACT

Methicillin Resistant Staphylococcus aureus Bacteraemia Surveillance and Infection Control

JENNY G. VU  University of Texas at Houston Medical School  Graduation: 2005

Sponsored by:  Stanley J. Reiser, M.D., Ph.D., Department of Surgery, Humanities & Technology, U.T. at Houston Medical School  and  Elizabeth Haworth, M.D., Imperial College School of Medicine, London, U.K.

Supported by:  The University of Texas Health Science Center at Houston;  NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words:  antimicrobial resistance, MRSA bacteraemia, surveillance, infection control, acute hospitals

The control of antimicrobial resistance in NHS Trusts and hospitals is a pressing health care problem, and the surveillance of Methicillin Resistant Staphylococcus aureus (MSRA) bacteraemia has been chosen by the Department of Health in England as an indicator of both antimicrobial resistance and infection control. It introduced mandatory MRSA surveillance by Trusts in April 2002.

The surveillance scheme and MRSA league tables, using the MRSA bacteraemia rate per 1000 bed days for NHS Trusts, were reported in CDR Weekly 21 June 2002. However, both epidemiologists and microbiologists argue that this rate does not adjust for case mix. A more appropriate measure is MRSA bacteraemias as a proportion of all bacteraemias per year since the denominator is ill, bacteraemic patients rather than all in-patients. Because the true bacteraemia figures were not routinely available, all positive blood cultures were used as a proxy measure. New league tables for the year April 2002 to March 2002 were created for NHS hospitals to compare MRSA bacteraemias as a proportion of all bacteraemias and MRSA bacteraemia rate per 1000 bed days.

An infection control survey was undertaken in acute hospitals within the South East region, focusing on resources for and constraints on infection control and the utility of data ranking. Of the 31 hospitals included in the survey, 15 replied*.

Microbiologists welcomed both re-presentation of MRSA bacteraemia data and the survey in helping establish a collaborative relationship with regional epidemiologists, though were skeptical over the league table approach to infection control.

*As of July 30, 2002. Surveys are still being conducted to develop a regional infection control profile.
ABSTRACT

Regulation, Expression, and Catalytic Activity of CYP3a13

MARY T. VU

UT at Houston Medical School

Graduation: 2005

Sponsored by: Henry W. Strobel, Ph.D., Department of Biochemistry & Molecular Biology

Supported by: The University of Texas Health Science Center at Houston; NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: Cytochrome P450, CYPa13, Cos M6 Cells, and Formaldehyde Assay

Cytochrome P450s are a diverse group of heme-containing proteins. Those belonging to the CYP3A subfamily are of particular interest due to their involvement in the metabolism of more than 50% of clinically active drugs. Furthermore, it has been shown that some of its members demonstrate sex-dependent expression. In his study, Huamin Wang showed that CYP3A9 was female-specific and demonstrated estrogen dependency. His results showed more than 10-fold higher expression of CYP3A9 in female livers than in male livers. Ovariectomized female rats had reduced expression of CYP3A9 in the liver. However, when these rats were treated with estrogen, the expression level of CYP3A9 was restored. Because mouse models are easier to understand and manipulate, CYP3a13, a probable orthologue of CYP3A9, was used to see if it showed similar protein expression and function. Cos M6 cell line was transfected with CYP3a13 in pCMVScript. Protein assays and Western Blots confirmed that CYP3a13 was expressed. To check the functionality of the protein, formaldehyde assays were performed using erythromycin, benzphetamine, and ethylmorphine as substrates. The metabolism of these drugs by CYP3a13 yielded results that were comparable to those of CYP3A9.
ABSTRACT

First Place, 2002 Frank Webber Prize for Student Research

COUP-TFII and GATA-4 but not USF Play a Role in CPT-1β Regulation

ELIZABETH ANN WARNER                     U.T. at Houston Medical School                     Class of 2005

Sponsored by: Jeanie B. McMillin, PhD, Department of Pathology and Laboratory Medicine

Supported by: The University of Texas–Houston Summer Research Program; National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676

Keywords: CPT, transcription, metabolism, myocyte, AMP kinase

Metabolically stressed myocytes with increased levels of AMP activate stress kinases such as AMP-activated protein kinase. This activation can be mimicked in rat neonatal cardiac myocytes with the compound 5-Aminoimidazole-4-Carbamoyl-1-β-D-Ribofuranosyl 5'Monophosphate (AICAR). Carnitine Palmitoyltransferase-1β (CPT-1β) is the rate limiting enzyme in fatty acid degradation; CPT-1β activation would contribute to the restoration of the AMP:ATP ratio. AICAR treatment stimulated CPT-1β luciferase reporter expression 2.3± 0.2-fold (p<10^-6). We hypothesized the metabolically regulated transcription factors USF-1 and 2 were involved in AMP kinase signal transduction. However, over expression of wild-type USF, a dominant negative form (A-USF), or mutation of the USF binding sites (E-box -252 and –315), did not significantly alter promoter response to AICAR treatment. Further analysis of promoter structure implicated Chicken Ovalbumin Upstream Promoter - Transcription Factor II (COUP-TFII) and GATA-4 as possible mediators of the AICAR response. Overexpression of COUP-TFII decreased promoter response to AICAR to 1.3± 0.2-fold (p<0.005). Mutation of the COUP-TFII binding site does not significantly affect the AICAR response, suggesting that COUP-TFII is acting at alternate binding sites. GATA-4 overexpression reduced AICAR stimulation to 1.4± 0.1-fold (p<0.005); binding site mutations increased response to 3.1± 0.2-fold (p<0.05). Our data suggests that promoter response to AICAR is mediated by multiple transcription factors and possibly unidentified cofactors. Further investigation of phosphorylation patterns is necessary to discern the regulation of CPT-1β transcription under stressful metabolic conditions.
ABSTRACT

Survival of End-Stage Heart Failure Patients on Short and Long-term Use of Left Ventricular Assist Systems

JANELLE WILLIAMS UT at Houston Medical School Graduation: 2005

Sponsored by: Heinrich Taegtmeyer, M.D., D.Phil, Department of Internal Medicine, Cardiology

Supported by: NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

Key words: Left Ventricular Assist Systems (LVAS), mechanical unloading

Background: Left Ventricular Assist Systems (LVAS) unload the failing heart and are used as a “bridge to transplantation”. Anecdotal reports suggest that survival of patients with advanced heart failure is inversely related to the duration of LVAS support.

Hypothesis: In a large group of patients, the survival is a function of duration of LVAS support and independent of the types of LVAS used.

Materials and Methods: We reviewed the clinical charts of 20 consecutive patients entered into a prospective study of functional and structural changes of the failing heart subjected to mechanical unloading. Of these patients, eight had a Jarvik 2000 (Group I) and twelve had a HeartMate Vented Electric Left Ventricular Assist Device (LVAD) (Group II) implanted.

Results: In Group I, four patients received a heart transplant (50%); three patients died while on support (37.5%); and one patient was still alive (12.5%). In Group II, three patients received a heart transplant (25%); five died while on therapy (42%); and five remain on therapy (33%). Of the seven patients that received transplants, the mean length of support was 84±62 days for the Jarvik implants and 235±12 days for the LVAD. Multivariate analysis revealed no difference in survival with respect to etiology, changes of biochemical abnormalities, or pharmacological treatments with heart failure.

Conclusion: Factors other than the length of support with the LVAS determine the survival of heart failure patients treated with mechanical unloading of the left ventricle. These factors may include length of symptoms and co-morbidities (e.g. diabetes, hypertension, obesity).
ABSTRACT

Effects of Parametric Alterations in Performance during Working Memory Tasks on Hemodynamic Response in Prefrontal Cortex of Individuals with and without Schizophrenia

AUDREY C. WOERNER  University of Texas at Houston Medical School  Graduation: 2005

Sponsored by: Joel L. Steinberg, M.D., Department of Psychiatry and Behavioral Sciences

Supported by: NIDDK T35, National Institute of Diabetes and Digestive and Kidney Diseases, T35DK07676-10

(3-5) Key words: Functional Magnetic Resonance Imaging (FMRI), Delayed Memory Task (DMT), Immediate Memory Task (IMT)

Individuals with schizophrenia have severe deficits in cognitive executive functions, specifically working memory. Previous studies have suggested that the prefrontal cortex is essential for working memory. Thus, dysfunction of prefrontal brain regions has been proposed as an explanation for the deficits in working memory in patients with schizophrenia. Each subject of the two experimental groups (individuals with schizophrenia and normal controls without schizophrenia) participated in 2 FMRI sessions. The behavioral protocol during each session was a rapid-presentation, stochastic, event-related design consisting of the following trials presented in random order: DMT, IMT, and a null trial (Rest, 2 s) over a total period of 10 minutes per session with a 5 minute rest period between sessions. The level of difficulty of each DMT and IMT trial was varied randomly by changing the number of digits for each trial, between 3 and 7 digits. A sagittal localizer scan and a high resolution 3D-SPGR anatomical scan were obtained immediately prior to the first FMRI session. For event-related analysis, the first stimulus (target) of each trial, the distracter stimulus during working memory, and the probe stimulus of each trial were regarded as separate events. The data were analyzed using Statistical Parametric Mapping software (SPM99). During equal levels of performance on a working memory task, individuals with schizophrenia had decreased levels of neuronal activity at the 0.001 level (uncorrected) in the dorsolateral prefrontal cortex compared to controls for both the 3 and 7 digit trials.
Undergraduates
Soluble Guanylyl Cyclase Inhibits the Migration of Vascular Smooth Muscle Cells

KARL ACKERMAN
East Stroudsburg University
Graduation: 2002

Sponsored by: Ferid Murad, M.D., PhD, Department of Integrative Biology & Pharmacology

Supported by: The University of Texas at Houston Medical School

Key words: smooth muscle cell migration, soluble guanylyl cyclase

The enzyme soluble guanylyl cyclase, which is activated by nitric oxide and produces cyclic guanosine monophosphate (cGMP). cGMP, in turn, regulates cGMP dependent protein kinases, ion channels, and phosphodiesterases. Nitric oxide is hypothesized to play a role in the inhibition of vascular smooth muscle cell migration after vascular injury. After angioplasty, various growth factors in the blood cause exposed vascular smooth muscle cells to migrate into the lumen of the blood vessel, impeding blood flow. To test sGC’s ability to inhibit this migration, rat vascular smooth muscle cells were isolated and cultured. A transwell migration assay was devised to measure the migration of the cells from the upper chamber to the lower chamber, with 2.6x10^5 cells/well used for the assay. 20 ng/ml platelet derived growth factor was used in each well, and wells were treated as follows: control (untreated); BAY, a benzylindazole allosteric activator of sGC, 5 μM; 8Br-cGMP, an analogue of cGMP, 50 μM; DETA-NO, a nitric oxide donor, 50 μM. It was found that 8Br-cGMP inhibited vascular smooth muscle cell migration over 50% of the control, BAY inhibited almost 70%, and DETA-NO inhibited over 80%. These results suggest that NO inhibits the migration through the activation of sGC since BAY, an allosteric activator of sGC, also inhibited vascular smooth muscle cell migration. Further studies will address the mechanism through which sGC inhibits this migration.
ABSTRACT

Isolation of *Myxococcus xanthus* genes required for exopolysaccharide biosynthesis and assembly.

