2003

Summer Research Program

Student Abstracts

THE UNIVERSITY of TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

Contents

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. 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 under-graduates.

The trainee's role in the laboratory is to participate to the fullest extent of her/his ability in the research project being performed. This involves carrying out the technical aspects of experimental analyses, interpreting data and summarizing results. The results are presented as an abstract and are written in the trainees' own words. The abstracts also convey an impressive degree of understanding of the complex projects in which they were involved.

To date, more than 1,300 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.

Student research training is supported by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and by financial support from the Medical School and Dental School and their departments and faculty.

Science education remains a vital and integral part of our nation's interests. The Medical School Summer Research Program, and the dedication of our faculty and deans exemplify the institution's commitment to training and educating the future leaders in our scientific communities.

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

Acknowledgements

This publication marks the completion of the nineteenth year of The University of Texas Medical School at Houston Summer Research Program. The longevity and success of the program are rooted in the overwhelming support received from the deans, faculty, staff and students of UTHSC-Houston.

Indicative of this support is the administrative assistance and financial support provided by the UTHSC-H Medical School. Sincere appreciation is expressed to L. Maximilian Buja, M.D., Executive Vice President for Academic Affairs, to Stanley G. Schultz, M.D., Interim 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.

Major financial assistance for our Program has also been provided by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) through a short-term research grant (2 T35 DK007676-11).

The success of our Summer Research Program depends primarily on the faculty who volunteer to mentor the trainees. These dedicated educators organize and guide the research projects that, for each student, includes data analysis, preparation on an abstract and public presentation of results. Our sincere thanks to all faculty mentors.

2003 MS-1 Medical Students

MS-1 Student	Page	Faculty Mentor	Department
Adams, Brook	9	Clyburn, Terry	Orthopaedics
Alford, April	10	Geng, Yong	Internal Medicine
Bailey, Christopher	11	McDonald, Glenn	Internal Medicine
Balldin, B. Christian	12	McKinley, Bruce	Surgery
Barreno, Ramon	13	Miller, Charles	Cardiothoracic & Vascular Surgery
Bartell, Holly	14	Ali, Asra	Dermatology
Borders, Charles	15	Actor, Jeffrey	Pathology
Chambers, Lisa	16	Scott, Allison	Orthopaedics
Cornforth, Katherine	17	DuPont, Herbert	Internal Medicine
Dahm, Paul	18	Ambrose, Catherine	Orthopaedics
Dang, Michelle	19	McDonald, Glenn	Internal Medicine
Delgado, Kristian	20	Bradley, Richard	Emergency Medicine
Even, Jesse	21	McDonald, Glenn	Internal Medicine
Fields, Brandon	22	Doursout, Marie-Francoise	Anesthesiology
Foltermann, Miles	23	Yee, Richard	Ophthalmology
Fowler, Aja	24	Eissa, Mona	Pediatrics
Galindez, Neil	25	McKinley, Bruce	Surgery
Hatfield, Brad	26	Lamki, Lamk	Radiology
Hernandez, Edgar	27	Ali, Asra	Dermatology
Hoang, Anthony	28	Geng, Yong	Internal Medicine
Jones, Kenyatta	29	Smith, Kevin	Otolaryngology
Karimullah, Mona	30	Kaplan, Heidi	Microbiology
Kasper, Erica	31	Koerner, Christine	Emergency Medicine
Kim, Hee Joon	32	Feldman, Robert	Ophthalmology
Knight, Matthew	33	Kao, Lillian	Surgery
Krolls, Tanya	34	Duvic, Madeleine	Dermatology
Martin, Stacey	35	Kiebzak, Gary	Orthopaedics
McFate, John	36	Porat, Eyal	Cardiothoracic & Vascular Surgery
Meehan, Eric	37	Scott, Allison	Orthopaedics
Mellnick, Vincent	38	Hickson-Bick, Diane	Pathology
Miller, Warren	39	Wojner, Anne	Neurology
Mogabgab, Owen	40	Grill, Raymond	Neurosurgery
Padalecki, Jeff	41	Cox, Charles	Surgery
Pai, Sher-Lu	42	Barron, Bruce	Radiology
Parrott, Justin	43	Steinberg, Joel	Psychiatry
Partesotti, Sebastian	44	Patrick, Charles	Plastic Surgery
Rabon, Shona	45	Groff, Janet	Famiy Practice
Reed, Brent	46	Ambrose, Catherine	Orthopaedics
Saunders, Bradley	47	Kulkarni, Anil	Surgery
Sedrak, Peter	48	West, O. Clark	Radiology
Smith, Marshall	49	Kozar, Rosemary	Surgery
Smith, Teresa	50	Northrup, Hope	Pediatrics
Turner, Dustin	51	Anderson, Kimberly	Surgery
Van Arsdall, Melissa	52	Taegtmeyer, Heinrich	Internal Medicine
Verner-Cole, Elizabeth	53	Kozar, Rosemary	Surgery
Weatherall, Justin	54	Kozar, Rosemary	Surgery

2003 Undergraduate Students

Student	*Page*	*Mentor*	*Department*
Aguillon, Claudia	57	Carter-Dawson, Louvenia	Ophthalmology
Ahn, Daniel	58	Mullani, Nizar	Internal Medicine
Amar, Neil	59	Murad, Ferid	Integrative Biology
Ban, Victoria	60	Zhou, Z. Hong	Pathology
Barron, Joshua	61	Mayes, Maureen	Internal Medicine
Birnbaum, Daniel	62	Swann, Alan	Psychiatry
Blanton, Lori	63	Lichtenberger, Lenard	Integrative Biology
Bokhetache, Imene	64	Jayaraman, Vasanthi	Integrative Biology
Bowhay, Elizabeth	65	Barnett, Ben	Internal Medicine
Chang, Katherine	66	Milewicz, Dianna	Internal Medicine
Chang, Yin	67	Kaplan, Samuel	Microbiology
Cosand, Louise	68	Phelps, Cynthia	School/Health Info Sciences
Devitt, Michael	69	Moody, Frank	Surgery
Eakin, John	70	Sereno, Anne B.	Neurobiology
Ellayda, Kathleen-Jo	71	McMillin, Jeanie	Pathology
Ellickal, Nirmal	72	Bick, Diane	Pathology
Elmore, Lauren	73	Wright, Anthony	Neurobiology
Gafur, Omar	74	Moody, Frank	Surgery
Galvan, Carmen	75	Morano, Kevin	Microbiology
Grubitz, Kenzie	76	Gray, Lincoln	Neurobiology
Hall, Allison	77	Ambrose, Catherine	Orthopaedics
Harkness, Melinda	78	Blackburn, Michael	Biochemistry
Haynes, Brandi	79	Fuentes, Francisco	Internal Medicine
Hernandez, Karina	80	Norris, Steven	Pathology
Holbrook, Andrew	81	Narayana, Ponnada	Radiology
Huang, Diana	82	Bean, Andrew	Neurobiology
Infante, Ernesto	83	Kaplan, Heidi	Microbiology
Itchon, Jean-Nicole	84	Cheung, Kim	Pediatrics
Khalil, Hassan	85	Penczek, Pawel	Biochemistry
Khalil, Mariam	86	Dial, Elizabeth	Integrative Biology
Kilgore, Kelly	87	Loveland, Katherine	Psychiatry
Ko, Mindy	88	Hagberg, Carin	Anesthesiology
Krajca, Justin	89	Dafny, Nachum	Neurobiology
Kronman, Rachel	90	Bradley, Richard	Emergency Medicine
Lee, Esther	91	Grotta, James	Neurology
Lemm, John	92	Taegtmeyer, Heinrich	Internal Medicine
Lerman, Beatrisa	93	Hereld, Dale	Microbiology
Li, Angie	94	Zhou, Z. Hong	Pathology
Li, Benjamin	95	Fujise, Ken	Internal Medicine
Liao, Jessica	96	Frost, Jeffrey	Integrative Biology
Lloyd, James	97	Fuentes, Francisco	Internal Medicine
Mayer, Matthew	98	D'Souza, Rena	Dental School
McGraw, Christopher	99	Loose, David	Integrative Biology
Mulloy, Benjamin	100	Clark, Richard	Integrative Biology
Papasozomenos, Harry	101	Bick, Diane	Pathology
Park, Hyun	102	Byrne, John	Neurobiology
Patel, Kiran	103	Veeraraghavan, Sudha	Biochemistry

Student	*Page*	*Mentor*	*Department*
Patterson, Lauren	104	Johnson, Philip	Internal Medicine
Pienkos, Elizabeth	105	Dafny, Nachum	Neurobiology
Proett, Jessee	106	Barron, Bruce	Radiology
Saeed, Madeeha	107	Schonbrunn, Agnes	Integrative Biology
Schnell, Aaron	108	Koehler, Theresa	Microbiology
Sen, Shiraj	109	Taegtmeyer, Heinrich	Internal Medicine
Sherill, Jennifer	110	Kaplan, Samuel	Microbiology
Tsai, Jessica	111	Bradley, Richard	Emergency Med
Udayamurthy, Anita	112	Bull, Joan	Internal Medicine
Uddeen, Sarah	113	Rahman, S.N.	Internal Medicine
Wadera, Sheetal	114	Marshall, Gailen	Internal Medicine
Wilson, Benjamin	115	Carpenter, Philip	Biochemistry
Won, John	116	Putkey, John	Biochemistry
Wu, Kelly	117	He, Xiangwei	Biochemistry
Zemo, Sessunu	118	Maloney, Donald	Internal Medicine

Medical Students

ABSTRACT

Comparison of Total Knee Arthroplasty Position and Alignment Using Two Techniques; Standard Open Procedure with Alignment Guides vs. An Infrared Based Navigation System-A Cadaveric Study

BROOK A ADAMS *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Terry Clyburn, MD, Department of Orthopaedic Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Aesculap, Radiological Systems Inc.

Key Words: total knee arthroplasty, navigational system, femur, tibia

Proper positioning of the components is critical for successful total knee arthroplasty (TKA). Concern with this positioning has led to interest in the development of "navigation" systems to guide proper placement of the components. The accuracy of these systems as compared to standard mechanical devices has not been shown. TKA was performed bilaterally on ten male fresh frozen cadavers with ages ranging from 61 to 81 years of age. The procedure was performed on five cadavers each by two surgeons. One side was chosen preoperatively at random to receive TKA with the navigation technique, while the standard approach was used on the contralateral side. Each surgeon used three extramedullary devices and two intramedullary devices on the contralateral tibias. Postoperative high quality plain radiographs were then taken of each knee in both the anterior-posterior and lateral planes to determine the alignment and position of the implants. Measurements were taken of the femoral and tibial components in both the sagittal and coronal planes. These measurements were carried out by three blind observers and averaged. The resulting data of the standard approach was then compared to data from the navigational technique. While the analysis of these measurements has not yet been fully completed, preliminary results show superior placement and alignment of the implants using the navigation system.

ABSTRACT

Apoptosis and Stiffness of the Arteries of Mice Prone to Atherosclerosis

APRIL C. ALFORD *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Dr. Yong J. Geng, MD, PhD, Department of Internal Medicine
Supported by: Alpha Omega Alpha Student Research Fellowship
Bristol-Myers Squibb Fellowship Program in Academic Medicine
American Federation on Aging Student Geriatric Scholar Program
Key Words: atherosclerosis, apoptosis, artery, smooth muscle cell, stiffness

Disappearance of vascular smooth muscle cells (SMC) via apoptosis in the arterial wall with atherosclerosis may lead to stiffening and weakening of the arterial tissue. Local immune response to atherogenic antigens or inflammation may activate the Fas ligand (CD95L)/Fas (CD95)/caspase death-signaling pathway which in turn triggers SMC apoptosis. To assess the role of the Fas/Fas ligand pathway in regulation of vascular SMC apoptosis in association with the arterial stiffness, we examined the arterial function and Fas ligand expression in the aortas of the genetically manipulated mice, which lack apolipoprotein-E. Immunohistochemistry with rat anti-mouse Fas ligand revealed positive immunostains in the arterial plaques but not in the normal arterial tissue. The Fas ligand immunostains appeared in the region with intense immunoreactivity toward CD1d, a lipid antigen presenting protein structurally similar to MHC class I molecules. *In situ* labeling of DNA fragments using the TUNEL technique illustrated numerous nuclei bearing this marker for apoptosis in the arterial wall. We further measured the aortic stiffness using non-invasive Doppler. We found that aging apoE mice developed stiffening with increased aortic pulse wave velocity (PWV). In contrast, apolipoprotein-J transgenic mice showed no major change in stiffness between the ages of 2- and 8-months. Heart rates for all animals were normal and ranged from 350 bpm to 530 bpm. These data suggest that increased expression of pro-apoptotic or proinflammatory genes may contribute to arterial apoptosis and stiffness during atherogenesis.

ABSTRACT

Angiotensin II Decreases Fibronectin Degradation by the Ubiquitin Proteasome Pathway in an In-Vitro Model of Vascular Fibrosis

CHRISTOPHER BAILEY *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Glenn A. McDonald, MD, Department of Renal Diseases & Hypertension
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Angiotensin II, Fibronectin, Ubiquitin, Fibrosis

Angiotensin II (AII) has been shown to be one of the most fibrogenic cytokines known and has been shown to increase fibronectin (FN) protein levels in multiple cell types. Previously, we have demonstrated that FN is a target protein for ubiquitin-dependent degradation. Additionally, we have shown that the von Hippel-Lindau tumor suppressor protein (pVHL) is required for ubiquitin dependent degradation of FN. The purpose of this study was to evaluate the role of AII in ubiquitin dependent fibronectin degradation in
endothelial cells. We demonstrated that AII increases fibronectin protein levels in mouse glomerular endothelial cells (mGEC) in a dose dependent fashion. To determine if AII effects on fibronectin protein correlated with alterations in fibronectin RNA levels we examined the effect of AII induced fibronectin RNA in mGEC[1]s. RNA levels were not increased by increasing doses of AII in duplicate samples. The dissociation between protein and RNA levels and our prior work prompted us to evaluate the ubiquitin-proteasome pathway. In co-immunoprecipitation experiments, we demonstrated that ubiquitin physically binds to fibronectin. We then utilized fluorescent deconvolution microscopy to confirm the co-localization of FN and ubiquitin. To further implicate the ubiquitin-proteasome pathway we evaluated the effects of AII in pVHL null cells (786-0 cells). Increasing doses of AII had no effect on fibronectin protein levels in 786-0 cells. AII increased fibronectin levels with the introduction of wild type pVHL (HA-VHL cells). To confirm that AII effects on fibronectin levels were do to protein degradation we evaluated the effects of AII by pulse chase analysis. We demonstrated that AII decreases protein degradation and significantly increases the half life of fibronectin in mGEC[1]s. Furthermore, AII had no effect on fibronectin half life in 786-0 cells while significantly increasing the half life of fibronectin in HA-VHL cells. These data demonstrate that AII decreases FN protein degradation in a pVHL dependent manner. These findings further support a role for the ubiquitin proteasome pathway in extracellular matrix homeostasis and may have implications in vascular sclerosis.

ABSTRACT

Coagulopathy Correction in Trauma Patients

B. CHRISTIAN BALLDIN *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Bruce A. McKinley, PhD, Department of Surgery

Supported by: Department of Surgery and Office of the Dean, The University of Texas Health Science Center at Houston-Medical School

Key Words: trauma, coagulopathy, PT, PTT, platelet, fibrinogen, FFP

Coagulopathy is a common complication of major trauma. Coagulation factors can be consumed rapidly with massive tissue injury and hemorrhage, and can require replacement with exogenous blood products, primarily fresh frozen plasma (FFP) and platelets. Recognition and correction of coagulopathy is a necessary part of early care of the severely injured patient. Development of standardized clinical protocol logic to detect and correct coagulopathy associated with major trauma is ongoing with the UT-Memorial Hermann Trauma Team. As part of this effort, data related to coagulopathy during shock resuscitation in the ICU is being reviewed. The variables of interest include prothrombin time (PT), partial thromboplastin time (PTT), platelet concentration ([plt]), fibrinogen concentration ([fib]), and fresh frozen plasma (FFP) and platelets given to correct coagulopathy.

Data from 79 severely injured patients (2000-2001) indicates moderate coagulopathy upon ICU admit (mean PT=15±1 sec [normal PT~11.5 sec]; [plt]=104±9 k/mm^3; [normal [plt]~250 k/mm^3]), and its persistence during the 1st 24 ICU hours with shock resuscitation (mean PT~14±0.2 sec; mean [plt]~95±5 k/mm^3]). Many of these patients received FFP and platelet transfusions (53% FFP, 46% platelet). Whereas [plt] tended to decrease ([plt]=90±5 k/mm^3 at 24 hr), [fib] increased linearly ~2.5x ([fib]=174±12 to 439±23 mg/dL; increased in 84% of patients) during the 24 hr resuscitation process.

Transfused FFP is a source of fibrinogen that may have contributed to [fib] increase. Association of times of FFP transfusion and measurement of [fib] or PT was unclear. Analysis of patient ICU data confirms need for development of a standardized, data driven protocol to help direct detection and correction of coagulopathy in the severe trauma patient starting in the emergency department (ED). ICU and ED data analysis is ongoing.

ABSTRACT

Acute Renal Failure in Type IV Thoracoabdominal Aortic Aneurysm Repair; Evaluation of Simple Cross-Clamping Versus Renal Perfusion with Warm and Cold Blood

RAMON X. BARRENO *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Charles Miller, PhD and Randolph van Eps, MD, PhD, Department of Cardiothoracic and Vascular Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11

Key Words: thoracoabdominal aortic aneurysm, acute renal failure

The role of adjunctive measures in protecting the kidneys during type IV thoracoabdominal aortic aneurysm (TAAA) repair, as opposed to simple aortic cross-clamping, remains unknown. This study evaluates the occurrence of acute renal failure (ARF) following type IV TAAA repair using renal perfusion with warm and cold blood versus the simple cross-clamp technique. Between January 1991 and March 2003, 128 type IV TAAA were repaired (10 were excluded because of short-term mortality or incomplete data). ARF was defined as postoperative doubling of creatinine and creatinine higher than 3 mg/dl or requiring dialysis. In 70 patients, distal aortic perfusion was performed to perfuse the renal and visceral arteries during the cross-clamping period. In 36 of these cases, renal perfusion was performed with blood at 4˚C with renal temperature monitoring. The simple cross-clamp technique without renal perfusion was employed in 48 cases. Of the 118 patients studied, ARF occurred in 38 (32%) and 18 required dialysis. The incidence of ARF in the simple cross-clamp group was 27%. Using warm blood perfusion the incidence of ARF was 20.1% which was significantly lower than an incidence of 50% in the cold blood perfusion group. Multivariate analysis revealed preoperative creatinine ($p=0.0003$), hypertension ($p=0.02$) and cold blood renal perfusion as significant independent risk factors for ARF development. ARF remains a significant clinical problem following type IV TAAA repair. Whereas perfusion with warm blood appears to give some protection as opposed to the simple cross-clamp technique, perfusion with cold blood surprisingly resulted in a higher incidence of ARF.