ANUPAM ADITI                   University of Southern California                             Class of 2004
Sponsored by:   Heidi B. Kaplan, Ph.D., Department of Microbiology and Molecular Genetics
Supported by:   The University of Texas Health Science Center at Houston Medical School
Key Words:       Myxococcus xanthus, gliding motility, calcofluor

*Myxococcus xanthus* exopolysaccharide (EPS) capsule, referred to as fibrils, is required for social gliding motility and fruiting body development. To identify genes involved in EPS biosynthesis and assembly, random mutagenesis with the miniHimar1 transposon was performed. Mutants were identified by their lack of reactivity with calcofluor white, a fluorescent dye that binds \( (1\rightarrow3)\)-\(\beta\)-D-glucopyranosyl units contained in the EPS. *M. xanthus* wild-type cells (DK1622) were electroporated with a plasmid containing the miniHimar1 kanamycin resistant transposon and plated onto kanamycin plates containing of calcofluor white (50 \(\mu\)g/ml). After incubation for six days at 32°C, the colonies were examined under UV light to identify non-fluorescent and therefore non-calcofluor reactive mutants. Thirty putative mutants were identified from the approximately 12,000 colonies screened and two mutants were studied in detail. To identify the genes into which the transposons inserted, the flanking DNA was sequenced. First, chromosomal DNA from each mutant was isolated, digested with the restriction enzyme *SacII*, ligated, and used to transform *E. coli* \(\lambda pir\) cells. *E. coli* cells containing the recombinant plasmids composed of the transposon (providing the origin of replication and the selectable kanamycin resistance gene) and the flanking *M. xanthus* DNA were identified. The plasmids were prepared for sequence analysis. The sequence of the *M. xanthus* DNA flanking the transposon will be compared to sequences in the databases to determine if the genes identified are homologues of known genes. Both of these mutants are defective in fruiting body formation as would be expected. Future analysis of these mutants will determine the specific roles of the mutated genes in surface motility and development.
Tumors need glucose and blood flow to grow. These two parameters are sensitive to changes in tumors with treatment such as Endostatin and can be measured by Positron Emission Tomography (PET). We have analyzed 19 solid tumors that were treated with Endostatin and PKI and imaged by PET. Regions of interest (ROI) were drawn on glucose images of tumors, and the values of blood flow, metabolism, and tumor size were obtained for baseline scans and at intervals of 28 days and 56 days post treatment. Our results show a great deal of heterogeneity in blood flow, glucose uptake, and tumor growth rates for different types of tumors. Metastatic lesions in the same patient were found to have different blood flow and metabolism rates. Changes in tumor blood flow, metabolism, and growth rates were also different with treatment for tumors in the same patient. The relative distributions of blood flow and glucose metabolism were sometimes different in the same tumor and changes in these parameters with treatment were different in regions of the tumor. In conclusion, there is a great deal of heterogeneity in tumor blood flow, glucose metabolism and tumor growth rates within the same tumor, the same patient and between tumor types. Rates of changes of these parameters were also found to be variable within the same tumor. Additional research is required to learn more about the role of this heterogeneity in quantitation of tumors by PET.
ABSTRACT

The Side Effects and Efficacy of Antiretroviral Treatment in HIV/AIDS Patients

DIONNE L. ALLEN                           The University of Texas at Austin                           Class of 2006

Sponsored by:       Roberto C. Arduino, M.D., Department of Internal Medicine, Infectious Disease

Supported by:       The University of Texas Health Science Center at Houston

Key words:            antiretroviral, CD4, viral load, adherence

This study was created to analyze the side effects and efficacy that HIV-1 infected patients may experience after commencing antiretroviral therapy. Efficacy was assessed by CD4 cell counts and viral load (HIV RNA copies/ml) response to antiretroviral therapy. Data was collected and analyzed from medical charts containing the HIV/AIDS history of 40 patients regularly examined by physicians at Thomas Street Clinic. During the first 4 weeks of therapy, the most common side effects experienced by patients were skin rashes (19%), nausea (17%), mild diarrhea (13%), vomiting (8%), and headache (5%), while 20% of patients had no complaints. However, after continuing treatment 65% of the patients had no complaints of side effects. Due to adherence to their antiretroviral therapy the majority of patients have experienced significant improvements concerning their HIV/AIDS status. Twenty-four (60%) of 40 patients have more than doubled their CD4 cell count, in which 18 (75%) of the 24 have quadrupled their CD4 cell count. Nineteen (59%) of 32 patients clinically diagnosed with AIDS who had a CD4 cell count < 200 cells/mm³ at baseline experienced a CD4 cell count increased to >200 cells/mm³ after at least eight weeks of antiretroviral therapy. The viral load of 57.5% of the patients was below limits of detection by week sixteen. In conclusion, antiretroviral therapy shows very promising results among the patients undergoing antiretroviral treatment. Although most patients may experience short-term discomfort the long-term effects seem to be greatly beneficial.
Angiotensin II Increases Fibronectin in an In-Vitro Model of Renal Fibrosis.

VICTOR BLACKETT Ohio Wesleyan University Graduation: 2004

Sponsored by:  Diane Hickson-Bick, Ph.D., Department of Pathology and Laboratory Medicine
RogerJ. Bick, Ph.D., Department of Pathology and Laboratory Medicine
Glenn A. McDonald, M.D., Department of Internal Medicine

Supported by:  The University of Texas Health Science Center at Houston Medical School

Key words:  renal failure, angiotensin II, fibronectin

Fibronectin (FN), a large adhesive glycoprotein, is a prominent constituent of the extra cellular matrix (ECM). Abnormalities in FN homeostasis occur in numerous disease states and is a prominent feature of renal fibrosis. Central to this process is the up regulation of fibrogenic cytokines. A prominent cytokine in this process is angiotensin II (ANG II). To define the role of ANG II in an in-vitro model of renal fibrosis we incubated mouse mesangial cells (MMC), mouse cortical tubular (MCT) and mouse tubular fibroblast (TFB) in the presence of ANG II. We demonstrate that ANG II causes a dose dependent increase in FN in each of the three cell types. To determine the molecular mechanism responsible for this increase in FN we evaluated the effects of ANG II on fibronectin RNA. In duplicate samples, increasing doses of ANG II did not result in an increase in fibronectin RNA. Thus we conclude that ANG II causes a dose dependent increase in the ECM protein FN. Furthermore, these effects are most likely due topost-translational processing. Additionally, we have developed an in-vitro model to allow the further interrogation of ANG II on the ECM.
ABSTRACT

Mannose binding protein gene polymorphisms as markers for susceptibility to infection with Cryptosporidium

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Sponsored by: Pablo C. Okhuysen, MD, Department of Internal Medicine, Infectious Disease

Supported by: The University of Texas Health Science Center at Houston

Key words: Cryptosporidium parvum, mannose-binding protein, single nucleotide polymorphisms

Cryptosporidium parvum is a protozoan parasite that frequently causes diarrhea in the general population and is transmitted from person to person or through contaminated water. The low infectious dose of this parasite and its ability to contaminate drinking water sources facilitates its potential for causing large-scale waterborne outbreaks. Upon exposure to the parasite the susceptibility to infection and clinical manifestations are variable and likely related to innate immunity. Since susceptibility to other intracellular infectious agents is associated with single nucleotide polymorphisms (SNP) of the mannose binding lectin gene, we investigated if polymorphisms in the MBL gene are associated with susceptibility to Cryptosporidium parvum as evidenced by the presence of anti-C. parvum seropositivity. To this end we conducted a study using samples collected from healthy volunteers who where tested for anti-C. parvum IgG antibodies. DNA from 38 subjects was studied for the presence of MBL SNPs (positions 52, 54, 57) using PCR and sequencing. Subjects with SNP in positions 52, 54 and 57 were classified as homozygous (O/O) or heterozygous (A/O) if no SNP were found. As shown in the table, subjects who were seropositive were more likely have MBL SNPs (38% vs 9% p=0.03, Odds Ratio=6, Fisher’s exact test).

<table>
<thead>
<tr>
<th>Anti-C. parvum</th>
<th>A/O or O/O</th>
<th>AA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive n=16 (%)</td>
<td>6 (38)</td>
<td>10 (62)</td>
<td>.03</td>
</tr>
<tr>
<td>Negative n=22 (%)</td>
<td>2 (9)</td>
<td>20 (91)</td>
<td></td>
</tr>
</tbody>
</table>

In this study we demonstrate that subjects with previous infection with C. parvum are more likely to carry MBL genotypes associated with deficient MBL production. The identification of SNP in the genes of the innate immune system that are associated with susceptibility to infection with enteric pathogens will have implications for risk assessment and control of these agents.
ABSTRACT

Dose Response Characteristics of Chronic Ritalin in Juvenile and Adult Rats

JANIE CASTILLO                           University of Texas at Brownsville                  Graduation:: 2003

Sponsored by:      Nachum Dafny, PhD, Department of Neurobiology
Supported by:      The University of Texas Health Science Center at Houston
Key words:           Methylphenidate, behavioral sensitization, dose response

Methylphenidate (MPD), also known as Ritalin, has been demonstrated to elicit time dependent adverse effect such as behavioral sensitization, a phenomenon in which increased locomotor activity and stereotypic behavior occur following repeated exposures to these drugs. Knowledge about this adverse effect of MPD is important because MPD is the most frequently used psychostimulant to treat children who are diagnosed with attention deficit/ hyperactivity disorder (ADHD). Although studies on other psychostimulants like cocaine and amphetamine have clearly indicated that females are more sensitive than males, little is known about the long-term effects of MPD in females. In order to investigate the long-term effects of MPD in females, a dose response experiment must first be established. Therefore, the objective of this study was to determine the dose response characteristics of MPD in juvenile and adult female Sprague-Dawley (SD) rats. A total of 48 juvenile female SD rats were divided into the following groups: Groups 1, 2, and 3 received 0.6, 2.5, or 10 mg/kg, MPD, i.p., respectively, for 6 consecutive days as juveniles and when they become adults (naïve juveniles, non-naïve adults), Groups 4, 5, and 6 received saline as juveniles and 0.6, 2.5, or 10 mg/kg, MPD, i.p., respectively, for 6 consecutive days as adults (naïve adults), and Group 7 received saline as juveniles and adults and served as the control. Following saline/MPD administration, the locomotor activity and stereotypic behavior of the rats were measured using a computerized activity monitoring system for two hours. All injections and measurements of locomotor activity and stereotypic behavior were performed in the afternoon (14:00h – 18:00h). Results showed that 1) the locomotor activity baselines were the same in both juvenile and adult rats, 2) only naïve adult rats receiving 0.6 mg/kg MPD showed behavioral sensitization, 3) naïve adult rats receiving 10 mg/kg MPD displayed tolerance and 4) non-naïve adult rats receiving 0.6 mg/kg MPD exhibited tolerance to repeated injection.

*MPD was a gift from Mallinckrodt, Inc.
The Centers for Disease Control and Prevention published new fluoride guidelines in August 2002, which aim to prevent any increase in the prevalence of dental fluorosis resulting from excessive fluoride intake. Fluorosis in its most severe form appears as dark-brown stain, pitting and chipping of enamel surfaces. The purpose of the study was to investigate the knowledge and prescription patterns of fluoride supplements among dentists practicing in San Antonio, Texas, where water supplies are yet to be fluoridated. Data were collected by a self-administered mail questionnaire that consisted of 13 open-ended and 29 pre-coded items, from 439 dentists. After one mailing, the effective response rate to the survey was almost 25%. Among the respondents, 81.6% were males and the mean number of years in practice was 19.9±11.1. Many respondents correctly identified that dietary fluoride supplements are useful in caries prevention (93%), cost effective (85.6%), and benefits adults as well (87.5%). Some 36.5% of the respondents incorrectly identified that systemic effects of fluoride supplements is more important than topical effects. Dietary fluoride supplement is recommended to begin at the age of 7 to 12 months and continue until the age of 16 years. Only 11.5% and 15.4% of the respondents correctly identified the beginning and discontinuing ages respectively. The results indicate deficiencies and ambiguity among respondents’ knowledge on fluorides and its recommendation to patients. Respondents could benefit from continuing education courses in the clinical knowledge of fluorides.
Interference of Traditional Chinese Medicines Chan Su, Lu-Shen-wan, Dan Shen and Ginseng on the Serum Digoxin Measurement of Three Digoxin Immunoassays

LEONARD CHOW
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Graduation: 2003

Sponsored by: Amitava Dasgupta, PhD, Department of Pathology and Laboratory Medicine

Supported by: The University of Texas Health Science Center at Houston

Key words: Digoxin, traditional Chinese medicines, fluorescence polarization, Roche assay, Beckman assay

Chan Su, Liu Shen Wan, Dan Shen, and Asian Ginseng are traditional Chinese medicines used to treat a number of conditions including cardiovascular disease because each of these drugs exhibits cardio active properties. Digoxin is a cardio active drug with a narrow therapeutic range (0.8-1.9 ng/ml). A patient taking digoxin may also take any of these Chinese medicines for its cardio tonic effects. Moreover, active components responsible for these effects in each of these medicines bear structural similarities to digoxin. Therefore, we studied the potential interference of these Chinese medicines with three digoxin immunoassays: fluorescence polarization immunoassay (FPIA), Roche digoxin immunoassay, and Beckman digoxin immunoassay. When very small amounts (2-5 l) of aqueous extract of Chan Su or Liu-Shen Wan (1 mg/ml) were added to drug free serum, we observed high digoxin like immunoreactivity with FPIA. In contrast when ethyl acetate extract of Dan Shen or micro-liter amount of ginseng extract were added to drug free serum, we observed modest digoxin-like immunoreactivity with the FPIA, but no apparent digoxin activity with the Roche and Beckman digoxin immunoassays. When aliquots of a digoxin pool prepared from patients receiving digoxin were supplemented with these Chinese medicines, we observed most significant interference with the FPIA. For example, a digoxin pool containing 0.7 ng/ml of digoxin, the apparent digoxin concentration was increased to 9.30 ng/ml (FPIA) in the presence of 5.0 l of Chan Su extract added to per ml of digoxin pool. The Roche and Beckman assays showed 5.35 and 7.30 ng/ml of digoxin concentrations respectively. When 20 l of ginseng was added to per ml of the same pool, the apparent digoxin concentrations were 1.28 ng/ml by the FPIA, 0.85 ng/ml by the Roche and 0.60 ng/ml by the Beckman digoxin assays. The presence of endogenous digoxin-like immunoreactive substances can have additive effects with these Chinese medicines in falsely increasing apparent digoxin levels by the FPIA. On the other hand, Roche and Beckman assays are free from interference from DLIS. We conclude that FPIA showed most significant interference with all four Chinese medicines we studied. Although Roche and Beckman digoxin assays showed significant interference with Chan Su and Lu-Shen-Wan, the two other Chinese medicines Dan Shen and Ginseng had no effect on both Roche and Beckman Assays.
ABSTRACT

Cell Permeability of Nemo IKK Inhibition Peptide

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Graduation: 2005

Sponsored by: Jaroslaw Aronowski PhD, Department of Neurology

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: Nemo, Inhibition, Permeability, IKK, Nf-kB

Nf-kB regulates transcription of various molecules, such as cytokines, that induce an inflammatory response after a stroke. The inhibitor-kB kinase (IKK) most likely regulates Nf-kB activity in the nucleus. Inhibition of IKK hypothetically will inhibit Nf-kB activity, thus decreasing inflammation in the brain. To further understand IKK regulation of Nf-kB, a cell-permeable peptide was designed after the noncatalytic subunit of IKK called NF-kB essential modulator (NEMO), or IKK gamma, which supposedly mediates formation of dimers critical for IKK catalytic activity. Its N-terminal is designed after the sequence from the Antennapedia homeodomain, which allows the peptide to penetrate cells. The N terminal possesses a biotin tracer that allows immunohistochemistry, namely antibody streptavidin-ALEXA 488, to trace the exact location of IKK inhibition of NF-kB activity. The peptide was initially delivered into the rat brains in a PBS solution and then in a DMSO/saline solution by injection into the striatum. Delivery in a PBS solution yielded no detection by streptavadin-ALEXA 488 because its antennapedia sequence is hydrophobic and reacts negatively with the PBS. Delivering the peptide in a DMSO/saline solution yielded slightly better results. Various troubleshooting strategies, including varying the solution’s volumes and concentrations and delivering the peptide in vivo, failed to improve its limited cell permeability. A more effective sequence should replace the antennapedia sequence in future experiments. Immunohistochemistry showed IKK inhibition in neurons and in unknown fibers along the needle tract. Further immunohistochemistry should eventually determine the identity of these fibers.
ABSTRACT

Return of Spontaneous Circulation in a High Volume Urban EMS System

ALLISON DRYDEN Baylor University Graduation:2004

Sponsored by: Richard Bradley, M.D., Department of Emergency Medicine

Supported by: The University of Texas at Houston Medical School

Key words: cardiac arrest, Emergency Medical System, return of spontaneous circulation

Return of spontaneous circulation (ROSC) rates in out of hospital cardiac arrests (OOHCA) are one determining factor for the competency of an EMS system. Systems with higher ROSC rates may help serve as templates for systems that have lower percentages. In order to determine the ROSC rates for the Houston (TX) Fire Department (HFD)- Emergency Medical Service (EMS) system, we reviewed all of the EMS charts related to cardiac arrests of presumed cardiac origin within the study period for the year 2000. We then used Microsoft Access to enter all of the data that was gleaned from the EMS charts. This data could then be examined through the use of queries related to outcomes that we specified. Using only cases in which the cardiac arrest stemmed from non-traumatic origin, we found there to be 811 total cardiac arrests within the study period. Out of this total, 327 (40%) had a positive ROSC. When the numbers were broken down further, ventricular fibrillation/ventricular tachycardia (VF/VT) showed the highest percentage of ROSC at 63%, followed by pulseless electrical activity (PEA) or rhythms other than VF/VT and asystole with a ROSC in 57% of cardiac arrest patients. Finally, asystole showed a ROSC percentage of 25%. These percentages may be considered above average; however, comparison is difficult due to the lack of published information on ROSC rates for other cities. Further examination of ROSC rates in other systems is needed.
ABSTRACT

Scleroderma Registry Sample Processing

KARINA EASTMAN  Mary Baldwin College  Graduation:  2003

Sponsored by:  Maureen D. Mayes, M.D., M.P.H., Department of Internal Medicine, Rheumatology

Supported by:  The University of Texas Health Science Center at Houston Medical School

Key words:  systemic sclerosis, Scleroderma, DNA repository study

Systemic sclerosis or scleroderma is a connective tissue disease characterized by the over production of scar tissue in the skin, internal organs, and blood vessels. Hardness of the skin is the most visible change caused by the disease. The etiology is still unknown. The goal of the Scleroderma family registry and DNA repository study is to investigate the genetic basis of scleroderma and identify candidate genes for the expression of the disease. Blood samples are received regularly in the laboratory and my goal is to manage the sample income by processing these samples efficiently. Initially, the blood is spun down in a centrifuge and the serum and plasma are measured and pipetted off for freezer storage. Red blood cell lysis solution is then added to the blood and the samples are set on a rocker and later spun down in an eppendorf centrifuge. The supernatant is poured off and cell lysis solution is added to the pellet and the tubes are set on the rocker overnight. At the end of the week 48 samples undergo DNA extraction using a repeater and colmbi tips. The DNA pellets are then stored in 1000 µL of DNA hydration solution at 4 °C. The concentration is later determined by a spectrophotometer. The O.D. 260nm absorbency, concentration (in µg/µL), and 260/280 ratio is recorded. Samples with very low concentration are amplified by PCR and the product is confirmed by electrophoresis. Processed and quantitated samples are then stored for genomic screening and to build the DNA repository for use by other investigators.
ABSTRACT

Bond Strengths of 5th and 6th generation Adhesives to Composite Matrix Bands

DAWN EVENS                                   Prairie View A&M University                                   Graduation 2005
Sponsored by: Rose-Marie Fay, D.D.S., M.S., Dental Branch, Restorative Dentistry, Biomaterials
Supported by: The University of Texas Health Science Center at Houston Dental Branch
Key words: bond strengths, 5th and 6th generation adhesives, composite matrix band

PURPOSE: To determine the bond strength of resin composite bonded to composite matrix material using 5th and 6th generation adhesives after storage for two time period.

MATERIALS and METHODS: Matrix material specimens (Access Crown), were fabricated using a 3 mm x 10 mm mold, and mounted in potting resin. Specimens were polished to 600 grit with SiC discs, and aged for 24 hours and 1 week before bonding. TPH Spectrum composite was bonded to the specimens with Clearfil SE Bond and One-Step adhesives. The bonded composite were built in the shape of an inverted, truncated cone. There were 8 specimens per condition for a total of 32 specimens. After bonding, the specimens were stored in water at 37°C for 24 hours. They were then debonded in tensile strength on the Instron testing machine at a cross-head speed of 0.5 mm/min.

RESULTS: After 24 hours, mean (s.d.) for One-Step was 24.3 (4.9) and for Clearfil SE Bond was 23.3 (7.1). After 7 days, the mean for One-Step was 16.4 (4.9) and for Clearfil SE Bond was 19.6 (5.9). Failure sites were mixed. Fisher’s PLSD statistics program was used.

CONCLUSION: Bond strengths were shown to be higher when the product was used immediately than over a period time. Also, overall the Clearfil SE Bond had a better bond strength than the One-Step for the two time periods.
ABSTRACT

Substrate specificity in recombinant plant fatty acid oxygenase

PAVOL FABIAN                                                  Tufts University                                    Graduation:  2005

Sponsored by:     Richard J. Kulmacz, PhD, Department of Internal Medicine
Supported by:     NIH GM 52170 and The University of Texas at Houston Medical School
Key words:          plant pathogen-induced oxygenase, fatty acid oxygenase, substrate specificity

Many plants have an inducible fatty acid oxygenase, called PIOX (Pathogen-Induced Oxygenase). PIOX has interesting structural and functional similarities with the two physiologically important human prostaglandin H synthase isoforms. Various constructs of A. thaliana PIOX protein, including the full-length PIOX alone and fusions of PIOX to the C-terminus of GST or Nus, were expressed in bacterial (E. coli cells) or baculoviral (Sf9 insect cells) systems. The oxygenase kinetic parameters of the various recombinant PIOX constructs were evaluated with several fatty acid substrates to compare active site structures. An oxygen electrode was used to measure oxygenase activity as the fatty acid concentration was varied form 5-300µM. Activity values were fitted to the Michaelis-Menten equation to estimate $V_{max}$ and $K_m$ (see table below). The similarities among the PIOX constructs in their fatty acid selectivity for both “good” substrates (18:2 and 18:3) and “poor” substrates (16:1 and 20:1) indicate that the mode of recombinant protein expression had little effect on PIOX active site structure.

<table>
<thead>
<tr>
<th>Protein Construct</th>
<th>16:1 (n-7)</th>
<th>16:1 (n-7)</th>
<th>18:2 (n-6)</th>
<th>18:2 (n-6)</th>
<th>18:3 (n-3)</th>
<th>18:3 (n-3)</th>
<th>20:1 (n-9)</th>
<th>20:1 (n-9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$K_m$ (µM)</td>
<td>Rel. $V_{max}^*$</td>
<td>$K_m$ (µM)</td>
<td>Rel. $V_{max}^*$</td>
<td>$K_m$ (µM)</td>
<td>Rel. $V_{max}^*$</td>
<td>$K_m$ (µM)</td>
<td>Rel. $V_{max}^*$</td>
</tr>
<tr>
<td>PIOX (Sf9)</td>
<td>57 ± 11</td>
<td>0.92</td>
<td>21 ± 4</td>
<td>1.1</td>
<td>38 ± 17</td>
<td>1.0</td>
<td>31 ± 5</td>
<td>0.53</td>
</tr>
<tr>
<td>PIOX (E. coli)</td>
<td>61 ± 10</td>
<td>1.5</td>
<td>21 ± 5</td>
<td>1.6</td>
<td>21 ± 5</td>
<td>1.0</td>
<td>27 ± 4</td>
<td>0.78</td>
</tr>
<tr>
<td>GST-PIOX (E. coli)</td>
<td>38 ± 5</td>
<td>0.98</td>
<td>16 ± 3</td>
<td>0.84</td>
<td>21 ± 2</td>
<td>1.0</td>
<td>16 ± 1</td>
<td>0.48</td>
</tr>
<tr>
<td>Nus-PIOX (E. coli)</td>
<td>45 ± 17</td>
<td>0.93</td>
<td>18 ± 5</td>
<td>0.91</td>
<td>37 ± 15</td>
<td>1.0</td>
<td>19 ± 3</td>
<td>0.47</td>
</tr>
</tbody>
</table>

*Relative to the value for 18:3 (n-3).
Identification of Novel Heat Shock Genes in *Saccharomyces cerevisiae*

**PATRICK A. GIBNEY**  
*University of Northern Iowa*  
Class of 2003

Sponsored by: Kevin A. Morano, Ph.D., Department of Microbiology and Molecular Genetics  
Supported by: The University of Texas Health Science Center at Houston Medical School  
Key words: heat shock, *Saccharomyces cerevisiae*, yeast

Human pathological states such as heart disease and cancer share many similar features with the cellular stress response in microbes. *Saccharomyces cerevisiae* provides a versatile model system to study the eukaryotic stress response. The goal of this research project was to characterize eight previously unknown, predicted heat shock-inducible genes. The characterization was accomplished through cloning, phenotype complementation assays, and gene expression analyses. One gene, *YER139c*, was found to have a temperature-dependent formamide sensitivity phenotype that was complimented by expression of the wild-type gene. Formamide is a protein-unfolding agent that exacerbates heat shock phenotypes. The heat induction pattern of *YER139c* was confirmed by Northern blotting. *YER139c* will now be studied further as a novel gene in the heat shock response. Interestingly, a putative suppressor of the formamide sensitivity phenotype was isolated in *YER139c*, which may provide further insight into the cellular roles of *YER139c* through genetic analysis.
ABSTRACT

A New Method of Endotracheal Intubation Using the Video Laryngoscope

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Sponsored by: Carin A. Hagberg, M.D., Department of Anesthesiology
Supported by: The University of Texas Health Science Center at Houston
Keywords: endotracheal intubation, video laryngoscopy, difficult airways