ABSTRACT

Tazarotene 0.05% Cream for the Treatment of Keratosis Pilaris

HOLLY L. BARTELL *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Asra Ali, MD, Department of Dermatology
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Tazarotene, keratosis pilaris, hyperkeratosis

Keratosis Pilaris (KP) is an autosomal dominant condition associated with dermatitis/eczema. It presents as follicular hyperkeratosis (skin plugs) most prominently on posterior upper arms, anterior thighs, cheeks, buttocks and trunk in up to 40% of the general population. The skin plugs can be distressing cosmetically. KP is difficult to treat, and no single treatment has been found to work effectively. KP is known to have a high number of cellular retinoic acid binding proteins. Tazarotene 0.05% cream was chosen as the preferred treatment since it is a retinoid and can interact with the receptors involved in KP. A placebo controlled double blind study is being performed to determine the effectiveness of Tazarotene 0.05% cream for the treatment of KP on the upper arms of patients enrolled. The criteria of redness, roughness, itchiness and number of lesions is being compared between the treated arm and placebo arm. Each patient received a vehicle cream and an active drug. The patient applied 1/4 of a teaspoon of the active drug to one arm and the same amount of the vehicle to the opposite arm every other day. The arm to which the active drug was applied was determined by randomization, and neither the patient nor the evaluator knew which arm received the treatment. Each patient enrolled followed up at 4-week intervals for a total of 3 follow-up visits. Data determining the effectiveness of Tazarotene 0.05% cream for the treatment of KP is pending.

ABSTRACT

A role for complement C5 in Granulomatous Response to the Mycobacterial Glycolipid Trehalose 6,6'-Dimycolate (TDM)

CHARLES W BORDERS III *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Jeffrey Actor, PhD, Department of Pathology
Supported by: Dean, The University of Texas at Houston – Medical School
Key Words: TDM, tuberculosis, granuloma

The molecular mechanisms underlying protective granuloma formation and control of bacterial growth during infection with Mycobacterium tuberculosis (MTB) are not yet completely understood. MTB-infected mice with natural deficiency in complement component C5 are unable to develop productive granulomatous responses, and are impaired in limiting organism growth within the lung. A model of granulomatous response using emulsified mycobacterial glycolipid trehalose 6,6'-dimycolate (TDM) was used to further address the molecular basis for this histologic dysfunction. Congenic complement C5-sufficient (B10.D2-H2d H2-T18c Hcl/nSnJ) and complement C5-deficient (B10.D2-H2d H2-T18c Hco/oSnJ) congenic mice were treated with TDM, and cytokine and chemokine responses were examined. Knockout mice deficient in C5a receptor (C5aR-KO) mice were also examined, relative to parental C57BL/6 controls. Six days after administration, lungs showed elevated protein for multiple inflammatory cytokines in all congenic, parental and knockout strains. Relative to other groups, lung weight indices were significantly elevated in the C5aR-KO mice. Lung tissue was examined histologically, and production of chemokines (KC, MIP-1 alpha and MIP-2) was also monitored. These findings indicate a role for C5 in mediation of chemotactic and activation events that are the basis for initiation and maintenance of granulomatous responses during murine tuberculosis.

ABSTRACT

Patella Alta in Ambulatory Patients with Cerebral Palsy

LISA ANN CHAMBERS *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Allison C. Scott, MD, Department of Orthopaedics
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Patella Alta, Cerebral Palsy, Pediatric

Introduction: In children with cerebral palsy, patella alta (elevated patella) can be caused by quadriceps weakness or spasticity, and/or hamstring spasticity. Over time, patella alta can result in decreased ambulation and osteoarthritis. The purpose of this study is to record the incidence and natural history of patella alta in ambulatory children with cerebral palsy (CP).
Materials and methods**:** 139 children with cerebral palsy and no previous orthopedic surgery were included in this retrospective chart review. 305 lateral knee x-rays were measured for patellar height using the method of Kushino and Sugimoto.
Results: A database of patellar height versus degrees of knee flexion was developed for three diagnosis groups: independent ambulators with bilateral invovlement, dependent ambulators and hemiplegics. In all three groups, the patellar height was statistically increased over normal, consistent with patella alta. The percentage of patients with patella alta as well as the degree of patella alta increased with degree of cerebral palsy. Correlation of the onset of patella alta with age was only seen in male independent ambulators and female hemiplegics.
Conclusions: Patella alta was present in all three diagnosis groups and increases in degree with the severity of cerebral palsy. Increase in patellar height with age was not documented in all groups; therefore treatment intervention may not be possible to prevent patella alta.

ABSTRACT

Markers of Intestinal Inflammation in *Clostridium difficile* and Enteroaggregative *Escherichia coli*

KATHERINE CORNFORTH *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Herbert L DuPont, MD, Deptartment of Internal Medicine
Supported by: Dean, The University of Texas Health Science Center at Houston-Medical School
Key Words: *Clostridium difficile*, Enteroaggregative *Echerichia coli*, intestinal inflammation markers

Clostridium difficile mediates antibiotic-associated diarrhea, and is a major pathogen in hospitals and nursing homes. Another common pathogen in intestinal inflammation is enteroaggregative *Escherichia coli* (EAEC), which is a major cause of diarrhea in children of developing countries, as well as in travelers. Our laboratory has previously shown the importance of fecal cytokine measurements in the pathogenesis of culture-proven inflammatory diarrhea. In order to better understand the patterns of inflammation associated with these organisms, stool samples from 48 patients at St. Luke's Episcopal Hospital who developed diarrhea and from 20 travelers to Guadalajara, Mexico who developed acute diarrhea were tested for known markers of intestinal inflammation. Markers tested include interleukin (IL)-8, IL-1β, and fecal lactoferrin. Results pending.

ABSTRACT

Formation, Entrapment Efficiency and Elution Characteristics of Antibiotic Laden 50/50 PLGA Microspheres

PAUL H. DAHM *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Catherine G. Ambrose, Ph.D., Department of Orthopedics
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: PLGA, Microspheres, Vancomycin, Cefazolin

Current treatment of osteomyelitis involves debridement, irrigation, and long term parenteral, high-dose antibiotics, which can be nephrotoxic and ototoxic. To limit this risk, a local delivery system is developed that allows a known concentration of antibiotics to be released over a six week period. Using a double emulsion solvent extraction technique, 50%/50% poly(DL-lactic-co-glycolic acid) (PLGA) microspheres are formed entrapping vancomycin and cefazolin within pores. Both vancomycin and cefazolin are released as the PLGA degrades. In addition, the results of degradation, glycolic and lactic acid are then utilized in the normal Krebs cycle. Four combinations of microspheres have been generated: 95% PLGA/5% cefazolin, 90% PLGA/10% cefazolin, 95% PLGA/5% vancomycin, 90% PLGA/10% vancomycin. The size of the microspheres formed range from 5.3 to 7.6 micrometers. Entrapment efficiency studies are being conducted to determine the concentration of antibiotic within the microspheres while in vitro elution characteristic studies are presently underway to determine the release kinetics. From previous studies, a linear release of antibiotics, culminating in degradation of the microspheres after four to six weeks, is expected. In addition, 50% of the original antibiotic utilized is expected to be contained within the microspheres.

ABSTRACT

An In-vitro Evaluation of the Ubiquitin-Proteasome Pathway in the Vasculature

MICHELLE DANG The University of Texas at Houston Medical School Class of 2006

Sponsored by: Glenn A. McDonald, MD, Department of Internal Medicine
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: fibrosis, vascular smooth muscle, endothelial cells, TGF-β

The extracellular matrix (ECM) is the external milieu that bathes all cells of the body, whose function is to provide structural support. Changes in ECM composition are prominent pathologic features of many diseases. We demonstrate that fibronectin is a target protein substrate for ubiquitin dependent degradation, which classically targets intracellular and membrane proteins for degradation. We will further examine the role of the ubiquitin proteasome pathway in fibronectin and extracellular homeostasis in vascular smooth muscle and endothelial cells. Fibrosis is scar tissue, caused by the accumulation of ECM through an excessive tissue repair response. We were able to develop an in-vitro model of vascular fibrosis by incubating mouse vascular smooth muscle and endothelial cells with TGF-β and evaluating fibronectin by Western blot analysis.

ABSTRACT

Correlation of Paramedic and Physician Decisions To Administer Thrombolytics for Acute Myocardial Infarctions

KRISTIAN DELGADO *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Richard N. Bradley, MD, FACEP, Department of Emergency Medicine
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Emergency medical services; acute myocardial infarction, treatment; alteplase; heparin

This prospective observational study is designed to determine if the LifePak 12 can safely and reliably determine ST elevation myocardial infarction (STEMI), and determine if paramedics can correctly utilize an inclusion/exclusion criteria checklist (IECC). Cardiovascular disease is the leading cause of death in the United States, with STEMI causing a significant proportion. It has previously been established that the interval from STEMI onset to reperfusion is a critical indicator of myocardial damage and mortality. Pre-hospital thrombolytic therapy (PHTT) can minimize this crucial interval and save many lives. This study calls for paramedics to obtain an ECG and to transmit it to an emergency physician (EP) for interpretation, also to complete an IECC and then validate each item with an online EP. We believe that the EP will not add any additional value to the paramedic's decision to give thrombolytics. This study will commence August 4, 2003. We will report the number of cases in which the LifePak 12 diagnoses a STEMI and compare this to the final retrospective diagnosis. We will also compare the paramedic's decision to include/exclude versus a retrospective decision by a cardiologist. Data will be presented in 2x2 data tables and analyzed using McNemar's test. We believe the data will support our accepting the null hypothesis that the probability of a decision to diagnose a myocardial infarction made in the field will be equivalent to the probability of the same decision based on our reference criteria.

ABSTRACT

Angiotensin II Decreases Fibronectin Degradation by the Ubiquitin Proteasome Pathway in an In-Vitro Model of Renal Fibrosis

JESSE L. EVEN *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Glenn A. McDonald, M.D., Department of Internal Medicine
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: angiotensin II, fibrosis, ubiquitin-dependent degradation

Angiotensin II (AII) is one of the most fibrogenic cytokines known and has been shown to increase fibronectin (FN) protein levels in multiple cell types. Previously, we have demonstrated that FN is a target protein for ubiquitin-dependent degradation. Additionally, we have shown that the von Hippel-Lindau tumor suppressor protein (pVHL) is required for ubiquitin-dependent degradation of FN. The purpose of this study was to evaluate the role of AII in ubiquitin-dependent fibronectin degradation. We demonstrated that AII increases fibronectin protein levels in mouse mesangial cells (MMC), proximal tubular cells (MCT), and interstitial tubular fibroblasts (TFB) in a dose-dependent fashion. To determine if AII effects on fibronectin protein correlated with alterations in fibronectin RNA levels, we examined the effect of AII induced fibronectin RNA in MMC, MCT, and TFB's. In all three cell types RNA levels were not increased by increasing doses of AII. The dissociation between protein and RNA levels and our prior work prompted us to evaluate the ubiquitin-proteasome pathway. In communoprecipitation experiments we demonstrated that ubiquitin physically binds to fibronectin in all three cell types. We then utilized fluorescent deconvolution microscopy to confirm the co-localization of FN and ubiquitin. To further implicate the ubiquitin-proteasome pathway we evaluated the effects of AII in pVHL null cells (786-0 cells). Increasing doses of AII had no effect on fibronectin protein levels in 786-0 cells. AII increased fibronectin levels with the introduction of wild type pVHL (HA-VHL cells). To confirm that AII effects on fibronectin levels were due to protein degradation, we evaluated the effects of AII by pulse chase analysis. We demonstrated that AII decreases protein degradation and significantly increases the half-life of fibronectin in MMC[1]s. Furthermore, AII had no effect on fibronectin half-life in 786-0 cells while significantly increasing the half-life of fibronectin in HA-VHL cells. These data demonstrate that AII decreases FN protein degradation in a pVHL dependent manner. These findings further support a role for the ubiquitin proteasome pathway in extracellular matrix homeostasis and may have implications in renal fibrosis.

ABSTRACT

NOS Isoforms Specificity During Isoflurane and/or Propofol Anesthesia in Rats Challenged with LPS

BRANDON FIELDS *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Marie-Françoise Doursout, Ph.D., Department of Anesthesiology
Supported by: Department of Anesthesiology
Key Words: Anesthetics, nitric oxide, nitric oxide synthase inhibitors

Objectives: The goal of this study was to investigate whether the nitric oxide (NO) pathway plays a role in the vasodilatation induced by isoflurane and/or propofol in rats subjected to lipopolysaccharide (LPS).
Material and Methods: Animals were chronically instrumented to continuously record mean arterial blood pressure (MAP) and heart rate (HR). Group 1 animals received isoflurane anesthesia in the presence and absence of LPS (20 mg/kg, IV) and N-methyl-L-arginine (L-NMA), a NO synthase (NOS) inhibitor. Group 2 animals received propofol anesthesia, IV, in the presence and absence of LPS and L-NMA. After completion of all protocols, staining and activity for constitutive (cNOS) and inducible (iNOS) was performed on previously harvested hearts.
Results: MAP decreased by 40% with propofol alone, by 60% in the presence of LPS and by 50% in the presence of LPS + L-NMA. MAP remained unchanged in the presence of isoflurane with and without LPS and L-NMA treatments. Specific staining for cNOS and iNOS on post-fixed heart sections show that propofol induced a marked iNOS production staining whereas isoflurane exhibited a noticeable eNOS production. L-NMA decreased iNOS production in both isoflurane and propofol hearts treated with LPS whereas L-NMA did not modify eNOS production in septic hearts in presence of isoflurane or profofol.
Conclusion: Our results suggest that an overproduction of NO through iNOS expression is likely accountable for propofol-induced decrease in MAP whereas eNOS expression is partly responsible for maintaining blood pressure during isoflurane anesthesia.

ABSTRACT

A Prospective, Randomized, Parallel-Group Study Evaluating the Effect of Topical Gatifloxacin, Moxifloxacin, Levofloxacin, and Ofloxacin on Corneal Epithelial Healing after Photorefractive Keratectomy (PRK)

MILES OTTO FOLTERMANN *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Richard W. Yee, MD, Department of Ophthalmology and Visual Science
Supported by: Dean, The University of Texas Health Science Center at Houston – Medical School
Key Words: cornea, photorefractive keratectomy, re-epithelialization

Photorefractive keratectomy (PRK) is a corrective refractive procedure entailing the removal of the corneal epithelium, followed by laser photoablation of the underlying stroma. Uncomplicated wound healing is fundamental in securing a satisfactory refractive outcome. As a prophylactic measure, topical antibiotics are used on the cornea before, during, and after surgery. Some antibiotics may delay re-epithelialization of the cornea themselves through cytotoxic mechanisms, disrupting wound healing and leading to corneal scarring. In order to determine which of the currently used antibiotics is least detrimental to re-epithelialization, four different antibiotics were used topically before, during, and after PRK, on four different study groups, respectively. Patients' post-surgical wounds were stained with fluorescein and photographed twice daily until complete re-epithelialization took place, to determine healing rates and elapsed time to complete healing. Wound surface areas were analyzed using a computer planimetry program. Mean elapsed time to healing for the four study arms were: ofloxacin 110 hours, standard deviation (SD) 32 hours; levofloxacin 104 hours, SD 31 hours; moxifloxacin mean 106 hours, SD 12.5 hours; and gatifloxacin 87 hours, SD 12 hours. Preliminary results indicate gatifloxacin promotes fastest healing, but results are not statistically significant at this point. More patients are currently being enrolled in the study, to enlarge the sample size, improve the power, and achieve statistical significance. Corneal haze formation is currently being followed, so that the elapsed time before formation, and permanency or transience of haze in each antibiotic group, can be better established.

ABSTRACT

Comparison of Self Body Image versus Actual Body Mass Index (BMI) in Adolescent Athletes

AJA J. FOWLER *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Mona A. Eissa, MD, PhD, Department of Pediatrics
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Body Mass Index, obesity, adolescent

Obesity in children and adolescents, a growing problem in the United States, has more than doubled since the 1970's (due largely to nutritional and exercise habits). These children are at higher risks for heart disease, high cholesterol, and high blood pressure (all risks that carry over into adulthood if there is no intervention). Adolescent athletes are not excluded from these risks either. Studies show that many adolescents who are also athletes face even higher risks of eating disorders in order to maintain or lose weight for their sport. In this study, adolescent athletes in the Aldine Independent School District were screened during routine sports physicals for their Body Mass Index (using CDC BMI guidelines), personal perception on their current weight, and what methods they used to achieve their desired weight. The study population consisted of 586 athletes: 408 African-American athletes (260 males, 148 females) and 178 Hispanic athletes (97 males, 81 females). Among this group, 26.11% were overweight (18.6% African-American, 7.51% Hispanic) and 18.95% were obese (12.12% African-American, 6.83% Hispanic). The majority of the overweight and obese groups consisted of African-American males (45.75% and 47.75%, respectively), with Hispanic males totaling 16.99% of the overweight group and 31.53% of the obese group. In terms of the overweight athletes' perception of their current weight, 71% of the African-American males and 80.77% of the Hispanic males perceived their weight as normal. The most popular method to achieve weight goals was exercise.