Since the introduction of the laryngoscope blade, innovators have attempted to perfect its design in order to improve visualization of the laryngeal structures and increase the success rate of endotracheal intubation. The purpose of this study was to determine if the MacIntosh Video Laryngoscope (MVL) is superior to the traditional MacIntosh Laryngoscope. The MVL design optimizes visualization by presenting an enlarged video image onto a monitor projected from a camera located at the distal end. The study included 101 anesthetized patients. Anesthesia was performed according to standard practices, except for the utilization of the MVL. Observations were recorded by looking into the patient’s mouth with the naked eye and viewing an image on a monitor. The MVL displayed partial glottic opening in 99% of the patients (82% full view), in contrast to 53% of the patients (36% full view) with the naked eye. Thirty-two patients were judged to be possible difficult intubations. Of these, the MVL revealed partial glottic opening in 96% (69% full view), whereas the naked eye only revealed partial glottic opening in 3% (0% full view). One or more of these conditions determined a possible difficult intubation: small mouth opening, limited neck mobility, or a Mallampati III or IV classification. These results suggest that the MVL is better than the standard MacIntosh laryngoscope for endotracheal intubation, especially for possible difficult airways. Further study in known difficult airways is warranted.
Expression of Synaptogyrin III in HEK293 Cells

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Sponsored by: Roger Janz, PhD, Department of Neurobiology and Anatomy

Supported by: The University of Texas Health Science Center at Houston Medical School

Keywords: synaptogyrin, synaptic vesicles, HEK293 cells, EGFP

Synaptogyrins are conserved, tyrosine-phosphorylated synaptic vesicle proteins. The synaptogyrin gene family consists of two neuronal isoforms (Synaptogyrins I/III), each with four transmembrane regions and cytoplasmic C- and N- termini. The localization and characterization of synaptogyrin I (Sgyr I) along with its role in synaptic plasticity has emerged in recent studies. To better understand the localization of synaptogyrin III (Sgyr III), we have constructed two Sgyr III expression vectors. Primers were designed to incorporate flanking BamHI/EcoRI restriction sites and subsequently used to amplify wild type and truncated forms of Sgyr III. Amplified DNA was inserted into the vector pEGFP-N1 using the BamHI/EcoRI restriction sites. Human embryonic kidney (HEK293) cells were transfected to examine the expression of the EGFP-Sgyr III fusion protein. EGFP expression was observed by fluorescence microscopy eight hours post-transfection. Protein samples from transfected cells were analyzed by SDS-PAGE and Western blot. Sgyr III blots revealed two bands at 55 and 60 kDa in wild type samples. Truncated samples showed no bands due to removal of the C-terminus containing the epitope recognized by the Sgyr III antibody. Fixed cells were processed for immunohistochemistry using antibodies against Calnexin, a marker for the endoplasmic reticulum. EGFP-Sgyr III and Calnexin, visualized with Alexa-568 coupled secondary antibody, partially co-localized, indicating Sgyr III was present on the endoplasmic reticulum. Ongoing studies using the EGFP-Sgyr III constructs in PC12 cells and hippocampal neurons will further elucidate the localization and function of this synaptic vesicle protein.
Correlation of Corneal Fibrosis and the Expression of a Vβ6

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Sponsored by: Richard W. Yee, M.D., Department of Ophthalmology
Supported by: The University of Texas Health Science Center at Houston Medical School

Keywords: integrin, TGFβ, αVβ6, corneal wound healing

The integrin αVβ6 is upregulated in pulmonary tissue during injury to activate TGFβ to begin the wound healing process. Inhibition of this integrin results in minimal fibrosis. Studies of PBK, an ongoing fibrotic disorder, has identified αVβ6 to be present in this diseased cornea, although absent in healthy cornea. The upregulation of αVβ6 in a corneal fibrotic condition suggests that there is a comparable role for αVβ6 in corneal healing as there is in pulmonary healing. If αVβ6 is required for corneal fibrosis, there are enormous implications for patients who undergo laser refractive surgeries. Inhibition of this integrin could result in a reduction of corneal scarring and haze, thus improving post-operative vision. As a preliminary study, healthy and post-LASIK cadaveric corneas were cut into halves, embedded in paraffin, and cut into 5 µm sections. The tissue was stained with a human/mouse chimeric anti-αVβ6 primary antibody and an anti-human HRP as a secondary antibody. As controls, the corneas were also stained using primary and secondary antibodies individually and without any antibody. The secondary antibody was identified to react nonspecifically with the human corneal tissue. To mediate this issue, the next sets of tissue were pretreated with murine Fc-block, mouse serum, or human serum. However, these blockers did not ameliorate the problem. Further studies may need to be performed with other blocking agents or with redesigned versions of the primary and secondary antibodies to determine whether αVβ6 is presenting post-LASIK corneas.
ABSTRACT

Bond Strength of Resin Composite to Dentin Contaminated with Blood

SHIREEN K. IRANI The University of Texas at Austin Class of 2003

Sponsored by: John M. Powers PhD, Dean of Research, Restorative Dentistry, Oral-Biomaterials

Supported by: The University of Texas Health Science Center at Houston Dental Branch

Key words: tensile bond strength, blood contamination.

The purpose of this study was to determine the effects of whole blood contamination on the bond strength of resin composite bonded to moist superficial dentin, using two different adhesive systems, Clearfil SE Bond (CB) (Kuraray America) and Clearfil SE Bond Plus (CBP) (Kuraray America).

Method: Freshly extracted human teeth were sectioned bucco-lingually and embedded in potting resin. Specimens were ground to superficial dentin using 600 grit SiC discs. Adhesives were bonded to the specimens according to the manufacturer's instructions using 5 surface conditions: Control Group (C), Blood/5 sec air dry/Adhesive (BA), Adhesive/ Blood/5 sec air dry (AB), Adhesive/Blood/5 sec water rinse/5 sec air dry (ABW), and Adhesive/Blood/5 sec water rinse/5 sec air dry/reapply adhesive (ABWA). Clearfil AP-X (Kuraray America) was bonded to superficial dentin in the form of a truncated cone (bonding surface area of 3 mm² and height of 5 mm). (n=8) for a total of 80 specimens. After bonding, specimens were stored in water at 37°C at 100% humidity for 24 hours. Specimens were de-bonded in tension using an Instron at a cross-head speed of 0.5 mm/min.

Results: In both adhesives C had the highest and AB the lowest bond strength values. For CB C>ABWA>BA>ABW>AB and for CB C>AB>BA>ABWA>AB. CBP had higher bond strength values than CB for all 5 surface conditions. Failure sites were mixed.

Conclusion: CBP had greater bond strength than CB under normal and blood contamination conditions.
ABSTRACT

Demonstration of the GABA activated chloride channel in mTAL cells

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Class of 2002

Sponsored by: Donald A. Molony, M.D., Department of Internal Medicine, Renal Diseases and Hypertension

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: flux assay, ST-1 cells, GABA receptor, $^{125}$I

Previous studies in this laboratory have shown that GABA receptor agonists protect against apoptosis in ST-1 cells, an established line of the mTAL (medullary thick ascending limb) of the mouse. Our hypothesis is that apoptosis results directly from inhibition of chloride efflux by GABA Cl$^{-}$ channel antagonists. The hypothesis was tested with a functional assay for the GABA receptor. Efflux of $^{125}$I was used to assess the permeability mediated by the GABA activated chloride channel in the presence of agonists, GABA and Muscismol, and antagonists, Bicuculline, all at concentrations of $10^{-6}$ M. The assay procedure was adapted from Venglarik et al (American Journal of Physiology, 259(2 Pt 1):C358-64, 1990 Aug). The cells, which were grown to 80% confluency on 35-mm plates, were incubated in modified HPBR containing 5.0 $\mu$Ci/ ml $^{125}$I for 45-75 minutes. The plates were washed 2x with 2 ml HPBR for 1 minute. After the wash, 1-ml aliquots of isotope free HPBR were added and removed sequentially at 30-second time intervals for 12 minutes. At the 4-minute time point, the HPBR wash solution was changed to one containing the agonist or antagonist. The rate constant was determined from the efflux data and immediately rose 350x above the baseline over a period of two minutes. Similar results were also seen with Muscismol. Bicuculline, the antagonist, did not show a change in the rate constant, as was expected. Unexpectedly, the addition of a GABA/Bicuculline combination yielded a greater increase in the rate constant than GABA. These preliminary results suggest that there may be other factors that need to be further investigated. The increased activity of the channel with the addition of GABA supports the hypothesis that the channel does function with a GABA receptor, and that GABA protects the cell from apoptosis while the Bicuculline’s inhibition of chloride efflux leads to apoptosis.

I would like to thank Otilia Mayorga-Wark and Dr. William Dubinsky for all of their help, support, and guidance.
ABSTRACT

Impulsivity and Aggression Differences Among Violent and Non-Violent Groups

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Sponsored by: Donald M. Dougherty Ph.D. Department of Integrative Biology and Pharmacology

Supported by: The University of Texas Health Science Center at Houston Medical School

Key word: Continuous Performance Test, Aggression, Impulsivity, Violence

Background: Prior Continuous Performance Test (CPT) studies have demonstrated a relationship between aggression and impulsivity. This project was a preliminary study of whether parametric manipulations of a CPT would enhance group discrimination between participants classified as violent or non-violent. Self-report questionnaires were used as collateral measures to confirm group differences.

Methods: Ten male and female participants, between the ages of 18 and 50, completed the Immediate Memory Task (IMT), a modified CPT procedure. The IMT requires the participant to respond to a briefly displayed (0.5 sec delay) 5-digit number if it was identical to the previous number. The three stimulus types included target (identical match), catch (four of five digit match), and novel (no match). Through parametric manipulation, three presentation probabilities of catch stimuli were studied and results of the two groups were compared. The Barratt Impulsivity Scale and Buss-Perry Aggression Scale were also completed as collateral measures of impulsivity and aggression.

Results: The findings of the CPT procedure were inconclusive. Differences in catch stimuli did not statistically differ between the violent and non-violent groups. The collateral impulsivity and aggression measures were compared, resulting in a differentiation between the violent (higher impulsivity and aggression scores) and non-violent (lower impulsivity and aggression scores) groups.

Conclusions: The violent group responded with more impulsivity and aggression than the non-violent group, however, the inconclusive IMT results were likely due to the small sample size.
Investigating Cell Division Protein Interaction with the Yeast Two Hybrid System

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Sponsored by:  William Margolin, PhD, Department of Microbiology and Molecular Genetics

Supported by:  The University of Texas Health Science Center at Houston Medical School

Keywords:  yeast two hybrid, cell division proteins

An essential part of prokaryotic cell division is FtsZ, a tubulin-like protein that assembles into a ring at the cell midpoint. Previous studies have shown that *E.coli* FtsZ interacts directly with FtsA and ZipA, essential proteins believed to serve different functions during division. However, a mutation in *ftsA* (*ftsA*) allows *zipA* knockout *E.coli* cells to survive, suggesting that the mutant protein (FtsA*) takes over the function of ZipA in its absence. One predicted mechanism to explain this bypass effect is that the FtsZ-FtsA* interaction might be stronger than FtsZ-FtsA. To test this hypothesis, a yeast two-hybrid assay was used to measure these protein interactions either as β-galactosidase activity or ability to grow in the absence of histidine.

Three clones were created: *pLexA-ftsA*, *pLexA-ftsA* *, and *pLexNLS-ftsA*. The *ftsA*-ftsZ system grew in the absence of histidine suggesting a positive interaction, while the *ftsA*-ftsZ system did not. The β-galactosidase liquid assay confirmed the known FtsA-FtsZ interaction, but suggested that there may be no FtsA*-FtsZ interaction. However, a β-galactosidase filter assay showed interaction with *pLexNLS-ftsA*-ftsZ. Therefore, these results are inconclusive. Further studies are currently underway using a *DivIVA-ftsA*-ftsZ-GFP protein interaction scheme. *DivIVA* normally localizes to *E.coli* cell poles. If *ftsA* and *ftsZ* interact, GFP should be targeted to the cell poles and would be visible as fluorescent polar spots. In the future, other protein interaction systems will examine FtsA*-FtsZ more closely in order to shed light on the FtsA*-mediated bypass of the ZipA requirement.
ABSTRACT

Are Mild Strokes Really Benign?