ABSTRACT

Modified Resuscitation of Traumatic Shock pre ICU

NEIL I. GALINDEZ *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Bruce A. McKinley, PhD, Department of Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: shock resuscitation, trauma, standardized protocol

Protocols developed by the UT-Memorial Hermann Hospital (MHH) Trauma Team for shock resuscitation in the ICU, massive transfusion pre ICU and other aspects of care ensure standard of care for major trauma patients. Research indicates need to control the early clinical course from ER to ICU. As part of a multicenter project, a standardized pre ICU shock resuscitation process was developed. Systolic blood pressure (SBP) <90 mmHg and heart rate (HR) >120 bpm identifies blunt trauma patients at risk of shock, and need for blood transfusion and base deficit (BD) ≥ 6 mEq/L indicates need for central venous monitoring to guide resuscitation. Hemoglobin concentration ([Hb]) ≥10 g/dL and central venous pressure (CVP) ≥10 mmHg are resuscitation goals to be maintained using blood and crystalloid fluid. This protocol was confirmed with collaborators during June-July. Initial implementation was part of this project, and involved encountering trauma patients in the ED. Several patients were screened. One patient met criteria. Data and process are summarized below:
Patient: young female; motor vehicle accident victim; transported via Life Flight (LF) to MHH ED. LF SBP=70, HR=136, ED SBP=84, HR=78, Hb=9.7, BD=6, CVP=2, indicating ongoing hemorrhage, metabolic stress. Exploratory laparotomy found spleen and liver injuries. During surgery, SBPmin=66, HRmax=127, Hb~7-10; BD=10-3, CVP~10; 9 units PRBC, 3 L crystalloid (NS). Interventional radiology (IR) procedure to control hemorrhage from liver injury; 4 units PRBC, 2 L LR; SBP~100-156, HR~70-140, hourly CVP=4, 7, 2; [Hb]=11.9, BD=1, indicating stabilizing hemodynamic function, ongoing hypovolemia. Upon ICU admit, SBP=127, HR=100, CVP=5, Hb=14.8, BD=7.

Combined with emergent interventions, pre ICU resuscitation stabilized SBP and [Hb] in this patient. Representative of most major trauma patients, ~6 hr is spent pre ICU, indicating need for definitive pre ICU resuscitation. Implementation is continuing to confirm this pre ICU strategy.

ABSTRACT

Advantage of PET Over CT for Cancer Diagnosis and Staging

BRAD HATFIELD *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Lamk M. Lamki, MD, FRCPC, Department of Radiology
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: PET Imaging, CT, cancer diagnosis

Purpose: A major tool for cancer diagnosis and staging is computerized tomography (CT), which identifies anatomical anomalies. Positron emission tomography (PET), is now available, and it detects physiological/metabolic changes. PET imaging utilizes deoxy-glucose radio-labeled with fluorine-18 (F-18-FDG), and malignant tumors display increased glucose (F-18-FDG) uptake. Hence, it is possible to detect cancers with high sensitivity using PET, and possibly even before anatomical changes are detected by CT.
Methods: To establish the possible additive advantage of using PET imaging, we retrospectively analyzed the CT and PET scans of 273 patients studied at The University of Texas – Houston Medical School between January and June 2003. The CT and PET findings were compared and any discrepancies were investigated. The discrepancies were then correlated with follow-up investigations. These included clinical notes, follow-up CT, MRI, ultrasound, and/or bone scan.
Results: Of the 273 patients, 65 lesions in 43 patients were identified by PET but not by CT. Follow-up data was available for only 19 patients to date. Of these, 12 lesions in six patients were confirmed to be malignant and detected only by PET. There were 25 other lesions in 18 patients that were detected by PET and not by CT but not confirmed to be cancerous as yet.
Conclusion: PET imaging detected confirmed new cancerous lesions in six patients. It may potentially impact staging of cancer patients and significantly contribute to their management.

ABSTRACT

Use of Fexofenedine HCl 60 mg to Decrease Pain of Sclerotherapy Treatment with Hypertonic Sodium Chloride

EDGAR HERNANDEZ *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Asra Ali, MD, Department of Dermatology
Supported by: Dean, The University of Texas Health Science Center at Houston—Medical School
Key Words: telangiectasias, spider veins, sclerotherapy, fexofenedine, antihistamine

Sclerotherapy is the primary choice of treatment in the management of cosmetically unacceptable lower extremity telangiectasias or "spider veins." Sclerotherapy is performed by the injection of hypertonic sodium chloride into enlarged veins. Many people experience a stinging pain for about 15-30 seconds at each injection site. The stinging pain may result from tissue injury caused by the release of histamine; therefore, suggesting that using an antihistamine such as Fexofenedine HCl 60 mg may decrease or eliminate the amount of pain experienced by the subjects during a sclerotherapy session. To understand this mechanism, 33 subjects were given both active and inactive medications at the initial visit. Patients took either active or placebo medication at two subsequent treatment sessions based on randomization. In order to standardize subject's pain thresholds, a dolorimeter evaluation was utilized. This device applies a set amount of pressure to the subject's skin, after which the subjects were instructed to rank the amount of pain experienced. At subsequent secondary and tertiary visits, patients were asked to rank pain based on a scale of 1-10 after the injections were administered and sensitivity was also evaluated. Results and conclusions will be pending, and further data will be submitted at the conclusion of the study.

ABSTRACT

Preparation of cDNA Inserts for Genetically Manipulating Embryonic Stem Cells

ANTHONY N. HOANG *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Yong J. Geng, MD, PhD, Department of Internal Medicine
Michael Wassler, PhD, Senior Research Scientist, Department of Internal Medicine
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: superoxide dismutase, clusterin (ApoJ), oxytocin

Multipotent stem cells have been used for cellular therapy for various diseases. Recent studies have documented a variety of genes involved in cell oxidative stress protection and growth may help stem cell survival and differentiation, such as superoxide dismutase (SOD), clusterin/apolipoprotein J (ApoJ), and oxytocin receptor (OTR), which contribute to cardiovascular cell protection and development. We hypothesized that transfection of these genes into stem cells may facilitate their growth and maturation in cardiac tissues damaged by ischemia. The goal of this project is to construct and subclone cDNA inserts coding for these genes into an expression vector for gene transferring. To accomplish this, cDNAs corresponding to SOD, OTR and ApoJ were first amplified from human heart cDNA library using PCR and then subcloned into plasmids. After transformation and propagation of the plasmids in *Escherichia coli*, cDNA inserts were cleaved and ligated into a mammalian expression vector. Plasmids containing cDNA inserts coding for SOD, OTR or ApoJ were transfected into mouse stem cells. Stable cells were selected with antibiotics and characterized for cardiovascular cell development and apoptosis regulation. PCR and restriction enzyme mapping revealed successful cDNA subcloning and positive transfectants were established. Further functional and morphological characterization will be conducted within the remaining time, and may be continued to the final stages of ESC lines, with overexpression of these individual genes. Fulfillment of this study may shed new insight onto the role of genetically manipulated stem cells for regenerative medicine.

ABSTRACT

Relief of Recurrent Migraine-Type Headaches with Septoplasty Surgery

KENYATTA M. JONES *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Kevin R. Smith, M.D., F.A.C.S., Department of Cosmetic Surgery and Otolaryngology
Supported by: Dean, University of Texas Health Science Center at Houston-Medical School
Key Words: deviated septum, migraine, septoplasty

The etiology of migraine and migraine-type headaches is often unclear, making proper diagnosis and effective treatment difficult. The purpose of this study was to determine if a simple surgical procedure (septoplasty)could provide significant headache relief for patients presenting with a deviated septum and migraine-type headaches. The study used a quasi-experimental self-control design. Of 188 sequential patients who had the septoplasty procedure performed, 149 (79.25%) initially presented with migraine-type headaches in addition to a deviated septum. For this subgroup, demographics and severity of the headaches were assessed with before- and after-treatment questionnaires. Prior to treatment, the average severity of the deviated septum was 2.6 on a scale of 1-3, the median duration of headaches was 8 years (range 1-60), and the median severity of headaches was 9.5 on a scale of 1-10. After treatment questionnaire responses are currently being collected, and will be compared with before-treatment responses using two-tailed Student's t-tests for quantitative variables and Chi-square analysis or Fishers Exact test for discrete variables. Other possible contributing factors (age, gender, and co-morbid conditions) will also be assessed. The results of this study will determine if a simple surgical procedure can provide significant relief of migraine-type headaches in selected patients, and may provide insight into the etiology of this type of headache.

ABSTRACT

Identification of the *Myxococcus xanthus* Genes Encoding Negative Regulators of *4442* Developmental Gene Expression

MONA KARIMULLAH *The University of Texas at Houston Medical School* *Class of 2006*
Sponsored by: Heidi B. Kaplan, Ph.D., Department of Microbiology and Molecular Genetics
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: *Myxococcus xanthus*, development, gene expression, regulation

Myxococcus xanthus is a Gram-negative soil bacterium that exhibits a unique developmental cycle in response to starvation at high density. During development the bacteria aggregate into haystack-shaped fruiting bodies in which cells differentiate into environmentally resistant spores that will germinate when conditions are favorable. To identify negative regulators of early development, a genetic screen was developed to isolate mutants that over expressed the gene monitored by Ω4442 Tn*5 lac*. The parent strain, DK4442 containing the Ω4442 Tn*5 lac* fusion, was electroporated with pMycoMar-tet^R, a plasmid containing the mariner transposon. The transformants were plated on nutrient agar containing oxytetracycine and after 7 days of growth, the colonies were overlaid with the chromogenic substrate of β-galactosidase, X-gal. One blue colony that over expressed the Ω4442 Tn*5 lac* fusion was identified from the 7,000 screened. The mutant expressed Ω4442 during growth and development at twice the level of the parent (67 β-galactosidase specific activity units compared to 31 U and 235 U compared to 127 U, respectively). Chromosomal DNA was isolated from the mutant, digested with restriction enzymes, ligated and used to transform *Escherichia coli*. The plasmid DNA will be sequenced and compared to the *M. xanthus* genomic database to determine the gene containing the transposon insertion. This information will be useful in developing a model for the regulation of *4442* gene expression.

ABSTRACT

The Role of Oral Activated Charcoal in the Management of Acute Poison Ingestions in the Adult and Pediatric Populations

ERICA KASPER The University of Texas at Houston Medical School Class of 2006

Sponsored by: Christine E. Koerner, MD, Department of Emergency Medicine
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: fibrosis, vascular smooth muscle, endothelial cells, TGF-β

Over 2.2 million poisonings occur each year. Gastric lavage (GL) followed by activated charcoal (AC), via orogastric/nasogastric tube (OG/NG), are commonly used to treat poisoned patients. AC therapy has been shown to be as efficacious as GL/AC. OBJECTIVES: To demonstrate that poisoned patients will drink AC without having the OG/NG tube inserted and that oral AC treatment is less time consuming. METHODS: A pilot study was conducted for 70 days at Lyndon B. Johnson General Hospital, an inner city hospital in Houston, Texas serving an 87% minority population. Poisoned Control was consulted as poisoned patients,' ages 1-65 years, were enrolled in the study as they presented to the Emergency Center (EC). Using a standardized script, healthcare workers gave AC solution to the patient telling them they had 20 minutes to drink. Patients were encouraged to drink in 5-minute intervals. After 20 minutes, the patients were told that they could continue to drink for another 10 minutes or have the OG/NG tube placed. Once AC was given orally (PO) or via OG/NG tube, patients were observed for complications for 2.5 hours. RESULTS**:** Fifty patients were observed and 68% (n=34) drank AC. The mean time for the three methods used involving AC was measured. The mean time for GL/AC (n= 10) treatment was 16.22 minutes, while the mean times for NG/AC (n= 6) and PO/AC (n=34) groups were 13.4 and 11.79 minutes, respectively. Therapy with PO/AC was demonstrated to be significantly faster than any therapy involving the NG tube (mean PO/AC= 1min, mean NG/AC= 4.8 min, p=.0175). CONCLUSION: We conclude that poisoned patients will drink AC and that oral AC treatment is faster than treatment with the NG tube or GL followed by AC.

ABSTRACT

Comparison of Reproducibility and Variability between OCT-3 Version 1 and OCT-3 Version 2

HEE JOON KIM *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Robert M. Feldman, MD, Department of Ophthalmology and Visual Science
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: OCT, reproducibility, RNFL

Glaucoma is a progressive optic neuropathy characterized by injury to retinal ganglion cells. Injury can be detected at the optic nerve head (ONH) and retinal nerve fiber layer (RNFL). Changes in these structures can be quantitatively monitored using an imaging device called optical coherence tomography (OCT). Previous studies have shown OCT-3 version 1 to generate reproducible ONH and RNFL thickness measurements. However, the latest OCT-3 version 2 contains modifications to the software designed to improve reproducibility in RNFL measurements. To evaluate improvements in RNFL measurements, data from version 2 were compared for reproducibility and variability to those of version 1. The cross-sectional images of the RNFL from 16 subjects (9 normal, 7 glaucoma) obtained from version 1 were reanalyzed using the new software and intra and inter observer variability calculated. The calculations were compared to those of the old software to determine if a significant difference in reproducibility existed between the two versions and to establish which variables should be considered for use in following glaucoma. For all subjects, RNFL thickness reproducibility was greater in all measured areas except the superior quadrant, where no significant difference was found. Overall, version 2 of the OCT Stratus software analysis has less variability than the previous version.

ABSTRACT

The Impact of Diabetes on Outcome in Patients with Necrotizing Soft Tissue Infections

MATTHEW T. KNIGHT *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Lillian S. Kao, MD, Department of Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Necrotizing soft tissue infections, diabetes mellitus

Background: The purpose of this study is to determine the clinical outcome of patients presenting with necrotizing soft tissue infections (NSTI's) who have diabetes.
Methods: A retrospective chart review of 43 patients admitted to LBJ Hospital between 1/01 and 12/02 was performed. Univariate analysis was performed using the chi-squared, Fisher exact probability, and student t-test.
Results: Forty-three patients were identified, of whom 46% were diabetic. These patients were older (50 ± 8 vs. 42 ± 16 years, p=0.04) and had more cardiovascular comorbidities (CAD: 35% vs. 0%, p=0.002; HTN: 45% vs. 13%, p=0.05) than their non-diabetic cohorts. They were also more likely to need Swan-Ganz monitoring (20% vs. 0%, p=0.04) and/or pressors (25% vs. 0%, p=0.02). Diabetics tended to have a longer length of ICU stay (13.6 ± 14.4 vs. 7.7 ± 11.1 days, p=0.07), a longer length of intubation (5.3 ± 7.6 vs. 1.4 ± 2.4 days, p=0.01), increased number of debridements (2.5 ± 2.0 vs. 1.8 ± 0.8, p=0.07), and increased infectious morbidity (30% vs. 17%, p>0.1). Of the patients who presented with lower extremity involvement (10/20 vs. 14/23), the rate of amputation was 30% vs. 7% (p>0.1). No statistically significant difference in mortality (2/20 vs. 1/23, p>0.1) was observed.
Conclusion: Diabetics who present with NSTI's are older and have more cardiovascular comorbidities. Furthermore, they tend to have a clinically worsened outcome and increased need for higher-level care. Given the small sample size, further prospective study is required.

ABSTRACT

Montelukast (Singulair) for Insect Bite Hypersensitivity in Patients with Chronic Lymphocytic Leukemia

TANYA B. KROLLS *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Madeleine Duvic, MD, Department of Dermatology
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: CLL, Singulair, leukemia, montelukast

Chronic Lymphocytic Leukemia (CLL) patients have an abnormal immune system including pruritic papulovesicular skin lesions which are thought to be insect bite hypersensitivity reactions (IBH). An IRB approved study was designed to determine 1) incidence of IBH in CLL patients, 2) its effect on quality of life, and 3) effect of therapeutic intervention with 10mg of montelukast qda. Out of 4000 MD Anderson patients with a CLL diagnosis, the 215 patients currently being followed for CLL were sent a short questionnaire to determine whether the patient had active itchy skin lesions. A second questionnaire based on the Skindex-29 was sent to patients that reported itchy skin lesions. Skindex-29 is validated as an instrument to measure effects of skin disease on patients' quality of life. The questionnaire was scored on a scale from 0-120 with 120 being the worst quality of life. Of the 215 initial questionnaires sent, 55 people responded and 19 reported itchy skin lesions. Of the 19 people sent the Skindex-29, 8 responded with a mean score of 21.8, range (2-45). Montelukast, originally used as asthma medication, has been proposed as a possible treatment for insect bite hypersensitivity in CLL patients. By tightly binding the CysLT1 receptor, montelukast inhibits leukotriene C4 released into the human skin following mosquito-bites and may therefore reduce the hypersensitivity reaction. In conclusion, insect bite hypersensitivity can be a significant problem in CLL patients and an effective treatment could greatly improve quality of life.

ABSTRACT

Is Fracture Risk Assessment Dependent on the Type of Quantitative Ultrasound Technology Used?

STACEY K. MARTIN *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Gary M. Kiebzak, PhD, Center of Orthopaedic Research and Education
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: calcaneal ultrasound machines, region of interest

Calcaneal ultrasound machines are an effective tool approved by the FDA to assess fracture risk. Three different ultrasound machines were used in the study: Sahara (Hologic, Waltham, MA), Achilles Express (Lunar, Madison, WI), and Achilles Insight (Lunar, Madison, WI). The Sahara and Achilles Express had a fixed transducer which did not allow for a modification of the location of the region of interest (ROI), while the Achilles Insight had an array of transducers that produced an image of the entire calcaneus and allowed the location of the ROI to be modified. Each patient had one foot scanned three times in each machine. The root mean square (RMS) of standard deviation (SD) and percent coefficient of variation (%CV) in the categories of stiffness, broadband ultrasound attenuation (BUA), and speed of sound (SOS) were calculated. The Sahara was found to have a RMS-SD of 1.45, 2.02, and 3.21 for stiffness, BUA, and SOS, respectively and a RMS-%CV of 1.63, 2.66, and 0.21 for stiffness, BUA, and SOS, respectively. The Achilles Insight was found to have RMS-SD of 1.67, 2.19, and 3.21 and a RMS-%CV of 1.65, 1.77, and 0.21. The Achilles Express was found to have RMS-SD of 1.92 and a RMS-%CV of 1.77, for stiffness. Analysis of the first fifteen patients suggests that having an image does not impact the reproducibility of the measurements, but does suggest that the image proves to be useful in determining the location of the ROI.

ABSTRACT

Analysis of Correlation Between Pulmonary Function Tests and Thoracoabdominal and Descending Thoracic Aortic Aneurysm Repair

JOHN A. MCFATE *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Eyal Porat, MD, Department of Cardio-Thoracic and Vascular Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Aortic aneurysm, pulmonary function test, TAAA, DTAA, forced vital capacity

Currently, there are no well delineated pulmonary function test guidelines for patients undergoing DTAA and TAAA repair. Moreover, there are no data describing its influence on the QOL, morbidity, and mortality of these patients. After the completion of this study, a methodical system will be used to help determine the risks of a patient undergoing TAAA or DTAA repair based on their pulmonary function data. Pre-operative PFTs consisting of spirometry along with other factors such as: co-morbidities, oxygen saturation, and smoking habits are evaluated for further consideration of post-operative complications from 30 patients undergoing DTAA or TAAA repair. Patients are interviewed to determine their past medical history and social history. Lung volumes are recorded from the pulmonary function lab to determine risk of pulmonary failure. Finally, oxygen saturation is monitored from the patient at rest, during a six minute walk, and post exercise. In addition, the patient answers questions from a survey to correlate their well being with the values mentioned before. These questions are scored with an SF-12 system. The number of days following the procedure was also evaluated to confirm the overall difficulty of recovery from the procedure. Patients are followed up by phone at six month intervals for the next three years to chart the progress and further results of their procedure.

1. Is there significant evidence to show that pulmonary function correlates with outcome of surgery?
2. Should patients with failing pulmonary values have a DTAA or TAAA?
3. What other factors can we look at to prove this further?
4. Can a system be created that predicts the outcome of the procedure based on PFTs and the other factors?

How many more patients should be included?

ABSTRACT

Surgical Treatment of Equinus Gait in Ambulatory Patients with Cerebral Palsy

ERIC T. MEEHAN *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Allison Scott, MD, Department of Orthopedic Surgery
Supported by: Dean, The University of Texas Health Science Center at Houston-Medical School
Key Words: Equinus, Calcaneal gait, Crouch gait

Equinus gait is one of the most common deformities in cerebral palsy. Heel cord lengthening is often used for correction, but there is controversy over the proper surgical technique. Postoperative risks include recurrent equinus, calcaneal gait, and crouch gait. A retrospective chart review of pre- and one year post-op clinical and gait analysis data was used in 42 children who underwent a tendoachilles (42 sides) or gastrocnemius lengthening (42 sides) to determine if one of the groups experienced better results post operatively. The two groups were then categorized into four based on the type of heel cord lengthening performed and pre-op ambulatory status (dependent or independent). The two dependent ambulatory groups were compared to each other and the two independent ambulatory groups were compared. Very little post-op kinematic or clinical data showed statistical significance between the two groups indicating that there was not a difference in the rate of recurring equinus, calcaneal gait, or crouch gait depending on the type of surgery performed. The dependent tendoachilles group and the independent gastrocnemius group were more flexed at the knee and dorsiflexed at the ankle, but it cannot be concluded that they are more likely to develop a crouch or calcaneal gait because there was a statistical difference between the groups on some of the pre operative kinematic data. More research is needed comparing the type of surgery in dependent or independent ambulators.

ABSTRACT

Cardiolipin and Hypoxia-induced Apoptosis in the Neonatal Rat Cardiomyocyte.

VINCENT MELLNICK *The University of Texas at Houston Medical School* *Class of 2003*

Sponsored by: Diane Hickson-Bick, PhD, Department of Pathology and Laboratory Medicine
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: cardiolipin, hypoxia, cardiomyocyte

Cardiolipin (CL) is a unique phospholipid that is ubiquitously present in mitochondria. It is essential for the normal function of the mitochondrial electron transport chain and energy metabolism. In tissues with a high respiratory demand like the heart, CL can account for 21% of the phospholipid in the inner mitochondrial membrane. The pathways affecting CL turnover in the heart are not well understood. Factors that regulate transcription of CL genes, or modulate activity by metabolic or hormonal means, are areas of current interest. CL content is decreased in several situations including aging, cardiac ischemia/reperfusion and stress-induced apoptosis. The acyl chain content of CL is also very sensitive to diet and changes in the CL structure can dramatically influence the efficiency of electron transport. Recent data also indicates a direct interaction between CL and cytochrome c. Cyt c is released from the mitochondrion in the early phase of programmed cell death (apoptosis). We have observed that apoptosis, as assessed by an increase in the activity of caspase-3 like enzymes, can be induced in the neonatal rat cardiomyocyte by incubating the cells in a hypoxic atmosphere in the absence of glucose. We have also observed that hypoxia-induced apoptosis is associated with a decrease in the intracellular levels of ATP and a decrease in the mitochondrial cardiolipin levels. This hypoxia-induced apoptosis is observed without reoxygenation of the cells and implies that reactive oxygen species (ROS) are not the initiators of this process.

ABSTRACT

Brain Computed Tomography Interpretation and Treatment Decision-Making Following Acute Stroke

WARREN R. MILLER *The University of Texas at Houston -Medical School* *Class of 2006*

Sponsored by: Anne W. Wojner, PhD, Department of Neurology
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: telemedicine, tPA, ischemic stroke, computed tomography

The ability to manage a variety of medical conditions using telemedicine has expanded considerably. We examined the ability of an experienced Stroke Team to read brain computed tomography (CT) scans and make appropriate thrombolytic treatment decisions using a telemedicine approach.

Sixteen (16) brain CT scans taken on patients presenting with "stroke-like" symptoms were obtained from a rural hospital; all scans were performed on a CT scanner in use since 1988. Original films were transported to the study center and read by a neuroradiologist to set a gold standard. Reviewers consisted of 4 physician faculty, 1 PhD nurse faculty, and 3 cerebrovascular fellows. Reviewers read each CT film directly in random order; a 3-week delay was then instituted, and scans were transported back to the rural hospital where they were again randomly ordered and transmitted across the telemedicine system for a second reading by the reviewers.

CT scans read in person: Percent agreement for thrombolytic treatment with the gold standard varied from 81% (nurse reviewer) to 88% (physician reviewers); 1 telemedicine-experienced physician demonstrated 100% agreement. *CT scans read remotely:* Percent agreement for thrombolytic treatment with the gold standard varied from 56% (senior physician) to 69% (1 physician fellow), 75% (nurse reviewer and 1 physician fellow), 81% (1 physician fellow), 88% (1 physician faculty), and 100% agreement (1 telemedicine experienced physician faculty and 1 physician fellow). No patients deemed ineligible for thrombolytic therapy by the gold standard were identified to receive tPA.

Agreement in direct and remote brain CT interpretation for determination of thrombolytic candidacy varies considerably. A more conservative approach to tPA treatment for telemedicine acute stroke patients is likely, although treatment rates may increase in proportion to telemedicine experience over time.

ABSTRACT

First Place, 2003 Frank Webber Prize for Student Research

Phosphodiesterase Inhibition Reduces Vascular Permeability Following Spinal Contusion Injury

OWEN MOGABGAB The University of Texas at Houston Medical School Class of 2006

Sponsored by: Raymond J. Grill, Ph.D., Department of Neurosurgery

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Christopher Reeve Paralysis Foundation
TIRR Foundation/Mission Connect

Key Words: spinal cord, contusion injury

Spinal cord injury (SCI) occurs in roughly 12,000 patients annually in the US. The vast majority of these patients experience permanent loss of function. Spinal cord contusion injury (SCI) results in disruption of the blood-spinal cord barrier (BSCB). The BSCB normally maintains the "immune privilege" of the spinal cord. Traumatic disruption of the BSCB results in vascular extravasation of blood-born substances normally excluded from the spinal cord, initiating a highly toxic inflammatory response that contributes to the destruction of spinal tissue and loss of function. Elevated levels of the intracellular signaling molecule cyclic adenosine monophosphate (cAMP) have been shown to be crucial in the development of vascular barrier function. Reduction of endothelial cAMP is believed to trigger increased permeability and relaxation of barrier tight junctions. The aim of this study was to determine whether the inhibition of cyclic nucleotide metabolizing phosphodiesterase enzymes (PDE's) could attenuate trauma-induced vascular leakage in the injured rat. Rolipram, a selective PDE4a inhibitor and Pentoxifylline (PTX), a non-selective PDE inhibitor were used tested in the injured adult rat spinal cord. Rolipram and PTX significantly reduced vascular permeability when assayed at 48 hours post-injury, the peak time point of vascular breakdown. We also demonstrate that Rolipram treatment attenuates the trauma-induced upregulation of glial fibrillary acidic protein (GFAP), an astrocytic cytoskeletal protein; a key event in the formation of the regeneration-inhibiting glial scar. Thus, the beneficial effects of phosphodiesterase inhibitors may extend beyond vascular repair following spinal cord injury.

ABSTRACT

The Effect of Enteral Nutrition on Intestinal Transit Associated with Gut Edema

JEFFREY R. PADALECKI *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Charles S. Cox, Jr, MD, Department of Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: intestinal edema, intestinal transit, enteral nutrition

Enteral nutrition has been shown to improve delayed intestinal transit associated with gut ischemia/reperfusion injury. We have shown that gut edema is also associated with delayed intestinal transit. We, therefore, hypothesized that enteral nutrition will improve delayed intestinal transit associated with intestinal edema. Rats underwent superior mesenteric vein partial occlusion and given 80 cc/kilogram of 0.9% saline (edema) $\pm$ enteral feeding (feeding) or sham surgery. At 12 hrs, FITC-Dextran was instilled into the gut via a duodenal catheter to evaluate intestinal transit. The small bowel was divided into 10 equal segments and transit was determined by the progression of FITC-Dextran and expressed as the mean geometric center (MGC). To determine if gut inflammation was associated with gut edema and dysfunction, myeloperoxidase (MPO) activity was evaluated in rat ileum. Tissue water was determined using the wet to dry weight ratio. In both edema and feeding groups, transit was delayed compared to sham controls. However, intestinal transit after feeding slightly improved the delay seen after edema alone. A significant increase in tissue water was seen in both edema and feeding groups compared to sham controls. There was no difference seen in MPO activity among groups. In conclusion, enteral nutrition slightly improved delayed intestinal transit associated with gut edema without inducing inflammation.

ABSTRACT

Increased F-18 Fluorodeoxyglucose (FDG) Uptake Following Radiation Therapy in Patients With Cancers

SHER-LU PAI *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Bruce J. Barron, MD, MHA, Department of Radiology

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11

Key Words: positron emission tomography (PET), F-18 fluorodeoxyglucose (FDG), radiation therapy

The purpose of this study was to evaluate fluorine-18-fluorodeoxyglucose positron emission tomography (F-18-FDG-PET) for the detection of radiation effects. PET imaging is a diagnostic modality that identifies changes in tissue metabolism. Following radiation therapy for cancers, increased FDG accumulation within the irradiated tissue can be identified. Accumulation in radiation induced skin burns, esophagitis, and post radiation uptake involving the pleura or great vessels has not been well characterized.

Seventeen patients with cancers who underwent radiation therapy were evaluated by PET imaging following a standard protocol. A retrospective analysis of findings was performed for several cases before and after radiation therapy. The remainder was a series of PET studies done after the therapy.

PET scans obtained after the therapy show significant increased FDG uptake compared to pre-radiotherapy images. The irradiated tissues also showed higher standard uptake values than the surrounding, non-irradiated regions. Once radiation effects were located in the patients, the standard uptake values of these regions were found constant. Patients may have abnormal FDG uptake in radiation port regions that can persist up to twenty years due to inflammation or tissue generation.

Abnormal FDG accumulation due to the effects of radiotherapy is a possible confounding variable in the evaluation of cancer. Recognizing FDG activity at sites of radiation induced inflammation and burns in cancer patients is an important distinction since it may be confused with malignancy or recurrence of disease and serve as a potential pitfall for misdiagnosis.

ABSTRACT

fMRI In Schizophrenia Research

JUSTIN PARROTT *The University of Texas at Houston Medical School* *Class of 2006*
Sponsored by: Joel L. Steinberg, MD, Department of Psychiatry and Behavioral Sciences
Supported by: The Saltzberg Research Fellowship, Summer 2003
Key Words: fMRI, working memory, schizophrenia

Purpose of the Study: Studies point to deficits in memory in people with schizophrenia. Specifically a type of short-term memory called "working memory" is affected. The prefrontal cortex, targeted by research as the working memory center, is therefore a possible site for deficit in schizophrenics. A new technique of fMRI study that is event-related allows the study of working memory tasks separate from other tasks involved. This measure may lead to an accurate representation of working memory in schizophrenics and an overall better understanding of the disease.
Methodology: Schizophrenic and normal control subjects performed working memory (WM) tasks in which a 3, 5, or 7 digit numbers are presented on a screen followed by a delay of zeros, and then another number is displayed. The memory tasks are delayed and immediate in character. The subjects are asked to remember the first number and compare it to the second, allowing for a short-term memory assessment. The subjects performed these tasks while fMRI scans were acquired in a 1.5 T MRI scanner.
Results: Signal processing techniques revealed that during the 3-digit WM, the schizophrenic subjects showed significantly less activation compared to the normal subjects in the left dorsolateral prefrontal cortex in the vicinity of Brodman's area 9.
Conclusion: These findings are consistent with theories in schizophrenia research that have postulated that deficits in prefrontal cortex are associated with this disorder.

ABSTRACT

The Effects of FGF-10 On Preadipocyte Motility

SEBASTIAN PARTESOTTI *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Charles W. Patrick, Jr., PhD, Department of Plastic Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Preadipocytes, FGF-10, motogenicity

Preadipocytes (PAs) are adipose precursor cells whose application-based biology (e.g., cell adhesion, cell motility, and response to various microenvironments) is under investigation with the ultimate purpose of utilizing these cells for the development of engineered adipose tissue to overcome limitations realized with current reconstructive surgery strategies. Recent studies show that fibroblast growth factor-10 (FGF-10) interacts with FGF receptors (FGFR-2) on the cell surface of PAs and that FGF-10/FGFR-2 interactions are necessary for proper adipogenesis in vitro and in vivo. Thus, the Patrick laboratory hypothesized that the presence of FGF-10 in the microenvironment may be important for influencing the motogenicity and/or mitogenicity of PAs during development of adipose tissue. The effect of FGF-10 on PA motility was studied by utilizing digital time-lapse microscopy to track cell movements of cultured rat PAs over a 15 hr period and a time step of 10 min. Quantitative measurements were conducted using off-line image processing and metrics included total distance, average distance traveled per time step, and cell velocity. These data were generated for side-by-side experiments of PAs cultured in nutrient media alone (negative control), in nutrient media plus FGF-10, or in nutrient media plus FGF-2 (positive control). A statistical comparison of distance and velocity traveled was made between the three groups to determine the relative effects of FGF-10 upon PA motility. Preliminary data analysis yields results that are inconclusive as to the effect of FGF-10 on PA motility. Full data analysis is in progress.

ABSTRACT

Relation of Child Behavior Problems to Intimate Partner Violence and Mother's Mental Health

SHONA K. RABON *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Janet Y. Groff, MD, MSPH, PhD, Dept. of Family Practice and Community Medicine
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: intimate partner violence, child behavior , women, children

Intimate partner violence (IPV) has been shown to affect a woman's mental health and the mental health of her children. This study examines the association of physically abused women's mental health with their children's behavioral symptoms. Three-hundred sixty abused women were enrolled in a RCT testing two interventions for IPV. Participants in this cross-sectional analysis of the baseline data (n=140) were English or Spanish speaking, ages 18 to 44, with children 18 months to 15 years old. Mental health was measured by the Brief Symptom Inventory-18, which assessed women's overall emotional distress and subscales of depression, anxiety and somatization. The Child Behavior Checklist assessed mothers' reports of total behavioral problems as well as internalizing and externalizing patterns of behavior. Regression analysis showed that all measures of abused women's emotional distress were significantly ($p<.001$) and positively associated with their children's total behavior problems and internalizing and externalizing scores. Mothers' emotional distress accounted for 10-16% of the variance in children's total problems, 14-20% of internalizing symptoms, and 3-6% of externalizing symptoms. Among the mental health subscales, women's anxiety and somatization were more strongly associated with children's total problem scores than depression. Results from this study suggest that the mental health of women experiencing IPV is closely associated with increased behavioral problems in their children, although some of this could be attributed to utilization of maternal self-report. Alleviating a woman's mental distress might serve as a viable option to prevent or decrease her children from demonstrating behavioral problems.

ABSTRACT

Comparison of DXA, Sunlight Omnisense 7000S, and Mechanical Test Results in Cadaver Long Bones

B. DEVIN REED *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Catherine G. Ambrose, PhD, Department of Orthopaedic Surgery
Supported by: Dean, The University of Texas Health Science Center at Houston Medical School
Key Words: BMD, DXA, SOS

Accurate assessment of bone mineral density (BMD) is a critical factor in evaluating risk of osteoporosis and bone fracture. Two techniques used to determine BMD are dual X-ray absorptiometry (DXA) and ultrasonic measurement of speed of sound (SOS) through bone. The Sunlight Omnisense 7000S is a multi-site bone sonometer measuring the velocity of ultrasound waves propagating along the long axis of a bone. In order to evaluate the accuracy of this diagnostic tool in determining BMD, SOS measurements obtained with the 7000S were compared to the results of both DXA scans and of mechanical compression testing on cadaver tibias. It was found that SOS measurements taken at 4.5 cm sections along a given specimen did not correlate well with DXA results for the same sections. However, SOS measurements taken at the mid-shaft location specified in the Sunlight procedure showed a good correlation to DXA results, when considered across all eight cadaveric specimens. The next step in this project will be to subject tibia cross sections to mechanical compression testing. This will allow comparisons of results from the three different tests for each tibia section, although this data is not yet available. Hopefully, this will provide insight on the diagnostic reliability of the Sunlight Omnisense 7000S at accurately measuring bone mineral density.