CHRISTINE E. JOY                              Rice University                              Class of  2003

Sponsored by:    James C. Grotta, M.D., Department of Neurology

Supported by:     The University of Texas Health Science Center at Houston Medical School

Key words:         mild stroke, thrombolytics, transcranial Doppler

It is unclear whether patients with relatively mild, fixed neurological deficits should or should not be treated with thrombolytics. In this study, we identified consecutive stroke patients for a 2 ½ year period that presented with mild or acutely resolving stroke symptoms and were not treated with conventional thrombolytic therapy nor intra-arterial procedures secondary to low NIHSS upon acute presentation within the first 6 hours. All patients were evaluated in the Emergency Department with transcranial Doppler using standard protocol and validated criteria. 42 patients with an admission median NIH Stroke Scale score of 3 points (range 0-6 points) were identified. In-hospital events included: fluctuations 2 (5%), stroke progression or recurrent stroke 6 (14%), and death 1 (2%). Overall discharge median NIHSS was 2 points (range 0-8 points). In the emergency room, 41% of all patients had either stenosis (n=7), or persisting proximal extra- or intracranial occlusion (n= 10) in the arterial distribution responsible for stroke symptoms. The presence of persisting arterial occlusion or a stenosis was found in 66% of patients with stroke progression while only 36% of patients with stable in-hospital course had persisting arterial lesions, NS. Although short-term prognosis appears good, there is at least a 20% chance of subsequent fluctuation, deterioration, or recurrent stroke during in-hospital stay. The coincidence of abnormal transcranial Doppler results with these events suggests transcranial Doppler’s predictive value for deterioration and therefore its significance in medical decisions regarding thrombolytic treatment.
The Effects of Neonatal Lesions on Parvalbumin-Immunoreactive Neurons in the Prefrontal Cortex of the Macaque Monkeys (Matata mulatta)

YOUNG SIN JUNG
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Sponsored by: Jocelyne H. Bachevalier, PhD, Department of Neurobiology and Anatomy

Supported by: The University of Texas Health Science Center at Houston Medical School

Keywords: development, GABA, parvalbumin, prefrontal cortex, schizophrenia

Recent studies support the hypothesis that structural and functional abnormalities found in the prefrontal cortex of schizophrenic patients might be caused by a neonatal insult to the medial temporal lobe (MTL). Alterations in the γ-aminobutyric acid (GABA) system, especially in parvalbumin-immunoreactive GABAergic neurons are thought to contribute to dysfunction of the prefrontal cortex in these patients. The late expression in development of the calcium buffering protein parvalbumin is thought to allow these neurons to be more vulnerable to early brain damage. However, there is conflicting evidence regarding whether the total neuronal density of parvalbumin-immunoreactive neurons in the prefrontal cortex is decreased, increased, or unchanged in schizophrenics. Based on previous findings that early damage to MTL impairs the normal development of neural structures distal to the site of injury, we investigated possible changes in parvalbumin-immunoreactive neurons in the prefrontal cortex, specifically in the dorsolateral cortex (area 46) caused by neonatal insults to the MTL in the macaque monkeys (Matata mulatta), who displayed some behavioral similarities to schizophrenics. Using unbiased stereological sampling, the density of parvalbumin-immunoreactive neurons in area 46 of two adult monkeys with MTL lesions (Group AH) and two unoperated adult controls were compared. A significant (p<0.05) deficit in parvalbumin-immunoreactive neurons in layer III in Group AH was observed. Thus, this study provides anatomical evidence that neonatal damage to MTL results in neuronal reorganization in those with early MTL damage that resembles some of the neuropathology observed in schizophrenia.
ABSTRACT

Effects of Insulin and Estradiol on Tyrosine Phosphorylation of Insulin Receptors and IRS-1 in Breast Cancer Cells

MICHELLE KAO University of Texas at Austin Graduation: 2005

Sponsored by: Victoria P. Knutson, PhD, Department of Integrative Biology and Pharmacology

Supported by: The University of Texas Health Science Center at Houston Medical School and The Department of the Army under award number DAMD 17-00-0460

Key words: insulin, Estradiol, Tyrosine Phosphorylation, breast cancer, diabetes

Insulin and estradiol are growth factors that play important roles in the growth and proliferation of cells. When insulin binds to the insulin receptors in the cell membrane, the receptors autophosphorylate and initiate a phosphorylation cascade in the signal transduction pathways that lead to cell growth and proliferation. Activation of this phosphotyrosine cascade is decreased by Leukocyte common Antigen-Related (LAR) protein tyrosine phosphatase, which dephosphorylates the insulin receptor and inhibits cell proliferation. From previous work in the lab, estradiol has been shown to decrease the expression of LAR in MCF-7 breast cancer cells. Therefore, both insulin and estradiol might have a synergistic effect on the tyrosine phosphorylation of the insulin receptors. To test this hypothesis, MCF-7 cells, a breast cancer cell line, were stimulated with insulin, estradiol, and a combination of both hormones. Cells were scraped and membrane fractions were extracted. The activation of insulin receptors was detected with Western blots, using anti-phosphotyrosine monoclonal antibody. Our preliminary data showed weak phosphotyrosine reactivity in all tested samples. Currently, we are optimizing conditions to increase the intensity of the phosphotyrosine signals. Subsequently, MCF-7 cells that over express and under express LAR will be examined to quantitate the phosphotyrosine content of the insulin receptor and IRS-1 upon stimulation of these cells with insulin and estradiol. It is anticipated that the data from these tests will lead to the development of treatments to inhibit the proliferation of breast cancer cells.
ABSTRACT

Administration of Sevoflurane associated with Post-Surgery delirium

YOAV KAUFMAN                           The University of Texas at Austin                 Graduation:  May 2003
Sponsored by:          David C Abramson, Ph.D., Department of Anesthesiology
Supported by:          The University of Texas Health Science Center at Houston Medical School
Key words:               Sevoflurane; Halothane; emergence delirium

From previous experience, children anesthetized under the rapid influence of Sevoflurane, a volatile anesthetic, have awakened in a greater state of delirium than with other anesthetic vapors. However, patients anesthetized with the more slowly acting Halothane have reflected a calmer awakening upon completion of the operation. We hypothesized that if patients are initially sedated under Sevoflurane for its rapid effect and later awakened while under the influence of Halothane, then these patients should awaken without agitation associated with Sevoflurane. Patients were randomized to either of two groups, group S (Sevo) or group H (Halothane). According to their designated group, anesthesia was induced in a controlled fashion with either Sevoflurane or Halothane in a mixture of oxygen and nitrous oxide. Once the patient was asleep, the alternate anesthetic agent was administered for the remainder of the surgery. At the end of the surgery, the gas was switched off and the patient was allowed to wake up. Caudally administered local anesthesia ensured that the patients would awaken pain free. In the recovery room, a nurse unaware of the anesthetic agent used assessed the apparent behavior and agitation of the patient. Our results have confirmed that our original hypothesis is true. Patients have expressed a much calmer and less frustrated behavior following a procedure completed under the initial influence of Sevoflurane and completion with Halothane. The results of the study are recommended for application on pediatric patients.
ABSTRACT

Specific Binding of Calmodulin in Neuronal Gap Junction Connexin 34.7 and Connexin 35

YENABI J. KEFLEMARIAM
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Graduation: May 2004

Sponsored by: John O'Brien, PhD, Department of Ophthalmology and Visual Science

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: Calmodulin Retina Surface Plasmon Resonance

Gap junctions are most noted for their ability to create channels that facilitate ionic or chemical intercellular communication between the cytoplasm of adjacent cells. Most noted for their roles in the electrical signaling/firing of neurons, gap junctions are made of six, circularly connected proteins, called connexins. These connexins, identified by their individual molecular weights, are composed of four transmembrane regions, an intracellular loop located between the second and third transmembrane region, and a tailing carboxyl terminus. Calmodulin, a calcium-binding protein, is believed to play a regulatory role in the closing of certain gap junctions when bound to particular regions of connexins in the presence of calcium. The intracellular loops and carboxyl terminus of Connexins 34.7 and 35 of hybrid bass retina were fused into a GST vector then bound to an immobilized anti-GST ligand. By utilizing Surface Plasmon Resonance, the binding capacities of both connexins were traced at different Calmodulin concentrations in the BIAcore 2000. There was significant binding of Calmodulin to the carboxyl terminus of both connexins coupled with no significant binding to the intracellular loops. Data analysis in a Scatchard plot shows that 0.2612 moles and 0.2861 moles of Calmodulin bound to the carboxyl terminus of Connexins 34.7 and 35 respectively while the corresponding association constants for the two were 0.1009 uM and 0.2728 uM respectively. Specific binding to the carboxyl terminus of both connexins demonstrates that Calmodulin may regulate certain gap junctions in neurons.
ABSTRACT

Concept Learning in Pigeons: The Scratch and Match Paradigm

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Sponsored by: Anthony A. Wright, Ph.D., Department of Neurobiology and Anatomy

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: concept learning, match-to-sample, Columba livia, scratch and match

Two experimentally naïve White Carneaux Pigeons (Columba livia) were trained to match-to-sample with three, different colored gravel stimuli. The apparatus was such that the subjects pecked down at stimuli on a horizontal plane, as opposed to the standard vertical array of stimuli used in matching-to-sample experiments. This, in combination with the three-dimensional gravel stimuli, mimicked the pigeon's natural behavior of digging in substrate for food. This “scratch and match” paradigm is thus more ecologically relevant than tasks using vertical pecking keys and appears to facilitate faster learning. Additionally, the use of three stimuli in training allowed for twelve different configurations of the stimuli. Six were used in acquisition training while the opposite six configurations were used to test the “untrained set.” This allowed for identification of whether configurational learning or “if-then” rule learning had taken place. Novel stimuli were then used to test for concept learning. Transfer of performance indicated that concept learning had taken place, while lack of transfer indicated that one of the above forms of learning had taken place. Neither bird reached acquisition criterion by the testing phase. As a result of this it was impossible to determine what kind of learning had taken place. This experiment should be repeated under fewer time constraints to determine whether or not the scratch and match paradigm does indeed facilitate faster concept learning in pigeons than standard matching-to-sample tasks.
ABSTRACT

Utilizing RNA Interference to Silence a *Dictyostelium discoideum* Gene Encoding a Homolog of Human G Protein-Coupled Gamma-Aminobutyric Acid Receptors

NATHANIEL H. LOO                         Texas A&M University                           Graduation:   2004

Sponsored by:       Dale Hereld, M.D., Ph.D., Department of Microbiology and Molecular Genetics

Supported by:        The University of Texas Health Science Center at Houston Medical School

Key words:          *Dictyostelium discoideum*, Gamma-aminobutyric acid receptors, RNA interference

*Dictyostelium discoideum*, used in studies of motility, signal transduction, and development, relies on secreted signaling molecules and receptors for intercellular communication. These pathways enable *Dictyostelium* to aggregate, form multi-cellular fruiting bodies, sporulate, and survive starvation. We identified seven *Dictyostelium* homologs of human G protein-coupled receptors for the neurotransmitter γ-aminobutyric acid. To determine their functions in *Dictyostelium*, we chose to block expression of one of them, GRL5, using the method of RNA interference (RNAi). GRL5 is the sole type 1 receptor and, by analogy with mammalian GABA receptors, is potentially required for the remaining GRLs to function. RNAi employs gene-specific double-stranded RNA to trigger degradation of the target gene's mRNA. We therefore made a GRL5-specific RNAi construct, consisting of two inverted GRL5 repeats separated by an unrelated “spacer” DNA fragment. When expressed in *Dictyostelium*, this would yield a double-stranded RNA hairpin structure. We created this construct by ligating a fragment of the GRL5 gene to each end of the spacer DNA and amplified both possible ligation products using polymerase chain reactions (PCR). The two PCR products were then "stitched" together through their common spacer sequences in a final PCR reaction. We are now in the process of subcloning this construct into an expression vector with a tetracycline-regulated promoter. The latter feature will provide the necessary control of the RNAi construct's expression in the event that GRL5 is essential. Mutant cell phenotypes will be compared to those of wild-type cells to gain insight into the function of GRL5.
ABSTRACT

Developmental dose response characteristics of acute Ritalin in female rats in a novel environment

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Sponsored by:      Nachum Dafny, PhD, Department of Neurobiology

Supported by:       The University of Texas Health Science Center at Houston Medical School

Key words:            Ritalin, methylphenidate, psychostimulants, ADHD

Ritalin, also known as methylphenidate (MPD), is a psychostimulant widely used to treat attention deficit/ hyperactivity disorder (ADHD) in children and adults. It has been reported that when psychostimulants such as cocaine and amphetamine are administered in a novel environment, the locomotor and stereotypic activities of test subjects are enhanced compared to those activities in a familiarized environment. However, similar studies have not been performed with MPD. The objectives of this study, therefore, are (1) to establish the acute dose response characteristics of MPD in both adolescent (35-45 days old) and adult (>60 days) female rats, (2) to determine whether environmental cues, i.e. novel versus non-novel surrounding, exert any impact on their response to MPD, and (3) to investigate whether early exposure to MPD in rats modulates their susceptibility to MPD in a novel environment when they become adult rats. Female Sprague-Dawley (SD; n=90) were divided into the following treatment groups: Groups 1, 2 and 3 were given 0.6, 2.5, or 10 mg/kg MPD, i.p., respectively, for six consecutive days when they were adolescent and again similarly treated with MPD when they became adults, Group 4, 5, and 6 received saline during adolescence and six consecutive days of 0.6, 2.5, or 10 mg/kg MPD, i.p., respectively, during adulthood, and Group 7 received saline throughout adolescence and adulthood and served as a control. A computerized activity monitoring system with 32 infrared sensors measured and recorded any changes in locomotor activity and stereotypic behavior for two hours following saline/MPD injection. Results showed that the locomotor baselines were the same in adolescent and adult rats. Further analysis revealed a similarity in the acute dose response characteristics of adolescent and naive adult rats to MPD. There was an augmented acute effect in adult rats pretreated with MPD as adolescents compared to naive adult rats that had been treated with saline as adolescents. Female SD rats tested in novel cages peaked faster but had a shortened duration of response to MPD when compared to previous experiments involving SD rats tested in well- habituated cages.