ABSTRACT

Evaluation of Anti-Orthostatic Tail Suspension as a Model for Aging Studies

BRADLEY M. SAUNDERS *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Anil D. Kulkarni, PhD Department of Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: AOS, mice, aging

Aging affects individuals through pronounced alterations to normal physiologic conditions. As a result, aged individuals are at risk for increased morbidity and mortality. Our aim is to develop the use of anti-orthostatic tail suspension (AOS) as a time-compressed aging model to study these changes. The practicality of AOS as a model for aging studies was evaluated with the following method. The experimental groups were as follows: 1) two month old mice (Y), 2) two month old mice with AOS (Y-AOS), and 3) sixteen month old mice (aged). The mice were sacrificed after seven days, and various tissues, including serum, brain, gut, muscle, and bone were harvested for future study. Samples will be evaluated with the following techniques. Immune function will be assessed by mitogen assays, cytokine studies, and proteomic/gene-expression studies. Brain tissue will be examined for evidence of oxidative stress. Musculoskeletal tissue samples will be investigated for evidence of physiologic and morphologic changes. Based on the hypothesis, it is anticipated that similar physiology will be observed between the young suspended mice and the aged mice. Preliminary results have shown depressed immune function and increased oxidative stress in both the Y-AOS and the aged mice as compared to the controls in Group 1. The next phase of this study is underway, and is focused on studying those changes that are specific to the musculoskeletal system. These results may lead to projects aimed at developing countermeasures directed against these pathologic changes.

ABSTRACT

Evaluation of Performance of CT and Angiography for Diagnosing Aortic Injury

PETER SEDRAK *The University of Texas Medical School at Houston* *Class of 2006*

Sponsored by: O. Clark West, MD, Department of Radiology
Supported by: Dean, The University of Texas Health Science Center at Houston Medical School
Key Words: aorta, wounds and injuries, Computed Tomography (CT), diagnostic performance

Acute Traumatic Aortic Injury (ATAI) is a consequence of blunt trauma, such as would result from motor vehicle collisions and falls from great heights. CT has become the primary diagnostic method, potentially replacing angiography as the gold standard. We evaluated the diagnostic performance of CT and angiography using a retrospective chart review.

Our patient population includes 81 patients who were either initially worked up for ATAI at MHH or were transferred to MHH for further evaluation of ATAI, among 2133 patients undergoing CT for chest trauma. The diagnostic performance of CT calculated when only direct signs of ATAI are considered positive: sensitivity 84.1%, specificity 99.8 %, PPV 88.7%, NPV 99.7%. If both direct signs and periaortic hematoma are considered positive: sensitivity 100%, specificity 98.9%, PPV 65.7% and NPV 100%.

Of the 69 patients who had initial CT the mortality count was 16 (23.1%) with 6 (8.7%) ATAI-related. Of the 12 who did not have initial CT, the 5 (41.7%) died including three (25.0%) ATAI-related.

The average time from admission to CT was 2:33 (hours:minutes). The average time from admission to surgery for patients who only had CT was 7:28 vs. 21:50 for patients who had CT and angiography.

Angiography was performed in 19 (82.6%) of 23 patients with equivocal CT scan (hematoma without direct signs of ATAI) and only 11 (27.5%) of 40 patients with a definitive CT scan. The proportion of patients undergoing angiograph was stable over time.

Conclusions: 1.CT is not definite in all cases. Exclusive reliance on direct signs of ATAI when interpreting CT would have resulted in falsely negative interpretations. Periaortic mediastinal hematoma should also be considered a positive CT finding warranting angiography. 2.Use of CT resulted in rapid diagnosis and treatment of ATAI. 3. Angiography is primarily to evaluate equivocal CTs and is usually not performed when CT is definitive.

ABSTRACT

Glutamine (Gln) or Arginine (Arg) Given During Gut Ischemia/Reperfusion (I/R) Differentially Modulates Gut Injury

MARSHALL A. SMITH *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Rosemary Kozar, MD, PhD, Department of Surgery
Norio Sato, MD, Department of Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11

Key Words: glutamine, arginine, ischemia/reperfusion, nitric oxide, myeloperoxidase

Shock-induced mesenteric I/R has been linked to early gut dysfunction and post injury multiple organ failure. The administration of early enteral nutrition following injury has been shown to decrease infections and multiple organ failure. Recently, the addition of immune enhancing agents to enteral diets has further decreased infectious morbidity. The purpose of the current study was to investigate the effects of the immune enhancing agents, glutamine and arginine, on gut function following mesenteric ischemia/reperfusion. Methods: In this pilot study (n=5/group) rats underwent a midline laparotomy and creation of jejunal nutrient sacs. Each sac was filled with 60 mM glutamine or arginine prior to 60 min superior mesenteric artery occlusion (SMAO) and compared to SMAO alone and sham laparotomy. After 6 hours of reperfusion, the jejunum was harvested for histology (Chiu score), myeloperoxidase activity (MPO), iNOS and HO-1 protein. Data are expressed as mean±SEM. Results: iNOS was increased with arginine (0.53±0.11) comparable to SMAO (0.36±0.08) but decreased compared to glutamine (0.31±0.05). HO-1 was equally increased in all groups compared to shams. MPO levels were increased with arginine (12.5±3.6) compared to SMAO (6.3 ± 1.6), glutamine (5.0 ± 0.4) and shams (2.9±0.6). Mucosal injury was also increased by arginine (4.0± 0.4) and SMAO (3.7± 0.3) compared to glutamine (1.6 ±0.3) and sham (0±0). Conclusions: Enteral arginine increased iNOS expression, mucosal inflammation and injury compared to enteral glutamine. These results suggest that the immune enhancing agents may differentially modulate jejunal inflammation and injury. Further investigations are warranted as these agents are currently administered together, along with nucleotides and omega-3 fatty acids, to critically ill patients.

ABSTRACT

Third Place, 2003 Frank Webber Prize for Student Research

Mapping Genes Involved in Multiple Congenital Anomaly Syndromes and/or Mental Retardation

TERESA K. SMITH *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Hope Northrup, MD, Department of Pediatrics
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: fluorescent in situ hybridization, bacterial artificial chromosomes, genomic mapping, developmental genes, congenital anomalies

In 5-10% of de novo apparently balanced translocations, the individual has multiple congenital anomalies and/or mental retardation. The translocation causes the disruption or dysregulation of a developmentally significant gene, resulting in the abnormal phenotype. My research project utilizes fluorescent in situ hybridization (FISH) to map the breakpoint of a de novo apparently balanced translocation, between chromosome 10 and chromosome 16 (10p12.3 and 16p13.2), in a patient with multiple congenital anomalies. A literature search yielded information about the involved chromosomal breakpoints. Candidate genes were identified using the Genome Browser on the UC-Santa Cruz website. Bacterial artificial chromosomes (BACs) were selected that contained all/portions of the candidate genes. Four BACs were chosen from each chromosome and ordered. The BAC clones were grown up, and the DNA was isolated and purified. The DNA was digested and labeled, using nick translation, to create probes. Experiments were conducted utilizing several fluorescent dyes (ULYSIS® and VYSIS®) for labeling. VYSIS® dyes proved to be the better choice because of availability of filters on the fluorescence microscope. FISH was performed, using normal chromosomal spreads. Three of these probes were found to bind to the correct chromosome. The remaining probes continue to be tested and modified. After optimization, the probes will be used to perform FISH on the chromosomal spreads from the patient. Once the translocation breakpoint is mapped to a specific BAC clone, specific genes responsible for the anomalies observed in our patient can be identified.

ABSTRACT

Surgery Shelf Exam Failure: Remediation Strategies and Policies in Medical Schools

DUSTIN A. TURNER *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Kimberly D. Anderson, PhD, Department of Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: shelf exam, remediation, clerkship failure

Medical Schools throughout North America use the National Board of Medical Examiners (NBME) surgical subset shelf exam as a method of evaluating students' fund of knowledge. Each year, a portion of the students will demonstrate proficiency in all aspects of the surgical clerkship but will fail the shelf exam. The purpose of this study is to: provide data about current remediation policies; detail outcomes of these strategies; and provide a foundation for discussion about efficacy of strategies. A 27-item questionnaire was mailed to all Surgical Clerkship Directors in the United States and Canada (n=140). Questions addressed remediation strategies and policies with regard to the NBME surgery shelf exam failure. Data were analyzed using descriptive statistics and x^2. One hundred clerkship directors responded (71%). When students fail the NBME shelf exam, $1/3^{rd}$ of schools (36.2%) require student to remediate clinically; 63.8% require to students remediate non-clinically. Success rates of students passing the shelf exam on the second take were similar regardless of the form of remediation (x^2 $p \leq 0.13$). One-third of surgical clerkships require students to remediate clinically upon failing the shelf exam. These policies cause strain on an over-burdened clinical system and student back-logging, which forces students to forgo elective clinical experiences that will enhance their medical armamentarium and result in additional medical debt load. The results of this study demonstrate no clear differences in the shelf exam success rates among those students who completed clinical versus non-clinical remediation.

ABSTRACT

Second Place, 2003 Frank Webber Prize for Student Research

Activation of PPARγ Restores Metabolic Flexibility and Improves Contractile Function in Failing Hearts from Zucker Diabetic Fatty Rats

MELISSA R. VAN ARSDALL *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Heinrich Taegtmeyer, MD, DPhil, Department of Internal Medicine
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: Type 2 diabetes, PPARγ, heart, energy metabolism, contractile function

The normal heart is insulin responsive, exhibits metabolic flexibility, and uses the most efficient substrate for a given workload and metabolic milieu. Insulin resistance in the myocardium causes metabolic maladaptation and contractile dysfunction. High-affinity ligands for PPARγ exhibit potent insulin-sensitizing properties in the setting of type 2 diabetes mellitus in liver, skeletal muscle, and adipose tissue. Their effects on cardiac metabolism and function are not known.

Hypothesis: PPARγ activation *in vivo* sensitizes the diabetic heart to insulin and induces a metabolic switch from predominantly fatty acid to glucose oxidation, resulting in a tighter coupling of metabolism and contractile performance.

Methods and Results: Hearts from male Zucker Diabetic Fatty (ZDF) Rats, administered either a PPARγ agonist (G1262570X, 8mg/kg, 2x daily) compound (ZDF-A) or vehicle (ZDF-V) for seven days, were perfused as working hearts (15cm H_2O pre-, 100cm H_2O afterload) for three consecutive 20-minute periods, with glucose (G), G + oleate (O), and with G + O + epinephrine (Epi; afterload 140cm H_2O). Cardiac power (CP) was significantly higher (1.5x) for ZDF-A versus ZDF-V hearts perfused with G or G + O. The acute increase in energy demand resulted in rapid increases in CP in both groups. Cardiac efficiency and oleate oxidation rate were not different between ZDF-A and ZDF-V hearts. However, glucose oxidation rate was significantly higher (~4x) in the ZDF-A hearts versus the ZDF-V hearts when perfused with G, G + O under normal workload and higher with Epi and increased afterload. No significant difference in these parameters occurred between hearts from compound- and vehicle-treated lean Zucker rats and Han Wistar rats used as controls.

Conclusion: Activation of PPARγ *in vivo* restores metabolic flexibility and results in a tighter coupling of oxidative metabolism and contractile performance through an increased capacity of the heart to oxidize glucose in the setting of insulin resistance in type 2 diabetes.

ABSTRACT

Metabolizable Nutrients Maintain while Nonmetabolizable Nutrients Diminish Actin Cytoskeleton Integrity of the Gut Following Ischemia/Reperfusion

ELIZABETH VERNER-COLE *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Rosemary A. Kozar, MD, PhD, Department of Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, T35 DK007676-11
Key Words: gut barrier function, enteral nutrition, cytoskeleton, Ischemia/reprefusion

Critically injured patients have decreased infectious morbidity when receiving early enteral nutrition. One proposed mechanism is by maintenance of the gut's barrier function. We have previously demonstrated that the metabolizable nutrients, glutamine and glucose, maintain the gut's energy supply and function whereas the nonmetabolizable solute, alanine, depletes energy and worsens gut function following ischemia/reperfusion. The purpose of the current study was to determine if metabolizable vs nonmetabolizable enteral nutrients differentially modulate the integrity of the actin cytoskeleton and thus barrier function. We hypothesize that glutamine (actively absorbed and metabolized) and fructose (passively absorbed and metabolized) will maintain actin cytoskeleton integrity while arginine (actively absorbed but not metabolized) will lead to breakdown of the cytoskeleton. Jejunal sacs were created in laparotomized rats and filled with 10mM glutamine, arginine, or fructose followed by superior mesenteric artery clamping for 60 minutes and 2 hrs of reperfusion. Deconvolution microscopy was used to assess integrity of the actin cytoskeleton and revealed intact epithelium in the glutamine and fructose groups, comparable to shams. In addition, rats administered fructose showed more intense F-actin staining. Arginine, however, demonstrated destruction of the cytoskeleton, with decreased F-actin in what little epithelium remained. In conclusion, the nonmetabolizable enteral nutrient, arginine, results in breakdown of the actin cytoskeleton, while the metabolizable enteral nutrients, glutamine and fructose, maintain cytoskeleton integrity. These results suggest that patients at high risk for gut ischemia/reperfusion may benefit from receiving enteral diets enhanced with metabolizable nutrients while nonmetabolizable nutrients should be cautiously administered.

ABSTRACT

Dose-Dependent Reversal of Mesenteric Ischemia/Reperfusion-Induced Gut Dysfunction Following Administration of the COX-2 Inhibitor, NS-398

JUSTIN M. WEATHERALL *The University of Texas at Houston Medical School* *Class of 2006*

Sponsored by: Rosemary A. Kozar, MD, PhD, Department of Surgery
Supported by: Dean, The University of Texas Health Science Center at Houston Medical School
Key Words: COX-2, PPAR gamma, NS-398

We have previously demonstrated that COX-2 plays a role in mediating gut dysfunction following mesenteric ischemia/reperfusion (I/R). The goal of the present study was to determine if NS-398, a COX-2 inhibitor, could reverse the effects of COX-2 on the gut. Methods: Rats were pretreated with NS-398 (3, 10, or 30 mg/kg) or vehicle 1 hr prior to 60 min of superior mesenteric artery occlusion (SMAO) and compared to sham laparotomy. After 2 hrs of reperfusion, ileum was harvested for measurement of PGE2 and 6-keto PGF, myeloperoxidase (index of inflammation), and PPAR (nuclear receptor which mediates stress kinase pathways). Results were analyzed by ANOVA with Tukey's post hoc, $p<0.05$ significant (n=5/group) Results: There was a dose-dependent decrease in prostaglandin production and myeloperoxidase activity following administration of NS-398. At 30 mg/kg, both PGE2 (3831 ± 538 pg/mg protein) and 6-keto PGF (3415 ± 477 pg/mg protein) were significantly decreased compared to SMAO vehicle (17369 ± 2201pg/mg protein, 19412 ± 1055 pg/mg protein, respectively). There was also a significant decrease in MPO (2.58 ± .19 ng/mg protein) down to sham levels (2.37 ± .44 ng/mg protein) compared to SMAO vehicle (7.24 ± 1.48 ng/mg protein). At 30 mg/kg, NS-398 increased DNA binding of PPAR. Conclusion: NS-398 decreased prostaglandin production and gut inflammation in a dose-dependent fashion following mesenteric I/R. NS-398 inhibition of COX-2 correlated with an increase in PPAR, and may be a mechanism by which NS-398 reverses the deleterious effect of COX-2 on the gut. COX-2 inhibition following shock-induced gut ischemia/reperfusion may therefore have important clinical implications.

Undergraduates

ABSTRACT

Production of Glutamine Synthetase in Rat Retinas with Elevated Glutamate

CLAUDIA AGUILLON *Texas Southern University* *Class of 2004*

Sponsored by: Louvenia Carter-Dawson, PhD, Department of Ophthalmology and Visual Science
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: glutamine synthetase, dihydrokainic acid, glutamate

Purpose: Glutamate is the major excitatory neurotransmitter in retina. Rapid removal and conversion to non-excitatory products is essential for normal retinal function. The major glial cell in retina, Müller cells, remove excess glutamate from the extracellular space via glutamate transporters on Müller cells and transfer it to the cytoplasmic compartment where it is converted to glutamine by the enzyme glutamine synthetase (GS). Blocking the glutamate transporter-1 (GLT-1) located on cone photoreceptors and some bipolar cells causes an increase in extracellular glutamate. An increase in extracellular glutamate will cause a concomitant increase in transport as well as metabolism of glutamate by glutamine synthetase. The purpose of this experiment was to evaluate the possible increased production of GS caused by raised extracellular glutamate.
Methods: Glutamate concentration was raised by monocular injection of dihydrokainic acid (DHK) in the vitreous of male Sprague-Dawley rats. DHK blocks glutamate transport by the GLT-1 transporter. The control eyes were injected with vehicle. Eyes were removed and dissected at 4, 7, and 10 days. Expression of GS was examined by Western blot analysis using PicoWest chemiluminescence.
Results: Raising extracellular glutamate concentration did not generate an increase in GS at any time point post-injection.
Conclusion: We conclude that the rise in extracellular glutamate induced by DHK was not sufficient to alter expression of glutamine synthetase.

ABSTRACT

Quantitation of Tumor Parameters

DANIEL AHN *Texas A&M University* *Class of 2004*

Sponsored by: Nizar A. Mullani; B.S.; Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: tumors, P.E.T., blood flow

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 21 solid tumors that were treated with Endostatin and PKI, and imaged by PET. Our goal was to define the parameters for monitoring tumor blood flow and glucose metabolism change in tumors following therapy, develop methods to measure anti-angiogenic changes in human tumors, and validate the methods using established phase 1 Endostatin Study data and manual analysis of data. We observed were pixel, slice and volumetric tumor parameters through different methods in order to see the relationship between flow, metabolism and size. Manual analysis of tumor data was conducted by drawing regions of interest around tumors in every slice, adding the date from the slices to produce total tumor volumetric measurements and obtaining tumor areas from slices. Our results showed that individual pixel-based analysis contains too much regional variation to be useful for PET analysis while volumetric measurements and slice-based analysis of the tumor should be done whenever possible. The observations from the manual analysis of PET data showed that the total tumor glucose and blood flow utilization are linearly related to total tumor volume. Further, tumor utilization of glucose and blood flow is higher at the rim than the center, and the glucose/flow ratio is increased in the center of the tumor compared to its edge. Finally, Endostatin reduced total tumor blood flow but not total glucose utilization of total tumor volume.

ABSTRACT

Anti-inflammatory Action of Nuclear Receptor Activators

NEIL K. AMAR *Houston Baptist University* *Class of 2004*

Sponsored by: Ferid Murad, MD, PhD, Department of Integrative Biology and Pharmacology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: protein expression; TO-901317; WY 14643

TO-901317 (TO), a Liver X receptor agonist, and WY 14643 (WY), a PPAR receptor agonist, are two important nuclear receptor activators that are believed to play a major role in the prevention of inflammation in a variety of cell types. A specific example involves the repression of inflammation-induced proteins in macrophage cells. To understand TO and WY's role in this process, macrophage-like RAW cells from mice were cultured and activated using treatments with lipopolysaccharide and interferon gamma. Additionally, TO or WY was added to the cell media followed by a 24 hour incubation period. A Western blot analysis was then performed using antibodies specific to proteins expressed in activated RAW cells—inducible nitric oxide synthase (iNOS) and intercellular adhesion molecule-1 (ICAM-1). iNOS is an important protein that catalyzes the production of nitric oxide, a molecule involved in numerous physiological and pathophysiological processes. ICAM-1 is a glycoprotein involved in cellular interactions and may also play an important role in the onset of atherosclerosis. A careful analysis of the Western blots revealed a decreased expression of iNOS in TO and WY treated cells as well as a decrease in expression of ICAM-1 in WY treated cells. This suggests that TO, WY, and other related compounds may have a significant role in the development of new anti-inflammatory drugs.

ABSTRACT

Image Digitization and Pre-processing for 3D Structure Determination of Macromolecular Complexes by Electron Cryomicroscopy

VICTORIA BAN *Rice University* *Class of 2006*

Sponsored by: Z. Hong Zhou, PhD, Department of Pathology and Laboratory Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: electron cryomicroscopy, image processing, human cytomegalovirus, basic phosphoprotein

Electron cryomicroscopy (cryoEM) and computer reconstruction is an emerging structural biology technique for determining the three-dimensional (3D) structures of supramolecular complexes, such as viruses and multi-component enzymes. In cryoEM, images of frozen hydrated complexes are recorded on photographic film and subsequently digitized in a high resolution microdensitometer. These images are then selected and evaluated by image pre-processing. My project focused on the structural determination of the mutant human cytomegalovirus, whose tegument protein, the basic phosphoprotein (BPP; pp150, ppUL32), had been tagged with a green fluorescent protein. To create a three-dimensional structure of the mutated virus, particle images were selected from cryoEM micrographs. Approximately two-hundred electron micrographs (one-hundred focal pairs) were digitized and then prepared for image processing. Subsequently, individual particles were boxed out from the digitized micrographs, and the quality of the micrograph was evaluated by determining the defocus range. Currently, a preliminary three-dimensional construction of the BPP-tagged human cytomegalovirus has been computed. The 3D localization of BPP and the identification of its interactions with other viral proteins in the intact virus are essential to the understanding of its roles in human cytomegalovirus infection.

ABSTRACT

Scleroderma Family Pedigree

JOSHUA A. BARRON *Yeshiva University* *Class of 2004*

Sponsored by: Maureen D. Mayes, MD, MPH, Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: scleroderma, family pedigree, ANA

Background: Scleroderma is a disorder of unknown etiology with generalized involvement of connective tissue. No single laboratory study can confirm the diagnosis. ANA patterns may be useful in diagnosis. Possible genetic relationships are to be investigated.
Methods: Pedigree charts were constructed on scleroderma patients using information provided by the scleroderma Family Registry and DNA Repository. The pedigrees were performed on 3 different sub-groups:

singleton families (N=387), multi-case scleroderma (MCS) (N=26), and multi-case auto-immune disease families (MCAIF) (N=112). Supplementary to family lineage, ANA results were added, and their pattern recorded in color. Additionally other autoimmune diseases were documented.
Results: Upon analysis of disease propensity it was found that among MCAIF the percentage was 9% male and 91% female, 10.26 % and 89.74% respectively in singleton families, and 7.69% and 92.31% respectively in MCS families. These numbers differ slightly from the expected 20% males 80% females in singleton families. Upon review of all cases of ANA positivity the following patterns were noted: Speckled 50.23%, Nucleolar 23.20%, Centromere 19.82%, Cytoplasmic 5.63%, Homogenous 1.13%, peripheral 0%. In MCAIF the patterns were Speckled 53.53%, Centromere 23.23%, Nucleolar 16.16%, Cytoplasmic 6.06% Homogenous 1.01%, peripheral 0%. Among all ANA+ family members the patterns were Speckled 70.96%, Centromere 12.90%, Nucleolar 8.06%, Cytoplasmic 6.45%, Homogenous 1.61%, peripheral 0%.
Conclusion: Future Analysis could look at birth order and the propensity of firstborns acquiring scleroderma. This would test the notion that children born later on should have a higher rate of scleroderma due to retained fetal cells.

ABSTRACT

Laboratory Measures of Impulsive Behavior in Adults – Yohimbine Administration

DANIEL S. BIRNBAUM *The University of Kansas - Lawrence* *Class of 2006*

Sponsored by: Alan C. Swann, MD, Department of Psychiatry and Behavioral Sciences
Donald M. Dougherty, PhD, Department of Psychiatry and Behavioral Sciences
Supported by: NIH Grant AA 12046; Pat R. Rutherford Junior Chair in Psychiatry
Key Words: yohimbine, norepinephrine, impulsivity, alpha-2, IMT/DMT

Impulsive behavior is characteristic of several psychiatric disorders. For bipolar manics, both increased impulsivity and increased amounts of the neurotransmitter, norepinephrine, occur concurrently. Based upon this phenomenon, the effects of increased norephinephrine in normal subjects will be examined to document a link between norepinephrine and state related changes in impulsivity. This will be achieved through the oral administration of yohimbine hydrochloride. Yohimbine blocks alpha 2 noradrenergic receptors that normally inhibit norepinephrine release. Computer based testing (IMT/DMT) will then determine if impulsivity has increased while self-questionaires will monitor mood and behavior effects of yohimbine. If a solid link between impulsivity and increased amounts of norepinephrine can be established as a generalizable phenomenon, it will spur new treatments for psychiatric disorders in which impulsivity occurs and raise understanding of how impulsivity varies with time. Five subjects completed the study, but one subject's data varied widely and was thus excluded as an outlier. Examining the other data reveals expected side effects for yohimbine: the largest dose increased systolic blood pressure (3 subjects) by at least 20 mm Hg and increased self-indicators consistent with the presence of yohimbine like restlessness, uneasiness, and tenseness. Two parts constitute the computer test: (IMT) a short delay time between stimuli & (DMT) longer delay time with distracters between stimuli. IMT is thought to test impulsivity, so it is important that overall, IMT revealed a positive relationship in change in scores to actual administration and quantity of yohimbine dosage. At the higher dosage, an average IMT increase of 2.96 over baseline occurred, with normal scores ranging from 3.36 to 13.45 on a 100-point scale. DMT scores related negatively to administration and quantity. However, effects varied. One subject registered little blood pressure change, and one registered little self-indicator change at the highest yohimbine dosage. Preliminarily, the data suggests a potential relationship between norepinephrine and impulsivity. Further testing will reveal the specificity of the relationship.

ABSTRACT

NSAIDs and Breast Cancer

LORI BLANTON *Lamar University* *Class of 2005*

Sponsored by: Lenard M. Lichtenberger, PhD, Department of Integrative Biology and Pharmacology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: NSAIDs, PC-NSAIDs, MTT assay

NSAIDs are a family of drugs which reduce pain, inflammation, and fever. Some common NSAIDs include Acetylsalicylic acid (ASA, or Aspirin) and Ibuprofen (IBU). NSAIDs are associated with gastrointestinal bleeding and ulceration. Thus, Dr. Lichtenberger developed PC-NSAIDs, which are NSAIDs bound to a phospholipid derived from soy lecithin. PC-NSAIDs not only reduced injury to the GI, but also enhanced therapeutic activity to inhibit pain, inflammation, and fever. Research indicates that use of NSAIDs can decrease the risk of many kinds of cancer, including breast cancer. We can predict that upon treatment with ASA and IBU, MCF-7 breast cancer cells in cell culture will show a reduction in cell number. Due to enhanced therapeutic effects when dealing with the GI tract, we can hypothesize that PC-NSAIDs will show greater efficacy at reducing cell number than unmodified NSAIDs. For the experiment, cells were seeded at 50,000 cells per well in a 24-well plate and generally allowed to incubate for forty-eight hours. The cells were treated with ASA and IBU to determine a dose response. The cells were then treated with PC-ASA and PC-IBU. Analysis was done by MTT assay. The MCF-7 cells did show a reduction in cell number when treated with ASA and IBU in a dose dependent fashion. PC-ASA and PC-IBU proved to be more effective at reducing cell number than unmodified NSAIDs. With more research, PC-NSAIDs could prove to be a safer, more effective way of preventing breast cancer.

ABSTRACT

Investigating Glutamate Receptor Binding Site Using Vibrational Spectroscopy

IMENE BOKHETACHE *The University of Houston-Downtown* *Class of 2005*

Sponsored by: Vasanthi Jayaraman, PhD, Department of Pharmacology and Integrative Biology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: glutamate receptors, glutamate, vibrational spectroscopy,

Glutamate receptors are excitatory ligand gated ion channels that are responsible for promoting fast synaptic communication between nerve cells in the nervous system. In order to investigate the kinetic steps that are involved in their ligand binding process, Fourier Transform Infrared Spectroscopy was used to probe the vibrations of the carbonyl groups of the protein backbone, and the asymmetric vibrations of the ligand, glutamate, carboxylate group. The infrared difference vibrational spectra for GluR2 and GluR4 between the unbound and the bound states indicate that glutamate induces the same structural changes on both of these AMPA subtype subunits, suggesting similarity in their behavior. Additionally the protein back bone vibrations indicate an increase in the absorbance suggesting that the protein is more ordered upon binding glutamate. Based on the previous spectroscopic investigations, glutamate is thought to first dock on the protein by interactions at the 1C carboxylate, followed by protein conformational changes. We have performed time resolved FTIR investigations which indicate that the protein and the ligand modes change approximately at the same rate. Future investigations will be aimed at using mutants that alter the rate of the ligand docking and protein locking steps so that these steps can be analyzed in more detail. The functional consequences of these mutations will also be investigation allowing us to draw correlations between the structural changes at the ligand binding site and functional changes in the receptor.

ABSTRACT

Assessment of the OraQuick Rapid HIV-1 Antibody Test for Use with Oral Fluid Specimens in a Known HIV Positive Population

ELIZABETH BOWHAY *The University of Texas at Austin* *Class of 2005*

Sponsored by: Ben Barnett, MD; Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: HIV testing, oral fluid

Studies have shown that the estimated 200,000 Americans who are unaware that they are infected with HIV contribute significantly to the number of new infections, but this may be prevented with increased accessibility to new rapid HIV diagnostic tests. The purpose of this clinical trial study was to test the sensitivity of the OraQuick Rapid HIV-1 Antibody Test in revealing a patient's HIV status by testing an oral fluid specimen. The study objective was to evaluate the safety and compare the diagnostic performance and sensitivity of the testing device when used to test oral fluid versus the traditional diagnostic methods of testing plasma specimens by licensed enzyme immunoassay (EIA) and Western Blot (WB). All study participants were prior known HIV positive subjects who, at the time of enrollment, did not meet the CDC criteria for AIDS. Patients were also HIV-antiretroviral naive, on a "drug-holiday" for a minimum of 30 days, or on highly active antiretroviral therapy less than two consecutive years. The total enrollment was fifty-four patients and all but two specimens were positive for HIV antibodies, resulting in a specificity of 96.3%. The two negative specimens were from patients who were diagnosed in the primary stage of HIV infection (PHI) and started anti-retroviral therapy before sereoconversion. The OraQuick device is a useful tool in diagnosing HIV infection; however, further investigation is needed for patients receiving therapy in primary stages of infection.

ABSTRACT

Abnormalities in Fibrillin-1-Containing Microfibrils in Scleroderma

KATHERINE W. CHANG *The University of Texas at Austin* *Class of 2005*

Sponsored by: Dianna M. Milewicz, MD/PhD, Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: systemic sclerosis, LTBP1, TGFβ-LLC, LAP

Scleroderma or systemic sclerosis (SSc) is a multisystem, autoimmune connective tissue disease characterized by cutaneous and visceral fibrosis and obliterative vasculopathy. Fibrillin-1, a glycoprotein that is a component of microfibrils in the extracellular matrix (ECM), binds directly to the latent-TGFβ-binding protein 1 (LTBP1). LTBP1 is part of the TGFβ-large-latent-complex (TGFβ-LLC), which also includes the latency-associated protein (LAP) and the mature form of TGFβ associated by non-covalent interactions. TGFβ, a profibrotic factor that regulates cell growth and matrix synthesis, must be activated to exert its functions. It is hypothesized that instability of fibrillin-1-containing microfibrils causes release of active TGFβ from the TGFβ-LLC and contributes to the pathogenesis of scleroderma. ECM fractions and media samples from 10 control and 10 SSc dermal fibroblasts were analyzed by Western blot analysis using polyclonal antibodies specific for LTBP1 and LAP. The SSc ECM fractions showed a significant decrease of the TGFβ-LLC and LTBP1 bands as compared to control samples. Furthermore, two-thirds of patients SSc media samples displayed an unique 75-kDa band recognized by the LTBP-1 antibody. Analysis with the LAP antibody revealed an increased number of protein bands compared to the control, suggesting proteolytic degradation of the TGFβ-LLC. These studies revealed that instability of fibrillin-1-containing microfibrils in SSc fibroblasts could lead to proteolytic degradation of TGFβ-LLC with release of a specific proteolytic peptide of LTBP1. Additional work will investigate the release of active TGFβ associated with degradation of TGFβ-LLC and its role in the pathogenesis of scleroderma.

ABSTRACT

Rhodobacter sphaeroides Has a Quorum-Sensing Regulon that Negatively Regulates the Putative Cellulose Synthase Operon

YIN CHU CHANG *The University of Texas at Austin* *Class of 2006*

Sponsored by: Rebecca Cox, PhD, Department of Microbiology and Molecular Genetics
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: *Rhodobacter sphaeroides*, cellulose synthase, quorum-sensing regulon

Rhodobacter sphaeroides is a metabolically diverse, free-living bacterium commonly found in freshwater lakes and ponds. Like many Gram-negative bacteria, *R. sphaeroides* has a quorum-sensing system that utilizes acylhomoserine lactone (HSL) as a response signal. In the absence of HSL, *R. sphaeroides ΔcerI* aggregates in liquid culture. Thus, the quorum-sensing regulator and the HSL synthase are referred to as C*erR* and C*erI*, respectively, for community escape response (c*er*). Typically, cell aggregation is caused by an exopolysaccharide layer, which in some bacteria also contains cellulose. Interestingly, *R. sphaeroides* DNA sequence data indicate that it has a homolog of *Agrobacterium tumefaciens* cellulose synthase operon (*cel*). Furthermore, *R. sphaeroides ΔcerI* fluoresces on calcoflour medium (an indication of β-1,4 linked polysaccharides like cellulose) and aggregated cells dissociate upon addition of cellulase. To determine whether the quorum-sensing regulon affects the expression level of the putative *cel* operon, we used a reporter plasmid, pRC35, which consists of a putative *cel* promoter fused with *lacZYA'*. Once *p*RC35 was conjugated into *R. sphaeroides ΔcerI* and *R. sphaeroides* 2.4.1 (wild-type laboratory strain), equivalent amounts of protein isolated from mid-logarithm phase aerobic cultures were analyzed in triplicate for β-galactosidase activity. In three separate trials we found that β-galactosidase activity in *R. sphaeroides ΔcerI* was three times higher than *R. sphaeroides* 2.4.1. Since levels of β-galactosidase activity reflect levels of *cel* promoter activity, this observed increase in *cel* expression indicates that the quorum sensing regulon negatively regulates the putative *cel* operon.

ABSTRACT

Getting Brains into Their Brains: Educating Youth about Mental Health Science

LOUISE DEBS COSAND *Colgate University* *Class of 2003*

Sponsored by: Cynthia L. Phelps, PhD, School of Health Information Sciences

Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
National Institute for Mental Health, Award: MH1917

Key Words: mental health, health informatics, education

In order to increase the numbers of students pursuing careers in mental health research, mental health information scientists are developing materials targeted at increasing youth awareness of the field. Effectiveness of informatics is positively correlated with effectiveness of supplementary hands-on activities. Thus, a field study of effective hands-on activities was conducted. Previously, hands-on neuroscience activities were tested with middle school students, high school students and science teachers. Data collected revealed factors important to effectiveness, such as interactivity, relevance to the neuroscience topic, and clarity of instructions. A new piece of curricula was developed based on these principles. 7 middle school science teachers volunteered to listen to a 5 minute explanation of neuron activity and then try the new activity. The teachers were given printed instructions and allowed to attempt the activity. Both observations and a post-test questionnaire served to collect data. Analysis of data revealed the importance of visual aids in instructions. Further, instructions needed to be succinct rather than thoroughly descriptive; the visual aids would replace the need for written descriptions. The findings provide guidance for future activity development and may improve knowledge transmission.

ABSTRACT

The Effect of Sensitization and Mast Cells on Gut Mucosal Permeability

MICHAEL DEVITT *Cornell University* *Class of 2006*

Sponsored by: Frank Moody, MD, Department of Surgery
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: dextran, fMLP, T. Spiralis

The bacterial toxin fMLP, when added to perfused ileum of a rat, causes a transient rise in the blood to lumen movement of macromolecules, in part through the release of mast cell mediators. Infection with Trichinella Spiralis results in an increase of mast cells in the gut. Perfusion with fMLP in T. Spiralis sensitized rats sustained an increase in the FITC-Dextran 4400 flux. It was hypothesized that the Dextran flux in the presence of fMLP in vitro will be further enhanced in T. Spiralis immunized rats, due to an increase in mast cells. Blood to lumen movement of Dextran during perfusion with fMLP would not be sustained in egg albumin sensitized rats, for they did not exhibit increased mast cells. The in vivo technique involved the perfusion of the distal ileum with Krebs solution at a rate of .25mL/min/g of tissue for 90 minutes, when fMLP at a concentration of 10^{-5} molars was added to the perfusion solution. The in vitro technique involved mounting ileal segments on Ussing Chambers and evaluating the permeability through mucosal to serosal movement of the Dextran 4400. The results were recorded flurometrically, and fMLP was added 30 prior to the Dextran. Results showed that fMLP caused an increase in membrane permeability which was not enhanced in T. Spiralis rats. Thus mast cell hyperplasia caused by T. Spiralis did not affect the fMLP induced increased in the permeability in vitro. The fMLP induced ileal permeability to Dextran in EA sensitized rats was not sustained. It can be concluded that an increase in mast cell number does not further increase fMLP-induced rise in flux.