*MPD was a gift from Mallinckrodt, Inc.
Cloning VAMP Gene from *Aplysia californica* to produce VAMP

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Graduation: 2003

Sponsored by: John H. Byrne, Ph.D, Department of Neurobiology

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: synaptobrevin, VAMP, *Aplysia*

Synaptic vesicle exocytosis is the process by which neurotransmitters are released, allowing for chemical synaptic communication. A key protein involved in this process is vesicle associated membrane protein (VAMP), also known as synaptobrevin. VAMP is a transmembrane protein found on synaptic vesicles. When VAMP forms a complex with the proteins synaptosomal associated protein of 25 kd (SNAP-25) and syntaxin, the synaptic vesicle can fuse with the presynaptic membrane and release its content. The VAMP gene was cloned from *Aplysia californica* to produce the corresponding protein, with the aim to raise a polyclonal antibody against it. The anti-VAMP antibody will be used to track the recycling of synaptic vesicles in future experiments. Briefly, total RNA was extracted from pleural pedal ganglia, and RT-PCR was performed to produce cDNA. cDNA coding for the VAMP gene was amplified using gene-specific primers in a PCR reaction, and the resulting product was isolated by gel electrophoresis and gel-extracted for subsequent analysis. The extracted product was then inserted into a pCR 2.1-Topo vector (Invitrogen), which was used to transform *E. coli*. Future experiments entail the purification of the vector from transformed colonies and the subsequent sequencing of the insert to verify its identity. Once the insert is sequenced and its identity verified, it will be ligated in an *Aplysia* expression vector, pNEX3, for further injection into *Aplysia* neurons.
Prevention of Chronic Pain Syndrome in Spinal Cord Injured Rats Treated With Phosphatidylcholine Associated Non-Steroidal Anti-Inflammatory Drugs

DANIELLE MARIE MILLER                  University of Northern Iowa                             May 2003

Sponsored by:     Lenard M. Lichtenberger, Ph. D., Department of Integrative Biology and Pharmacology
Supported by: The University of Texas Health Science Center at Houston Medical School
Key words:          Spinal Cord Injury, Chronic Pain Syndrome, Phosphatidylcholine, Non-Steroidal Anti-Inflammatory Drugs

Background: Spinal Cord Injury (SCI) contributes to the development of chronic pain syndrome which becomes increasingly debilitating over time. Chronic pain in SCI patients is treated with analgesics including Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). A family of phosphatidylcholine (PC) associated NSAIDs have been developed by our laboratory that possess low gastric toxicity and enhanced therapeutic activity. The therapeutic effectiveness of PC-Ibuprofen and Ibuprofen at the prevention of chronic pain syndrome in rats with SCI was investigated.

Methods: Contusive SCI was induced at thoracic level 8 in female Sprague-Dawley rats. Rats were administered saline, Ibuprofen, or PC-Ibuprofen (NSAID dose of 25 mg/kg) twice daily for a period of 3 weeks followed by a 2 week period without treatment. Von Frey Hair and Randall Selitto assessments were performed on the hind paws two hours after morning dosing on days 8, 22, and 36 post-SCI surgery.

Results: Von Frey Hair assessment showed a tendency for PC-Ibuprofen treated rats to have increasing sensitivity after SCI. Randall Selitto assessment showed saline treated rats had decreasing pain thresholds after SCI, indicative of the development of chronic pain syndrome. The pain threshold of PC-Ibuprofen treated rats remained at pre-SCI baseline levels and was significantly higher than the pain threshold of both Ibuprofen and saline treated rats. In both the Von Frey Hair and Randall Selitto assessments, when NSAID treatment was discontinued, sensitivity and pain thresholds dropped respectively.

Conclusion: PC-NSAIDs were more effective at the treatment of chronic pain syndrome than conventional NSAIDs, however, continued NSAID treatment is needed for the prevention of chronic pain syndrome.
ABSTRACT

High Resolution Three-Dimensional Structure of Gammaherpesvirus Capsids

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Fall 2002

Sponsored by: Z. Hong Zhou, Ph.D., Department of Pathology and Laboratory Medicine

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: three dimensional structure, Gammaherpesvirus Capsids

The gammaherpesvirus subfamily in the herpesviridae includes both the Lymphocryptovirus and Rhadinovirus genera and consists of DNA viruses associated with the development of cancers. While extensive biochemical efforts have been undertaken to characterize the infection and pathogenesis of human Gammaherpesviruses (including Epstein-Barr virus and Kaposi’s sarcoma-associated herpesvirus, KSHV), their three-dimensional (3D) structural studies have been limited due to difficulties in isolating these human viruses. Rhesus Macaque Rhadinovirus (RRV), the closest homolog of KSHV, is used in this lab as a model system for the 3D structural studies of KSHV and other gammaherpesviruses. Previous work in the lab involved embedding highly purified RRV capsids in vitreous ice and imaging in a 300 keV electron cryomicroscope equipped with a field emission electron source. My work focused on the computer data processing of these images. More than 100 high resolution electron micrographs with a total of >10,000 RRV particle images had been analyzed. Defocus and resolution values are computed and recorded for 42 images. These analyses indicated that the image resolution extends to an unprecedented 8 Å. Further data processing will be carried out to compute the 3D structure of the capsid from these high resolution images.

Acknowledgement: We acknowledge contributions by Christine O’Conor, Michael Sherman, Sanket Shah, Xue-Kui Yu, Blossom Damania and Dean H. Kedes.
ABSTRACT

Additional research project by Ms. Mirza

Web-Based Teleconference for Clinical Pathology

ZOHRA M. MIRZA University of Houston Fall 2002

Sponsored by: Nguyen, Andy (Nghia), M.D., Department of Pathology and Laboratory Medicine

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: Teleconference, clinical pathology, web

In order to determine whether teleconference can be implemented on the World Wide Web to facilitate presentation of interesting clinical pathology cases between teaching hospitals in an economical manner, the Department of Pathology designed a teleconference system using off-the-shelf components. The core components of the system are video web servers to transmit video images of pathology cases. Peripheral cameras for microscopic and gross images are connected to the video web servers and allow for bi-directional transmissions of images from two conference sites, both with high-speed T1 Internet connection. A graphic user interface is designed for the web browser to facilitate multiple views of presentation materials. A prototype program was also developed to allow for capturing images presented during conference to saving them into a database for later reference. The video quality was deemed adequate despite some latency in transmitting images. Audio communication by telephone using speakerphone is used to accompany video images during conference. Speakers with multiple microphone extensions and Microsoft Net Meeting for video conferencing are being considered. The teleconference system offers ease of use and low maintenance for our residents. Research was carried out on existing teleconference systems and compared with the quality and cost of our system. Investigation was done to incorporate better search options and a more sophisticated organization scheme for image files in the database for effective presentation. The research results were added to a paper draft that will be published as soon as it is finalized.
ABSTRACT

Role of Type I secretory Phospholipase A₂ in the Surface Hydrophobicity Changes of the Gastrointestinal Tract

MELANIE ROSE MONTGOMERY                  Louisiana State University                                 May 2004

Sponsored by:       Elizabeth J. Dial, Ph. D., Department of Integrative Biology and Pharmacology
Supported by:       The University of Texas Health Science Center at Houston Medical School
Key words:            type I secretory Phospholipase A₂, phosphatidylcholine, hydrophobicity

Background: The surface hydrophobic barrier property of the gastrointestinal (GI) mucosal lining is maintained by phospholipids, namely phosphatidylcholine (PC). The secretion and/or activation of secretory phospholipase A₂ (sPLA₂), a lipolytic enzyme in the GI tract, could disrupt the gastric hydrophobic barrier which increases the potential for translocation of damaging luminal factors into tissue and blood. Type I sPLA₂ is a pancreatic digestive enzyme found in the duodenal lumen and stomach. We hypothesized that traumatic stress disrupts the GI surface barrier by mechanisms involving expression/ activation of PLA₂.

Methods: Type I sPLA₂ activity was measured in tissue samples and gastric and intestinal washes of rats after administration of lipopolysaccharide (LPS), a bacterial component that when introduced mimics the sepsis that occurs after traumatic stress. Sprague-Dawley rats were given IP injections of LPS at a dose of 5 mg/kg 1 and 5 hours before euthanasia. Tissue samples of stomach, ileum, and pancreas were collected. The stomach and intestine were flushed with 2mL of saline, and entire fluid contents collected. Samples were incubated in solution with ¹⁴C labeled DPPC substrate for 30 minutes in 37ºC water bath. Reaction was stopped and supernatant containing the radioactive labeled free fatty acids was counted.

Results: Type I sPLA₂ did not change in the stomach and ileal tissue samples but appeared to decrease in the pancreas tissue and increase in gastric and intestinal fluid during the 5-hour period.

Conclusion: During times of traumatic stress, type I sPLA₂ from the duodenum may be refluxed into the stomach and disturb the hydrophobic lining of mucosal barrier. This can make the barrier more permeable to the translocation of acids and toxins into other tissues.
ABSTRACT

Abnormalities in Fibrillin 1-containing Microfibrils in Fibroblast Cultures of Patients of Different Ethnic Groups

WEIQING NG  
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Class of 2005

Sponsored by:  Dianna M. Milewicz, M.D., Ph.D., Department of Internal Medicine

Supported by:  The University of Texas Health Science Center at Houston Medical School

Keywords:  FBN-1, Fibrillin-1, Scleroderma

The FBN1 gene encodes for fibrillin-1, a major element of extracellular matrix (ECM). FBN1 mutations cause Marfan syndrome. Fibroblasts established from patients with Marfan syndrome show little or no microfibrils when analyzed by immunofluorescence or metabolic analysis. Explanted fibroblasts from unaffected skin of scleroderma (SSc) patients however, showed a prominent meshwork of fibrillin-1-containing microfibrils like the control cells. Paradoxically, metabolic studies displayed an absence of fibrillin-1 in the ECM in a majority of the SSc fibroblast cells. Extended metabolic studies verify that fibrillin-1 in the ECM of SSc cells degraded at a faster rate than that of control cells. These results indicate that the microfibrils made by SSc cells are unstable and suggest that an intrinsic defect in fibrillin-1-containing microfibrils may contribute to scleroderma. Experiments were done to confirm that this hypothesis is applicable to cells from SSc patients of different ethnic groups. Metabolic analysis examined fibrillin-1-containing microfibrils from cells explanted from SSc patients of different ethnic backgrounds. These results showed a significant decrease in fibrillin-1 concentrations in the ECM of SSc fibroblasts from American Indians and African Americans after 96 hours compared to that of control cells. This supports the hypothesis that abnormalities in fibrillin-1-containing microfibrils may be involved in the pathogenesis of SSc among all ethnic groups. Experiments are currently underway to investigate the Hispanic population.
Microgravity severely inhibits immune function. With growing emphasis on long-term space flights, ensuring optimal immune function in microgravity is a vital concern. An important issue yet unknown, is the effects of microgravity on growth and tumorigenicity of tumors. Therefore, B16 mouse melanoma cells were used in an in vitro study to investigate the effects of modeled microgravity (MMG). The following evaluations were performed for the static (flask-grown) cultures and MMG (bioreactor-grown) cultures which include: growth, melanin production, protein levels, VE-cadherin levels, urokinase production and apoptosis.