ABSTRACT

Evidence for More Robust Reflexive Priming in Schizophrenia

JOHN L. EAKIN *The University of Texas at Austin* *Class of 2006*

Sponsored by: Anne B. Sereno, PhD, Department of Neurobiology and Anatomy
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: schizophrenia, semantic priming, attention

We were interested in the role that attention plays in disordered thought processes frequent in schizophrenia. Specifically, we examined the role of reflexive and voluntary attentional processes in the semantic domain by using a category-switching manipulation based on Neelys 1977 work with normal subjects. Neely used this category-switching paradigm to separate semantic priming that would occur automatically for a related but unexpected word from semantic priming that would occur for a word from an expected but unrelated category. We tested 7 schizophrenic patients (SzP) and 10 control subjects on a similar lexical decision task. Probe stimuli were either words from 1 of 2 categories ("Animal" or "Clothing") or pronounceable non-words. Prime stimuli were the words "Animal", "Clothing," or "Neutral." SzP were told that when the prime word was "Animal" or "Clothing," then 80% of the time the following probe would be a word from the opposite category. Probe words following the "Neutral" prime could be from either category equally. Using these categories and the same short (250 msec) and long (2000 msec) SOAs as Neely, we found that SzP are greatly facilitated at the sort SOA for related but unexpected words, demonstrating more reflexive priming than controls. We also found in SzP inhibition at the long SOA for related but unexpected words but no facilitation for unrelated but expected words, suggesting that at the long SOA SzP can inhibit their reflexive tendencies but have difficulty voluntarily refocusing their attention on the opposite category. In sum, SzP demonstrated hyper reflexive priming and absent voluntary priming—that is, they remembered to inhibit the related category but failed to attend to the opposite but expected category.

ABSTRACT

Estrogen Effects on Neonatal Rat Cardiomyocytes

KATHLEEN-JO F. ELAYDA *Loyola University Chicago* *Class of 2005*

Sponsored by: Jeanie B. McMillin, PhD; Department of Pathology and Laboratory Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: estrogen, inducible NO synthase, serum response factor, cardiomyocytes

The role of estrogen in gender-specific differences in the occurrence of cardiac disease has been established in a number of studies. It has been shown that 17β-estradiol stimulates the expression of inducible nitric oxide synthase (iNOS) in cardiomyocytes, which is significant because of the major role played by NO in the response of heart tissue to ischemia. To measure the transcriptional effects of 17β-estradiol, e.g. iNOS expression, on neonatal rat cardiomyocytes, we removed estrogen from the cell culture media via charcoal-stripping. However, this also removed growth factors from the media, after which the myocytes did not survive. We finally established a viable model of estrogen depletion, which involved adding insulin and albumin to serum-free media. We were then able to show the stimulation of iNOS expression in cardiomyocytes by 17β-estradiol using western blot analysis, confirming the results of Nuedling, et al (Cardiovascular Research 43: 666, 1999). Transcriptional responses to estrogen appear to depend on the presence of a serum-response element (SRE) in the candidate gene. Gel shifts from estrogen-treated myocytes demonstrated serum response factor (SRF) binding to a consensus SRE that was supershifted by anti-SRF. There was no detectible difference between control and estrogen-treated binding, and no induction of Rel A binding, where NF-κB is a known iNOS gene activator. However, estrogen induced a more rapidly migrating band at 0.5 and 1 hour that was not supershifted or competed by anti-SRF. The results suggest that the SRE binding protein induced by estrogen may represent recognition of the SRE by cooperative or antagonistic binding proteins, e.g. Nkx-2.5 or YY1. This type of interplay may be important to fine-tune the estrogen response.

ABSTRACT

Cardiac Protection from Septic Shock

NIRMAL S. ELLICKAL *Case Western Reserve University* *Class of 2006*

Sponsored by: Diane Hickson-Bick, PhD, Department of Pathology and Laboratory Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: UCP2, UCP3, apoptosis, cardiomyocytes

Lipopolysaccharide (LPS) is a major component of bacterial outer walls that profoundly affects mammalian cells. A clinically important response to LPS is endotoxic shock. In the heart, programmed cell death (apoptosis) and depression of cardiac function are recognized sequellae of endotoxic shock. Studies from this laboratory have uncovered an innate protective phenotype of the newborn rat heart against LPS-induced cell death. In the adult heart sub-lethal doses of LPS can condition and confer resistance to LPS injury by reprogramming myocardial gene expression. These observations suggest that the heart has innate mechanisms that, if activated, can defend it from toxemia. Our earlier results using neonatal rat cardiomyocytes indicated that LPS treatment causes a transient change in the mitochondrial membrane potential and an increased activation of the mitogen-activated protein kinase (MAPK), p38. Using Western blot analysis and confocal laser microscopy we have shown that the loss in mitochondrial membrane potential is temporally associated with an increase in the expression level of mitochondrial uncoupling proteins, UCP2 and UCP3. This is also associated with a decrease in the cellular ATP levels. UCP proteins uncouple oxidative phosphorylation and thereby facilitate a proton leak across the mitochondrial membrane. Increase in UCP levels, because of their uncoupling properties, may act to protect the mitochondria by reducing their production of reactive oxygen species (ROS). Both UCP3 and ATP levels tended to return to control levels in a similar time frame to the recovery of the membrane potential.

ABSTRACT

Pigeons Learn Matching to Sample Using Gravel Stimuli

LAUREN C. ELMORE *The University of Texas at Austin* *Class of 2006*

Sponsored by: Anthony A. Wright, PhD, Department of Neurobiology and Anatomy
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: matching to sample, concept learning, pigeons

Two pigeons (Ron and Alex) were trained to match to sample using gravel stimuli in a digging task. The first phase of training began with four different colors of gravel stimuli. The pigeons participated in eight-trial daily sessions in which they dug in a sample pot, ate three seeds, and then chose one of two other pots in which to dig. They were rewarded with seeds for digging in the matching pot. After fifteen days of training with Ron, and eight days with Alex, acquisition of the task had not occurred. For phase two, the number of stimuli used was reduced to two. Acquisition was apparent after six and eight days for Ron and Alex respectively, at which point transfer trials were begun. Phase three, transfer trials, consisted of two daily transfer trials embedded in the usual eight trial daily session. Six of the phase two training trials were used to track baseline performance, and one transfer trial was composed of two totally novel gravel stimuli, and the other trial was composed of the two stimuli colors that had been cut out of the original training stimuli. It should be noted that the novel stimuli were only truly novel on the first day of transfer, as the two colors were reused every day. They are referred to as novel because they are more novel than the familiar stimuli which the birds trained with during phase one. The object was to compare performance on the novel and familiar transfer trials. Transfer tests indicate that Ron and Alex have both acquired the matching to sample concept as their performance is well above chance. However, Ron performed almost equally well on novel and familiar trials whereas Alex performed better on familiar trials.

ABSTRACT

Effect of Mast Cells on Gut Mucosal Permeability

OMAR ARIF GAFUR *The University of Texas at Austin* *Class of 2006*

Sponsored by: Frank G. Moody, MD, Department of Surgery
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: fMLP, mast cells, sensitization

Traumatic stress causes bacterial overgrowth in the lumen of the gut. E. Coli, a bacterium found in the gut, produces a toxin called fMLP. Treatment with doxantrazole, a mast cell stabilizer, negates fMLP-induced transient increase in Dextran flux in vivo. An increase in mast cells following infection with T. Spiralis sustained the response to fMLP. We hypothesize that ileum from a Trichinella Spiralis immunized rat will have an enhanced flux of FITC-Dextran 4400 movement in vitro. In contrast, we predict that ileum from egg albumin sensitized rats, with no mastocytosis, will not have a sustained response to fMLP perfusion of the ileum. Perfusion and Ussing Chambers were used to measure the fluxes of Dextran 4400. In contrast to our hypothesis, mastocytosis caused by T. Spiralis does not further affect the fMLP induced increase in permeability of rat ileum in vitro. The fMLP-induced increase in membrane permeability to Dextran 4400 in egg albumin sensitized rats studied in-vivo revealed a similar prolongation of the fMLP response as seen with T. Spiralis even though mastocytosis does not occur in this sensitized model. Although the results negate our hypothesis, mast cells do play a critical component in the fMLP response.

ABSTRACT

Isolation of High Copy Suppressors of the Uncharacterized Stress Gene YER139C in Saccharomyces cerevisiae

CARMEN GALVAN *University of Houston-Downtown* *Class of 2004*

Sponsored by: Kevin A. Morano, PhD, Department of Microbiology and Molecular Genetics
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: stress, heat shock, transcription, yeast

All organisms, from bacteria to higher eukaryotes, possess a highly conserved heat shock response that is important for coping with various stress conditions, including heart disease and cancer in humans. Advances in genomics have allowed the systematic identification of new genes involved in this response. In yeast, the predicted gene YER139C was found to be essential for cell viability during heat shock in the presence of formamide, which is a heat simulator that causes protein unfolding. The molecular function and biological role of YER139C are unknown. The goal of this study was to use genetics to isolate genes that suppress the temperature sensitive growth phenotype, possibly identifying proteins that interact with the Yer139C protein, thereby helping to place it within a known cellular pathway. The initial screening resulted in approximately 100 putative high copy genomic library suppressors, which were further categorized into nine groups. After re-testing for suppression, two genes, *RPB5* and *RPB9*, which encode subunits of RNA polymerase II, were found to restore wild type growth. *RPB5* is required for cell viability under normal laboratory conditions, whereas *RPB9* is only essential for cell growth under temperature extremes. The identity of a third possible suppressor is currently under investigation. The isolation of two RNA polymerase subunits suggests that YER139C may play a role in transcription, possibly under stress-activated conditions. The presence of YER139C homologs in mice and humans further suggests a conserved role in transcription in mammals.

ABSTRACT

Normal Perception of English Phonemes Depends on Frequency and not Amplitude Modulation

KENZIE GRUBITZ *University of Chicago* *Class of 2004*

Sponsored by: Lincoln Gray, Ph.D., Department of Otolaryngology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Hearing, speech perception, phonologic continuua

Recent research has shown that children with dyslexia are overly sensitive to small variations in linguistic output and less sensitive to phonological categories. Given this information, we wondered if it would be possible to create stimuli which make normal adults respond in a way similar to children with dyslexia. A computer generated continuum of five tokens ranging from /ga/ to /ka/ was used as a control, and then the continuum was modified in two ways. The first manipulation maintained the frequency modulations of the token while eliminating amplitude modulations. The second manipulation maintained the envelopes, but the fine structure of the tokens was identical. Each group of tokens was randomized and all possible pairs of tokens were played repetitively to 10 adults with normal hearing. By using multidimensional scaling to analyze their response times to changes in the stimuli, it was shown that subjects perceived the first set of modified stimuli similarly to the control, while they perceived the second set of stimuli differently to the control. Whereas the first set of modified sounds were perceived categorically, the second set were perceived without respect to phonological boundaries. These results show that our perception of English phonemes is sensitive to the fine structure of phonemes rather than the envelope. From these results, we might be able to begin to help dyslexic children improve their phonologic perception by training them to hear fine structure differences between phonemes.

ABSTRACT

Grading Implant Wear Using Radiographs

ALLISON HALL *Tulane University* *Class of 2005*
Sponsored by: Catherine G. Ambrose, PhD, Department of Orthopaedic Surgery
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: total hip arthroplasty, acetabular cup, femoral head, polyethylene wear, *in vivo*

Total hip arthroplasty is one of the major concentrations of orthopaedic surgery and research. A typical implanted device replaces both the acetabular cup and the femoral head. The acetabular portion contains a layer of polyethylene that can be worn away over time. Polyethylene wear is a major complication for orthopaedists, causing the development of osteolysis and loosening or failure of the hip replacement. Several different manual and computer-aided techniques currently exist to take *in vivo* measurements of the polyethylene wear. Research has shown that computer-aided techniques produce the most accurate results. In this study, a computer program was developed to determine the degree of wear from an anteroposterior radiograph. The program is composed of graphics code written in C++ and is designed for use on a Windows operating system. The users of this program will be able to load a series of radiograph images and input a small amount of information to pinpoint the locations of the acetabular cup and the femoral head over time. The output of the program will be an *in vivo* measurement of polyethylene wear. Orthopaedists will be able to utilize this program to quickly obtain precise results with little effort, as opposed to existing manual techniques. At this time, the program consists of a user-interface and many different functions that will facilitate input from the user. Further development of this program will complete the creation of an accurate method for the *in vivo* measurement of polyethylene wear that can be utilized by surgeons and researchers throughout the field of orthopaedics.

ABSTRACT

Regulation of IL-6 Gene Expression by Adenosine in ADA-deficient Mice

MELINDA G. HARKNESS *University of Houston-Downtown* *Class of 2003*

Sponsored by: Michael Blackburn, PhD, Department of Biochemistry and Molecular Biology
NIH Grant # HL70952

Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program

Key Words: adenosine, IL-6, clara cells

Asthma is a chronic inflammatory disease of the lungs that affects more than 15 million Americans. Although the incidence rate is on the rise, the mechanism of disease is still unknown. Previous studies have implicated the signaling nucleoside, adenosine, in the development and progression of asthma. Evidence includes the observation of elevated adenosine levels, as well as increased expression of adenosine receptors in the lungs of asthmatics. Adenosine is produced in response to damage and is regulated by the catabolic enzyme adenosine deaminase (ADA). Therefore, ADA-deficient mice develop severe lung inflammation due to accumulation of adenosine. However, the mechanisms by which adenosine induces changes in the lungs of these mice are not known. The goal of this project was to determine if IL-6 levels were elevated in an adenosine-mediated manner in ADA-deficient lungs and to begin to test which adenosine receptors were involved. Examination of IL-6 transcript levels using real time rtPCR revealed that IL-6 was significantly elevated in the lungs of ADA-deficient mice. In addition, elevations in IL-6 were reversed in ADA-deficient mice treated with ADA enzyme therapy suggesting that adenosine is mediating IL-6 levels in this model. In order to examine which receptors may be involved, lung epithelial clara cells were cultured and directly exposed to adenosine and adenosine receptor antagonists. Preliminary data suggests that the A_1 adenosine receptor may be involved in adenosine-mediated IL-6 production in these cells. Experiments are currently underway to help us better understand the role of adenosine receptors in the production of IL-6.

ABSTRACT

Cardiovascular Reduction in African American Women

BRANDI J. HAYNES *The University of Texas at San Antonio* *Class of 2003*

Sponsored by: Francisco Fuentes, MD Department of Internal Medicine- Cardiology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: African American Women CVD Prevention

African American women have a higher cardiovascular mortality than women in other ethnic groups. Cardiovascular disease (CVD) knowledge helps in the reduction of cardiovascular disease risk factors; therefore, an educational bilingual tool was developed to inform patients with cardiovascular disease of the risk factors. The tool was administered at the LBJ Hospital clinic where most of the patients were indigent and Spanish-speaking. The tool was written on a 4^{th} grade level to facilitate understanding of the information.

A database of risk factors and basic CVD knowledge of each patient was obtained prior to and after the administration of the tool. The number of questions they answered correctly before (I) and after (F) were recorded along with each patients' gender, weight, presence of high blood pressure, and presence of diabetes.

Seventy-one patients were screened and 32 were evaluated for the study. A cohort of 14 African American (AA) women was compared to a cohort of 10 non-African American women (OE) to observe the difference in CVD knowledge after administration of the educational tool. AA women had an average of 5.85 right answers before the administration of the tool and 7.35 after. OE women had an average of 6 right answers before and 7.8 after the administration of the tool.

We conclude that a significant increase in knowledge was demonstrated in both women cohorts, with no dissimilarities among ethnic groups.

ABSTRACT

Differential Reactivity of C6 Peptides in Lyme Disease Patients

KARINA M. HERNANDEZ *University of Texas at El Paso* *Class of 2004*

Sponsored by: Steven J. Norris, Ph.D., Department of Pathology and Laboratory Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: C6 peptides, Diagnosis, Lyme Disease

Lyme disease is a tick-borne illness caused by the spirochetes *Borrelia burgdorferi, Borrelia garinii,* and *Borrelia afzelii*. This disease is clinically diagnosed by the manifestation of erythema migrans, a bull's-eye shaped skin lesion which is seen in less than two-thirds of patients and only early in the course of infection. Detection of antibodies against *Borrelia* antigens can also be used to confirm diagnosis. The antigenic variation protein, VlsE has recently shown to be useful for the immunodiagnosis of lyme disease. The C6 peptide, a 26 amino acid, immunodominant conserved region of VlsE, was used in an enzyme-linked immunosorbant assay (ELISA) to detect the presence of serum antibodies directed against C6. The hypothesis of this study is that sera infected with a *Borrelia* species is more reactive to the C6 peptide derived from the infecting species. Sera from rabbits and mice infected with a known *Borrelia* species were more reactive to their respective peptide. Nineteen human samples from patients in Germany, where infection with all three *Borrelia* species is known to occur, were tested by ELISA using the C6 peptides. Sera from Lyme patients were reactive with all three C6 peptides, except for one borderline sample. The *B. garinii* peptide exhibited a higher reactivity in most serum samples, whereas the *B. burgdorferi* or the *B. afzelii* peptide were more reactive in some. These results suggest that with further refinement a VlsE-based ELISA may be used to determine the infecting *Borrelia* species.

ABSTRACT

Development of Diffusion Tensor Support for Multiple MR Scanners

ANDREW B. HOLBROOK *Duke University* *Class of 2005*

Sponsored by: Ponnada A. Narayana, PhD, Department of Radiology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: diffusion tensor imaging, magnetic resonance imaging, analysis software

Diffusion tensor imaging (DTI) of tissue water, based on magnetic resonance imaging (MRI), provides important information about the tissue organization at the microscopic level. DTI allows a noninvasive detection of pathology with improved sensitivity and specificity. For example, the anisotropic diffusion of tissue water in the brain can be exploited to track the fiber organization and the connectivity of various regions in the brain. Disrupted connectivity is implicated in a number of neurodevelopmental, neuropsychiatric, and neurological disorders.

Since generation of DTI from MRI involves the analysis of hundreds and thousands of images depending on the encoding scheme, robust and user-friendly processing software is critical for the analysis of data. The software in the mentor's laboratory, while very powerful, was limited to the analysis generated on a General Electric (GE) MR scanner. Additionally, this software was limited to the analysis of data acquired with a predefined set of encoding schemes.