Results indicate that modeled microgravity causes a significant alteration in some properties. Growth is inhibited in the bioreactors and is ¼ of that in the static flasks. Melanin production in the bioreactors, however, is 1.5 times higher than in the flasks, despite the inhibited growth in MMG conditions. Preliminary data show there is an increase in apoptosis in the bioreactors. Further additional experiments are required in the areas of VE-cadherin levels and urokinase production. Preliminary results show that there is a significant increase in tumorigenicity in the bioreactor-cultured cells as compared to the flask-cultured cells, when inoculated with animals. This further suggests that MMG may play a role in altering tumor cell characteristics, and studies will be continued to further explore the mechanisms and actual role MMG plays.
ABSTRACT

Use of the Grp78 Promoter in Systemic Gene Therapy for Cancer

LAURA E. OLSON                    Rice University                    Graduation:    2003

Sponsored by:      Joan M. C. Bull, M.D., Department of Internal Medicine, Oncology

Supported by:      The University of Texas Health Science Center at Houston Medical School

Key words:           targeted systemic cancer gene therapy, grp78 promoter, MTLn3 mammary adenocarcinoma

A key limitation in modern cancer therapy is the lack of an adequate systemic therapy that can target metastatic cancer. We are developing a systemic administration system in which a patient’s tumor could be transiently transfected with the herpes simplex virus tyrosine kinase gene. The gene would be preferentially expressed in tumor cells through the control of the glucose-regulated protein promoter, grp78. The grp78 is a promoter selectively activated solely in cells starved for glucose, such as is found in the anaerobic environment of a tumor. Patients could then be treated with the known antiviral agent ganciclovir to selectively kill the cells that express the viral kinase. We performed preliminary experiments in a rat MTLn3 mammary adenocarcinoma model to test the suitability of the grp78 promoter for tumor specific protein expression. Using an extruded cationic liposome as a systemic delivery vehicle for plasmid DNA, I intravenously injected DNA with the grp78 promoter controlling the Chloramphenicol Acetyltransferase reporter gene along with the pSV-β-Galactosidase Control Vector as an internal control to show the delivery efficiency of the liposome complex. Though not optimized, my experiments produced several useful observations. We demonstrated the DNA:liposome complex to have toxicity between 200 and 300 µg of DNA. Pending histological analysis, we observed liver abnormalities in animals injected with high dosage of the DNA:liposome complex. This toxicity was not observed in animals injected with either the DNA or the liposome alone. Future studies are planned to elucidate the nature of this toxicity and to demonstrate selective tumor cell gene expression.
ABSTRACT

Preparation of transient receptor potential channel-fluorescent protein fusion vector

STEPHEN M. OLSON : University of Northern Iowa Graduation: 2003

Sponsored by: Barbara M. Sanborn, PhD, Department of Biochemistry and Molecular Biology

Supported by: The University of Texas Health Science Center at Houston; HD38970; Merck AAAS Interdisciplinary Undergraduate Research Award

Key words: TRPC, gene fusion, PCR-based mutation

Myometrial smooth muscle cells depend on an increase in calcium derived both from intracellular store release and entry from the extracellular environment to stimulate contraction. Calcium influx is mediated in part by transient receptor potential channel (TRPC) proteins. There are seven known members of the TRPC subfamily, and it is assumed that they may combine in various ways to form tetrameric calcium channels. In order to determine which TRPC proteins associate with each other, three TRPC cDNAs were fused with fluorescent proteins. Using PCR based mutation, the stop codon in each sequence was replaced with the codon for an amino acid and unique restriction sites were added so that the cDNA could be removed from its original vector. It was then ligated in frame into a vector containing the sequence for a fluorescent protein. The mutation was confirmed by DNA sequence analysis. hTRPC3 was successfully fused with both yellow and cyan fluorescent proteins. hTRPC4 was mutated, but the results have not been confirmed and the fusion construct has yet to be generated. While the PCR was successful with hTRPC1, the PCR product has yet to be ligated into the original vector. These fluorescent fusion proteins will allow the laboratory to determine which TRP proteins associate with each other in the myometrium through fluorescent imaging techniques such as fluorescence resonance energy transfer (FRET) and to determine if the properties of the channels change depending on the composition.
ABSTRACT

Yeast two-hybrid screening of human placenta cDNA library using fortilin as bait

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Graduation: 2004

Sponsored by: Ken Fujise, MD, Institute of Molecular Medicine, Research Center for Cardiovascular Diseases

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: Fortilin, Yeast two-hybrid system, Yeast mating, Protein-to-protein interaction, Reporter genes

Purpose of the study: Fortilin is a 173 amino acid protein predominantly localized in the nucleus. Fortilin has been shown to prevent cells from undergoing apoptosis. In addition, the depletion from certain cancerous cells of fortilin causes spontaneous apoptosis. Fortilin is unique because it does not share structural similarities with other anti-apoptotic proteins such as Bcl-2 and IAP family proteins. The purpose of my summer research study is to identify a protein(s) that specifically interacts with fortilin. The identification and characterization of such proteins would help us understand the mechanism of the anti-apoptotic function of fortilin.

Methods: First, the cDNA of fortilin was cloned into the pGBKT7 yeast expression vector and expressed in a yeast cell line. It was found that the presence of fortilin alone self-activated the β-galactosidase reporter gene. We then generated a fortilin deletion mutant lacking C-terminus 35 amino acids (fortilin Δ1-135) and tested it in the same system. We found that fortilin Δ1-135 did not activate the reporter gene by itself. A yeast-mating was performed using AH109 (MATα) containing fortilin Δ1-135 and Y187 (MATα) containing human placenta cDNA library. Diploid yeast cells were plated on synthetic quadruple drop-out plates, lacking adenine, histidine, tryptophan and leucine (SD/-Ade,-His,-Trp,-Leu).

Summary of Results: Plates are currently incubated at 30°C for the diploid yeast cells that activate reporter genes, which enable cells to survive on the quadruple drop out plate.

Conclusion: Yeast two hybrid system is a viable system to identify a novel protein-to-protein interaction.
ABSTRACT

Mutant Screening of COMP, Matrilin-1, and Matrilin-3 in a Coxa Vara patient

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Graduation: 2004

Sponsored by: Jacqueline T. Hecht, Ph.D., Department of Pediatrics

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: coxa vara, COMP, Matrilin-1, Matrilin-3

Coxa vara describes any decrease in the femoral neck-shaft angle that is less than 120-135° and occurs as part of many genetic syndromes and as an isolated abnormality. Children with coxa vara display a waddling between two and six years with ambulation. Coxa vara often occurs as a new event in a family but can also follow an autosomal dominant pattern of inheritance. The etiology of this condition is poorly understood but may result from mutations in cartilage matrix genes that are important for joint formation. Likely gene candidates include cartilage oligomeric matrix protein (COMP), Matrilin-1, and Matrilin-3. Mutations in these genes cause multiple epiphyseal dysplasia (MED) and pseudoachondroplasia (PSACH), both of which are associated with abnormalities of the capital femoral epiphyses, which form the hip. In this study, sequencing of COMP, Matrilin-1, and Matrilin-3 was performed on the DNA from one patient with coxa vara. The COMP gene is encoded by 19 exons, matrilin-1 gene by 8 exons and matrilin-3 by 8 exons. The exons of these three genes were PCR amplified and sequenced. These sequences are being analyzed for mutations. Thus far, two variants have been identified: one in exon 5 of matrilin 3 gene and one in exon 10 of the matrilin 3 gene. Neither causes a change in the protein coding sequence and thus are polymorphisms and not an etiologic cause of coxa vara. Five of the exons remain to be analyzed and three are being amplified for sequencing.
Cloning and Preliminary Characterization of a Novel Estrogen Regulated Gene

DANIELLE L. RANKIN  
University of Houston  
Graduation: 2003

Sponsored by: Peter J. A. Davies, M.D., Ph.D., Department of Integrative Biology, Pharmacology and Physiology

Supported by: The University of Texas Health Science Center at Houston

Key words: Estrogen, cloning, characterization, PCR

Estrogen is a vital female steroid hormone and it achieves its function by binding to an estrogen receptor, which binds to estrogen responsive elements within the promoters of target genes. The purpose of this study was to clone and characterize a novel estrogen induced gene (EIG121). We first confirmed estrogen induction of EIG121 by a real-time RT-PCR assay of RNA obtained from human endometrial biopsies (placebo and estrogen replacement therapy for three months) and MCF-7 cells (treated with vehicle or estradiol for 24 h). To clone EIG121, we first extracted RNA from MCF-7 cells and performed RT-PCR using primers that covered the whole open reading frame. The PCR product was ligated into the pGEM-T vector and the expression vector, pEGFP-N1, respectively. Then DH5α cells were transformed and grown on Ampicillin/X-gal (for pGEM-T) or Kanamycin (pEGFP-N1) plates. Colonies were quickly screened by real-time PCR. Selected colonies of EIG121-pGEM were then confirmed by restriction digestion with Sac I. The screening of the EIG121-pEGFP colonies and sequencing of EIG121 in these two vectors are still in progress. An expression profile of EIG121 was compiled by BLAST searching against EST databases. By this method it was found that EIG121 is expressed in many tissues and it is over-expressed in endometrial cancer and colon cancer. In summary, we confirmed that EIG121 is induced by estrogen and we also successfully cloned EIG121 into two vectors.
Abstract

Effect of Superoxidase Dismutase on Stem Cells and Ischemic Heart Failure

CHENG RUAN  Texas A&M University  Graduation: 2005

Sponsored by: Yong Jian Geng, M.D., PhD, Department of Internal Medicine, Cardiology

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: Superoxidase Dismutase, Stem cells, Ischemic Heart Failure, Apoptosis

Ischemic heart disease occurs when narrowing of heart arteries causes a deprivation of oxygenated blood to heart tissue causing apoptosis (cell death) and ultimately leading to a heart attack. Research on animal models has shown that stem cells are capable of regenerating heart tissue up to 30% by injecting stem cells directly into the ischemic area. The cells, however, have difficulties surviving because of hydrogen peroxide buildup in cells due to a lack of oxygen. This creates oxygen free radicals that are deadly to healthy cells. Superoxidase Dismutase (SOD) is an antioxidant enzyme that shields cells from the poisonous oxygen free radicals. It is one of the scavenger proteins that may prevent cell apoptosis in infarct areas of the heart. This enzyme converts superoxide anions to hydrogen peroxide, which in turn is decomposed into water. Western blot analysis reveals SOD expression in mouse testes, dog fetal heart, and mouse heart; however it is not expressed in adult stem cells derived from dog bone marrow cells. To investigate if SOD can be used for therapeutic purposes, such as gene therapy, PCR was used to amplify DNA from fetal heart libraries. Once the DNA is put into an expression vector, it is transfected into stem cells. The ultimate goal is to see if SOD can help regenerate heart tissue more efficiently than just using regular stem cells.
ABSTRACT

Assessing Fracture Healing Using Quantitative Ultrasound (QUS), Mechanical Response Tissue Analysis (MRTA) and Dual X-Ray Absorptiometry (DXA): Phase 1

STEVEN J. SCHRODER
Texas A&M University
Class of 2003

Sponsored by: Catherine G. Ambrose, Ph.D., Department of Orthopaedic Surgery

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: quantitative ultrasound, fracture healing, tibia

Typical fracture assessment includes mechanical manipulation and radiographic analysis. These non-invasive, in vivo evaluation techniques are quite subjective and can lead to complicating diagnoses amongst clinicians. X-rays provide a satisfactory method for visual identification of callus growth yet is only able to do so weeks succeeding the initial injury and physiologic reaction until denser callus forms. Furthermore, the manipulation of the appendage only enables for speculative progression of bone formation and can only be done sparingly as to not hamper bone formation. Henceforth, the need for an objective, quantitative technique for analyzing fractures has become a more pronounced issue. The use of quantitative ultrasound (QUS) has been well documented as a method for fracture assessment.

This study analyzes how effective the commercially available Omnisense 7000S QUS (Sunlight Ultrasound Technologies, Tel Aviv, Israel) is in the determination of an artificial fracture gap in cadaver tibia specimens. Initial longitudinal QUS speed of sound measurements were obtained for pairs of cadaver tibias and subsequent artificial fractures were implemented. Post fracture, follow-up QUS measurements were acquired and the process was repeated with progressively larger fractures until QUS signaling terminated. The information attained through QUS testing was then compared to dual x-ray absorptiometry (DXA) density measurements and bone material properties to determine the existence of an overall correlation for bone stiffness. To date, results are pending further experimentation and data analysis. Ensuing in vivo research will build upon this opening investigation and hopefully validate this novel approach to monitoring fracture healing.
Although numerous studies have investigated the relationship between spatial attention and saccadic eye movements (EMs), these studies have variously reported that attention facilitates, inhibits, or has no effect on EMs. Some research has suggested that inhibition only occurs when the fixation point disappears before the onset of the target. In the present study, we examined whether fixation condition modulates attentional effects. Sixteen subjects were instructed to attend to a fixation point and, in separate blocks of trials, make an EM towards (saccade, reflexive task) or away from (antisaccade, voluntary task) the target stimulus. A cue at fixation preceded the onset of the target in each condition; this cue was either informative (arrow) or neutral. The informative cue was always 100% accurate, revealing the direction of the required EM prior to target onset. A variable delay interval between the presentation of the cue and the target was used to discourage anticipations. For each task, there were three fixation conditions: gap (cue offset 200 msec before the target), step (cue offset simultaneous with target onset), and overlap (cue remained present). An infrared eye tracking system registered subjects' eye position and a computer recorded their response times (RTs) and EM accuracy. We found that fixation condition did not affect the attentional modulation of saccade latency. That is, regardless of fixation condition, the informative cue facilitated voluntary EMs, but did not significantly affect reflexive EMs.
New Susceptibility Breakpoints for ESBLs

KELLY R TIERNEY University of Houston Class of 2004

Sponsored by: Audrey Wanger, Ph.D., Department of Pathology
Supported by: The University of Texas Health Science Center at Houston Medical School
Key words: ESBL, MIC, Enterbacteriaceae, cephalosporins, susceptibility

ESBLs (extended spectrum β-lactamases) are enzymes in Enterobacteriaceae, such as Klebsiella pneumoniae and Escherichia coli, which attack third generation cephalosporins. ESBLs may be susceptible to one or more extended cephalosporins in vitro, but in vivo none of these drugs are effective. To screen for an ESBL an Enterobacteriaceae must have a MIC of ≥2µg/mL for extended cephalosporins. When confirming ESBL production, the organism should be tested with cefotaxime, cefotaxime/clavulanic acid, ceftazidime, and ceftazidime/clavulanic acid. A decrease in ≥3 two-fold dilutions should be seen when the clavulanic acid is present. To alleviate the need to test for ESBLs, the NCCLS (National Committee for Clinical Laboratory Standards) is considering changing breakpoints for susceptibility to cephalosporins from ≤8 to ≤2; however, by lowering these values, some ESBLs may be overlooked. To determine if the change in MIC effects the identification of ESBLs, the MICs of 107 ESBL positive Enterobacteriaceae to cefotaxime, ceftriaxone, ceftazidime, and ceftazidime/clavulanic acid were determined using Etest. 43 of the 107 Enterobacteriaceae had an MIC ≤2 and would therefore not be considered ESBLs. Testing with ceftriaxone or ceftazidime detected 100 out of 107 ESBLs, and is therefore the most effective cephalosporins for testing. By testing the susceptibility with both of these cephalosporins, only 2 out of the 107 ESBLs were overlooked; therefore the new breakpoints suggested by the NCCLS are adequate detectors of the β-lactamase enzyme when testing against ceftriaxone and ceftazidime.
ABSTRACT

Regulation of the rabbit Cyp7a promoter by nuclear receptors

CHESTER C. TSAI                          University of Texas at Austin                                Class of  2004

Sponsored by:           David Loose-Mitchell, PhD, Department of Integrative Biology
Supported by:            The University of Texas at Houston Medical School
Key Words:               Cyp7a, LXR, RXR, Luciferase

Bile acid excretion represents the only way in which the human body can eliminate significant amounts of cholesterol. Cholesterol is metabolized into bile acids by 14 enzymes. Cholesterol 7alpha hydroxylase, (Cyp7a) is the rate limiting and first of these enzymes. Two nuclear receptors, the liver X receptor (LXR-alpha) and the retinoid X receptor (RXR-alpha) have been shown to stimulate the activity of the Cyp7a promoter in mice and rats by interacting with a DR4 sequence; interestingly these receptors appear not to work on the human Cyp7a promoter. The DR4 sequence is similar in rats and mice, and is also found in the rabbit Cyp7a promoter. We sought to determine if LXR and RXR regulated transcription of the rabbit Cyp7a promoter. LXR and RXR cDNAs were cotransfected into Cos-1 cells in addition to rabbit reporter constructs that contained a gene coding for luciferase attached to 5' deletions of the Cyp7a promoter. The cells were grown in DMEM media containing 10% FBS and Penstrep, and were lysed 24-40 hours after transfection. A luciferase assay was performed to determine the amount of luciferase transcribed by the cells. In the experiments using the 137 bp deletion of the Cyp7a promoter, LXR and LXR/RXR stimulated promoter activity, however RXR by itself had an even greater stimulation. Using the 1076 bp construct, there was also a LXR/RXR stimulation of the promoter activity, however RXR alone had no effect.
**ABSTRACT**

Comparison of toxin protein levels in regulatory mutants of *Bacillus anthracis*

PINAR ULUG  University of Rochester  Class of 2003

Sponsored by: Theresa M. Koehler, Ph.D, Department of Microbiology and Molecular Genetics

Supported by: The University of Texas at Houston Medical School

Key words: anthrax, toxin, *Bacillus anthracis*

*Bacillus anthracis* produces the anthrax toxin proteins protective antigen, lethal factor, and edema factor. The toxin genes, *pagA*, *lef*, and *cya*, are located on pXO1, one of two virulence plasmids in this species. Toxin gene expression is positively regulated by the pXO1 gene *atxA* and by genes on the chromosome: *sigH*, encoding a sigma factor; *abrB*, a transition state regulator that negatively regulates *sigH*; and *spo0A*, a transcription factor that negatively controls *abrB*. Previous investigations of toxin gene regulation have employed attenuated mutants missing pXO2, a virulence plasmid predicted to encode additional gene regulators. One pXO2 gene, *acpA*, positively regulates capsule synthesis by *B. anthracis*. We examined toxin synthesis by mutants of a fully virulent pXO1+, pXO2+ strain. Western blotting results indicate that pXO2 does not affect toxin gene expression and confirm previous reports in which gene regulation was tested using attenuated strains. PA levels dropped significantly for an *atxA* mutant, but PA synthesis was unaffected by an *acpA*-null mutation. Steady-state levels of PA were higher in an *abrB*-mutant relative to the parent strain, and the deletion of either *spo0A* or *sigH* resulted in significantly reduced PA synthesis. We also compared toxin synthesis by *atxA*, *acpA* and double mutants cultured in different growth conditions. Significantly higher toxin levels were detected in cultures grown in NBY medium incubated in 20% CO2 compared to CA medium incubated in 5% CO2, yet the same pattern of regulation was observed in each growth condition.
ABSTRACT

Scratch and Match: A test of concept learning in the pigeon (*Columbia livia*) using a modified matching-to-sample paradigm

CATHARINE J. WEI                                      Cornell University                                      Class of 2004

Sponsored by:      Anthony A. Wright, PhD, Department of Neurobiology and Anatomy

Supported by:       The University of Texas Health Science Center at Houston Medical Schyool

Keywords:            Concept learning, matching-to-sample, pigeon, same-different, ecological relevance

The ability to learn concepts, like language, is traditionally regarded as unique to humans. Whether animals have the ability to learn concepts remains controversial. A typical procedure to explore concept learning in animals is matching-to-sample. In matching-to-sample, the animal is trained to select the comparison stimulus that matches the sample stimulus. It is possible that failures to find concept learning in pigeons may have resulted from methodological shortcomings rather than an inability of pigeons to learn abstract relational concepts. The ecologically relevant scratch and match paradigm integrates a traditional laboratory design with the natural predisposition of pigeons: instead of pecking at video-images, the pigeon is allowed to view and interact with 3-D gravel stimuli from a natural distance. In 1994, Wright and Delius trained pigeons in a scratch and match task with black and white gravel but failed to find concept learning. To determine why the pigeons failed to transfer and whether concepts can be learned via an ecologically related paradigm, the acquisition and transfer of a same-different concept was investigated in one pigeon, *Columbia livia*, trained to match-to-sample by digging in red, green, and blue gravel stimuli for grain reward. Color, rather than texture was the discriminative stimulus in novel testing. Twenty-four training days (192 trials) without reaching criterion show delayed acquisition. Chance level performance on unfamiliar configurations prior to complete acquisition supports the possibility that the pigeon learned specific configurations of the training stimuli and not stimulus-specific ‘If-then’ rules. While training trial performance during novel transfer testing was significantly different from chance (p<0.05), transfer to novel stimuli was not, thus indicating that a concept was not learned.
ABSTRACT

Functional Screening of Jak3 Inhibitors in Human lymphocytes

QIAN WU University of Texas at Austin Graduation: 2004

Sponsored by: Robert A. Kirken, Ph.D. Department of Integrative Biology and Pharmacology

Supported by: The University of Texas Health Science Center at Houston Medical School

Key words: Tyrosine kinases, tyrosine phosphorylation and kinase assay

Janus tyrosine kinase (Jak)3 is a critical protein tyrosine kinase selectively expressed in T lymphocytes, natural killer cells and monocytes. Jak3 is absolutely required for mediating signals generated by T-cell growth factor (TCGF) cytokines like interleukin (IL)2. IL2 and other TCGFs activate Jak3 which then phosphorylates a number of substrates such as signal transducer and activator of transcription (Stat). This signaling cascade promotes gene transcription and a functional immune system. However, these same pathways have been found to be overly active in many lymphoid-derived diseases such as allergy, leukemia and lymphoma. Thus, identification of selective Jak3 inhibitors might reverse these diseases. Here we attempt to identify Jak3 inhibitors and develop an assay for rapid measurement. We have employed in vitro kinase assays and treatment of intact cells with various drugs. Next Jak3 tyrosine autophosphorylation, which correlates with its activity, was measured by antiphosphotyrosine Western blot. Some drugs were effective at concentrations as low as 1 nM. However, this technique was time consuming. We are now developing a rapid and high throughput screen that combines the kinase reaction with a peptide-based ELISA assay using either a generic tyrosine kinase substrate (E4Y) or Jak3 autoactivation loop. Jak3 kinase activity can be measured by monitoring tyrosine phosphorylation via an antibody-mediated colorimetric assay. This method should allow for the screening of possible therapeutic agents to battle T cell mediated diseases as well as reduce the drug assay time from five days to four hours.
A study conducted by Kato et. al (Dig. Dis. Sci. 46:1690-9, 2002), found that the gastric toxicity of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), increases in rats with experimentally induced joint inflammation. Gastric toxicity, or the capacity for the NSAIDs to damage epithelial tissue in the stomach, is a common concern for patients receiving chronic doses of NSAIDs. Many patients are taking NSAIDs to fight inflammatory conditions or joint inflammation. Though the NSAIDs may alleviate inflammation and pain, they may also exacerbate gastric damage. It has also been shown in the past that phosphatidylcholine (PC) association of NSAIDs reduces the ability of the drug to disrupt the mucosal hydrophobic barrier in the stomach, thus decreasing epithelial damage. In order to corroborate Dr. Kato’s results and to determine whether PC-NSAIDs decrease the gastric damage as compared to traditional NSAIDs, an inflammatory response was induced in rats using Complete Freund’s Adjuvant (CFA). Two different groups of CFA injected rats were challenged with (20mg/NSAID/kg) of indomethacin or PC-Indomethacin, 4 and 14 days after the induction of joint inflammation. Four hours after NSAID treatment, the rats were euthanized and the stomachs removed and inspected for lesions. The data revealed a tendency for rats with joint inflammation to experience greater NSAID-associated gastric damage compared to rats without inflammation, and that PC association significantly decreases the gastric toxicity of NSAIDs in rats with adjuvant-induced arthritis.
Analysis of Human Neuropeptide Tyrosine Gene Polymorphisms in the ARIC Cohort

DAISY ZAMORA                             University of Texas at Brownsville                             Class of 2004

Sponsored by:      Molly Bray, PhD, Human Genetics, School of Public Health
Supported by:       The University of Texas Health Science Center at Houston School of Public Health;
                             The University of Texas Health Science Center at Houston Medical School

Key words:           Neuropeptide Y, obesity, polymorphism

Obesity has been proven to increase the risk of developing cardiovascular disease, high blood pressure, diabetes mellitus, and certain cancers, among other physical and emotional complications. Although the genetic components of obesity are largely unknown, evidence suggests that Neuropeptide Tyrosine (NPY) may contribute to the development of this disorder. NPY plays an important role in the hypothalamic regulation of energy homeostasis by promoting a positive energy balance through alterations in feeding, basal metabolism and other metabolic pathways. The purposes of this study are to determine the association between eight polymorphisms in the NPY gene and both obesity and obesity-related quantitative traits (e.g., anthropometry, blood glucose and insulin levels, physical activity levels, and dietary profile), and to characterize the effects of variation in the NPY gene in predicting incident coronary heart disease and stroke. The DNA samples used in this study were gathered by the Atherosclerosis Risk in Communities (ARIC) study, which is a 12-year population-based longitudinal study from which a comprehensive amount of information has been collected. The variant sites studied were selected for research on the basis of their potential linkage to obesity and obesity-related measures and are as follows: -880 2bp insertion/deletion (I/D), -441 A→G single nucleotide polymorphism (SNP), -399 C→T SNP, 69 17bp I/D, 1201 A→G SNP, Leu7Pro, 5325 T→C SNP, and 7499 A→G SNP. DNA fragments containing polymorphisms were amplified using a standard Polymerase Chain Reaction (PCR) protocol. The PCR product will then be extended using dideoxynucleotides and loaded onto a mass spectrometer to obtain DNA sequencing data. Multiple logistic and linear regressions will be used to evaluate data and determine if interindividual variation within the NPY gene contributes to the development of disease.
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