With the acquisition of a Bruker, 7 Tesla MR scanner for in vivo animal studies, there was a need to modify the existing software to accommodate data acquired on different types of scanners using different encoding schemes. Using IDL (Interactive Data Language), these objectives were accomplished. It was then evaluated successfully using the MR images generated on water phantoms using the Bruker scanner. In addition, the software continued to work on the human brain MRI data acquired on the GE MR scanner using various icosahedral encoding schemes.

ABSTRACT

Binding of Actinin-4 and SNAP-25 to Hrs

DIANA S. HUANG *Cornell University* *Class of 2006*

Sponsored by: Andrew Bean, PhD, Department of Neurobiology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Actinin-4, SNAP-25, Hrs, endosome

Endocytosis is an essential process by which cells internalize nutrients from the extracellular environment as well as retrieve proteins and lipids that are added to the plasma membrane during fusion of secretory vesicles. Molecules are taken up by endocytosis into membrane-bound organelles called endosomes, which function to sort these molecules, separating those to be recycled and those to be degraded. Hrs is an endosome-associated protein that has been found to interact with a number of proteins including actinin-4. Actinin-4 is an actin-binding protein, and the interaction of hrs with it has been suggested to tether endosomes to actin filaments. We have previously shown that an endosome receptor for hrs is SNAP-25 and in the present study, we examined whether actinin-4 and SNAP-25 would bind to hrs simultaneously. To test this, we purified recombinant Hrs and SNAP-25 by affinity chromatography and immobilized pure actinin-4 on glutathione sepharose. We incubated the immobilized actinin-4 with hrs and SNAP-25. We also examined a number of controls: actinin-4/hrs, actinin-4/SNAP-25, GST beads/hrs/SNAP-25. After washing, we separated the proteins with a 12% gel, transferred them to nitrocellulose membrane, and probed the membranes using Hrs and SNAP-25 antibodies. We observed that hrs, actinin-4, and SNAP-25 can form a complex, but based on the apparently direct binding of actinin-4 with SNAP-25, we cannot determine if SNAP-25 and actinin-4 are binding to hrs simultaneously.

ABSTRACT

Identification of *Myxococcus xanthus 4494* Negative Regulators

ERNESTO INFANTE JR. *The University of Texas at Brownsville* *Class of 2005*

Sponsored by: Heidi B. Kaplan, Ph.D., Department of Microbiology and Molecular Genetics
Supported by: Dean, Graduate School of Biomedical Science,
The University of Texas Health Science Center at Houston
Key Words: *Myxococcus xanthus*, *4494*, mutagenesis, negative regulation

Myxococcus xanthus, a Gram-negative, rod-shaped bacterium, exhibits the complex behavior of fruiting-body formation on solid surfaces during periods of insufficient nutrients at high cell density. Within these fruiting bodies, cells differentiate into spherical myxospores capable of withstanding starvation and desiccation. The extracellular signal involved in this response is termed A signal. An important objective in *M. xanthus* research is to characterize the regulation of A-signal responsive genes. The early development gene, *4494*, is a target of the A-signal pathway, but is regulated independently of the known A-signal transducers: SasS/N/R and EcfA/ReaA/B. The *M. xanthus* strain DK4386 containing Ω4494 Tn*5 lac* was mutagenized by electroporation using the pMycoMar-tet^r plasmid to identify negative regulators of *4494*. Mutants containing a mariner transposon inserted within a gene encoding a *4494* negative regulator would be dark-blue upon exposure to the chromogenic substrate for β-galactosidase, X-gal. Two dark-blue colonies (A-11 and A-12) were observed from approximately 2000 colonies screened on nutrient plates containing oxytetracycline. Both A-11 and A-12 showed a two-fold increase in β-galactosidase specific activity during growth and development compared to the parental strain (30 U compared to 14 U and 70 U compared to 35 U, respectively). Chromosomal DNA of both strains was digested, re-ligated and electroporated into *Escherichia coli* cells that were screened for tetracycline resistance. The cloned *M. xanthus* chromosomal DNA upstream of each transposon insertion will be sequenced to identify the genes interrupted by the transposon insertions. Identifying the *4494* negative regulator(s) will further our understanding of the regulation of early development in *M. xanthus*.

ABSTRACT

Health-Related Issues in Foster Care Children

JEAN-NICOLE G. ITCHON *The University of Texas at Austin* *Class of 2004*

Sponsored by: Kim K Cheung, MD, PhD, Department of Pediatrics
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: foster care, children, health issues

The medical clinic at Harris County CPS provides comprehensive pediatric health care to children in protective custody. Initial physical exams done on intake to CPS reviewed multiple health problems. A retrospective medical chart review was performed on all intake patients (total of 546) seen between July and December 2002. Patients' age ranged from 0-5 years (47.3%), 6-10 years (25.5%), and 11-18 years (27.2%). An approximate 1:1 male-to-female ratio was found. The broad range of ethnicities included 37.6% African American, 32.6% Hispanics, 16.3% Anglo, and 13.5% either mixed or unknown. The six highest-ranking diagnoses for all children included URI (20.3%), dermatological findings (13.9%), head lice (8.2%), heart murmur (6%), asthma (4.6%), and otitis media 93.8%). The most common medical diagnosis was URI (34%) for the 0-5 year age group, head lice (14%) and URI (13%) for the 6-10 year age group, and various psychological concerns (19%) for the 11-18 year age group. ADHD, behavioral problems, and depression were the most common. Obtaining medical or immunization records was a major problem. A preliminary analysis of the immunization status was done. In the 0-5 year age group, 61% of the immunization records were unavailable for review. In school age children (ages 6-10), records were available in only 33%. Many of the children were found to have significant dental health problems. About 17.4% were noted to have caries. Children in protective custody enter with a multitude of health concerns that need to be addressed.

ABSTRACT

Computational methods in EM protein structure determination

HASSAN A. KHALIL *University of Houston* *Class of 2006*

Sponsored by: Pawel A. Penczek, Ph.D., Department of Biochemistry & Molecular Biology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: single particle reconstruction; electron microscopy; defocus

Single particle reconstruction is a method of determining the three-dimensional (3-D) structure of biological macromolecules with molecular masses ranging from few hundred kD (kilo-Daltons) to millions of Daltons. Particle images are obtained by electron microscopy (EM) using either stain or cryo and are aligned and corrected for the transfer function effects of the microscope. The 3-D structures are affected by the microscope settings, most prominently the defocus, and by the reconstruction technique. In this study, (a) computational methods were developed to account for defocus change across tilted micrographs, and (b) integrated multi-reference and reference-free alignment algorithms were implemented to align 2-D particles. Defocus varies across tilted micrographs and particles obtained from different regions of a micrograph have different transfer function parameters. We divided tilted 16S proteosome micrographs into bands and treated particles obtained from each band as a separate defocus group. The power spectrum of each band was calculated using averaged overlapping periodograms and its defocus was estimated using its 1-D rotational power spectrum.

Reconstruction procedures require that particles be aligned. The implemented procedure was based on the following strategy: For a set of heptameric complex particles, we aligned each particle using the partial average of all other particles to avoid the bias of the current particle. After each particle was aligned, it was re-inserted into the average.

The defocus estimation technique worked well on untilted micrographs. For tilted micrographs, however, further work is needed to enhance band signal. The alignment algorithm produced satisfactory results and was used to align the heptameric complex particles.

ABSTRACT

The Role of Phosphatidylcholine on the Intestinal Mucosa in an Animal Model

MARIAM A. KHALIL *University of St. Thomas* *Class of 2005*

Sponsored by: Elizabeth Dial, PhD. Department of Integrative Biology and Pharmacology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: phosphatidylcholine, ischemia, reperfusion, myeloperoxidase

Ischemia/reperfusion (I/R) of the Superior Mesenteric Artery causes injury as well as inflammation to the gut. It interrupts the blood supply and, thus, this model is used to cause traumatic stress to the animal for the purposes of our study. We hypothesized that phosphatidylcholine (PC) protects the small intestinal mucosa from injury by maintaining its hydrophobicity. In the laboratory we administered two different formulations of PC to rats and varied the doses. PC (90G) which contains 90% PC was administered orally to the rats in doses of 100mg/kg and 300mg/kg. P35 which is comprised of 35% PC was administered in the same way with the dose of 100mg/kg. We waited for a period of two hours prior to causing injury to the rats. Rats underwent ischemia for 1 hour and reperfusion for 2.5 hours and were anesthetized with isoflurane during the 3.5 hour period. Then, animals were sacrificed and serum, intestinal flush, lung and ileum tissue samples were collected for analysis. We then tested ileum tissues for the amount of myeloperoxidase present. Myeloperoxidase is an enzyme that indicates inflammation and is produced by neutrophils. Rats that were challenged with (I/R) had a high amount of myeloperoxidase present. Those that were dosed with PC showed a significant decrease of myeloperoxidase. Amount of hemoglobin present in the intestinal flush was also measured. Results indicated that rats pretreated with PC showed tendency to bleed less than the ones that received no treatment.

ABSTRACT

Emotion Recognition in Autism

KELLY L. KILGORE *University of Houston* *Class of 2004*

Sponsored by: Katherine A. Loveland, PhD, Department of Psychiatry and Behavioral Sciences
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: autism, emotion, facial and auditory stimuli

Autism is a developmental disorder that impairs social and communication skills. Natural conversations contain rapid changes in facial expressions, tone of voice, and gestures. Children with autism have difficulty understanding these multi-modal social cues, perhaps because they do not attend to them. This study examined the ability of children with autism to perceive emotion across modalities, with and without verbal instructions to draw their attention to relevant cues. Children with autism (n=41) and controls (n=27) of similar age, verbal and nonverbal mental age, and gender were videotaped while viewing 14 brief vignettes. Each video contained a split-screen presentation of one person, displaying a different emotion (afraid, angry, happy, sad, or surprised) on each side of the display, with one vocal track, de-synchronized from both sides, matching only one side's emotion. In the first task, subjects only watched the videos, and percent of time looking at the matching side was coded (PL task). Then, subjects viewed the vignettes again and were asked for each to tell which side was talking (VBL task). Based on repeated analysis of variance measures, controls matched auditory with visual emotion more accurately than autism subjects on both tasks ((F (1,66)=4.18, p=.045). However, both groups performed better on the VBL than the PL task (F (1,66)=67.85, p=.000), and the groups differed on the PL (F (1, 67)=9.91, p=.002) (Control > Autism), but not the VBL task. These results suggest that children with autism have more difficulty than controls perceiving emotion intermodally, but with structure, they can improve their perception of social-emotional information.

ABSTRACT

Has the Practice of Airway Management changed?

MINDY KO *Rice University* *Class of 2005*
Sponsored by: Carin A. Hagberg, M.D., Department of Anesthesiology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: advanced airway management, anesthetic trends

The modification of guidelines for management of the difficult airway and the introduction of new interventions mediate the re-evaluation of the current trends in the practice of airway management. Following Ethics approval, information regarding preoperative evaluation and airway management was collected. Airway management, outcomes, and prediction of difficulties were compared in 530 patients undergoing surgery at Memorial Hermann Hospital during the years of 1999-2001 (Period 2). This sample was compared to a larger retrospective study that was conducted during the years of 1991-93 (Period 1) by the University of Toronto. Alternative techniques for intubation including all methods other than direct laryngoscopy under general anesthesia (DL/GA) are noted below. There was a significant decrease in the use of traditional mask ventilation correlating with a significant increase in the use of the laryngeal mask airway (LMA). With exploration into the uses of the LMA, this device has replaced traditional mask ventilation in many cases. Furthermore, the use of assistive aids (i.e. fiberoptic and intubating stylets) has become more extensively utilized. This data represents a preliminary analysis of an ongoing study. Continuation of this study is warranted in order to determine whether or not the practice of airway management has really changed.

Results:

	Period 1	**Period 2**
Total (n)	22,542	530
DL/GA	80.1%	82.8%
Alternative Technique	1.5%	0.8%
Regular Mask	14.9%	4.3%†
LMA	2.8%	12.1%†
Other Supraglottic Devices	-	0.8%
Total ≥ 3 Laryngoscopies	1.4%	0.6%
Fiberoptic Assist	0.1%	1.3%
Intubating Stylets	0.03%	6.8%†
Predicted Difficult Airway	-	11.1%
Limited Neck Mobility	-	2.1%
Small Mouth Opening	-	2.8%
Mallampati ≥ III	-	6.2%

† $p<0.01$

ABSTRACT

Behavioral responses of chronic Ritalin® treatment in naïve and pretreated female spontaneously hypertensive rats

JUSTIN A. KRAJCA *Texas A&M University* *Class of 2003*

Sponsored by: Nachum Dafny, PhD, Department of Neurobiology and Anatomy
Alan C. Swann, MD, Department of Psychiatry and Behavioral Sciences

Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program

Key Words: Methylphenidate, Ritalin®, Sensitization, Attention Deficit Hyperactivity Disorder, ADHD, Chronic

Use of the psychostimulant methylphenidate (Ritalin®, MPD) has increased rapidly in treating Attention Deficit Hyperactivity Disorder (ADHD) in children and adults. Studies have shown that recurring exposure to psychostimulants such as MPD can cause behavioral sensitization, an enhanced response to the effect of the drug following each repeated exposure. However, the long-term consequences of MPD usage are still unknown. Therefore, the objective of the present study was to determine whether repeated exposure to low (0.6 mg/kg) and moderate (2.5 and 10.0 mg/kg) doses of MPD in adolescent, female spontaneously hypertensive rats (SHR), an animal model for ADHD, would alter their behavioral responses to the drug when they became adults. The SHR were randomly divided into two groups: (1) received intraperitoneally (i.p.) saline as adolescents and treated with 0.6, 2.5, or 10.0 mg/kg MPD i.p. as adults (i.e., naïve adults; N=12 per each dose), and (2) received 0.6, 2.5, or 10.0 mg/kg MPD i.p. as adolescents and again similarly treated as adults (i.e., pretreated adults; N=12 per each dose). Computerized infrared photocell motion sensors were used to record locomotor activities (e.g., total distance, horizontal and vertical activities, stereotypic movements) for 2 hours after saline/MPD injection. Results showed different dose-response characteristics of MPD between adolescent and adult SHR. In addition, adult naïve rats exhibited sensitization to 2.5 mg/kg MPD while the pretreated adults did not sensitize to any MPD dose used, as measured by all four motor indices studied. Furthermore, the naïve adult rats exhibited greater intensity in their responses to the 2.5 mg/kg dose as compared to the pretreated adults. These findings suggest that MPD pretreatment in adolescent female SHR could modulate their behavioral responses in adulthood.

MPD gift from Mallinckrodt, Inc.

ABSTRACT

Report of a Preliminary Study on the Effects of a Quality Management Intervention for the Treatment of Community-Acquired Pneumonia (CAP) on the Interval from Triage Time to Antibiotic Administration (ABx) and Rate of Blood Culture (BC) Collection Before Antibiotic Administration

RACHEL ESTHER KRONMAN *The University of Texas at Austin* *Class of 2006*

Sponsored by: Richard N. Bradley; MD; Department of Emergency Medicine.
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Community-Acquired Pneumonia, antibiotic, blood cultures.

CAP affects about 3 million people/year in the US and is responsible for 45,000 deaths. It is the leading infectious cause of mortality and the sixth most common cause of mortality in the US, and one of the most common reasons for adult hospitalization (25% of the diagnosed cases require hospitalization). A decrease in the interval from the time the patient arrives to the ED (Emergency Department) to ABx results in shorter length of stay, lower mortality, and less cost. In preparation for a before-and-after, interventional study on the interval from triage time to ABx and rate of BC collection before ABx, we conducted a CPHS-approved, retrospective study prior to research. Our study questions were: 1) What was the mean interval from triage time to ABx? 2) What percentage of the intervals were under 191 minutes? 3) What was the rate at which BC were obtained before ABx? Our preliminary research consisted in reviewing all adult ED with a diagnosis of CAP from June 2002. There were 25 patients diagnosed with CAP; we were able to locate 21 of their charts, but three of these were missing essential data. The median interval from triage time to ABx was 677 minutes with a 95% CI of 402 – 858 minutes. The interval was < 191 minutes in 0 of 19 cases. Fourteen of 19 cases (74%) had BC obtained before ABx, which is below our goal of 88%. We need to conduct a quality management intervention study for the treatment of CAP in the ED.

ABSTRACT

The Effects of Glypromate in Lesion Volume and Functional Deficits with MCAo Suture Model in Long-Evans Rats

ESTHER HYUN-KOUNG LEE *University of Texas at Austin* *Class of 2005*

Sponsored by: James C. Grotta, M.D., Department of Neurology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: MCAo model, glypromate, ischemic stroke

Because of its low molecular weight, glypromate is able to cross the blood-brain barrier and has been shown to rescue neurons following brain injury. With stroke being the third leading cause of death in the United States and the cause of serious, long-term disability, there is need for a more efficient and effective treatment of stroke. The purpose of this study is to determine if glypromate decreases lesion volume and improves functional recovery in the Middle Cerebral Artery Occlusion (MCAo) suture model of ischemic stroke in Long-Evans rats. Prior to surgery, the body weight and rectal temperature of the rat is measured, and the animal is then subjected to the MCAo via suture (75 min) under isofluorine anesthesia. Before drug delivery, these rats are pre-tested using behavior-testing (footfault, forelimb placing, circling, postural reflex and tail-forelimb pushing) 75 minutes after inserting the suture in order to ensure the animal indeed has had a stroke. The suture is then removed and drug delivery of the vehicle control (succinate buffer), glypromate, or caffeinol (10 mg/kg caffeine and 0.32 g/kg ethanol-positive control) is administered for 3 hours at 3 mg/kg/hr. After 72 hours, body weight, rectal temperature, behavior, and lesion volume via TTC staining of 27 male, Long-Evans rats (300-400 g) are measured. Due to unexpected hyperthermia in a number of our rats, this experiment was stalled in order to determine the cause of this problem which turned out to be due to heating of the animals during shipping, consequently, final results of these studies are still pending. To date 11 of the 27 animals have been analyzed.

ABSTRACT

Lipotoxicity in Failing Human Heart: Evidence for Triglyceride Accumulation in Diabetic and Obese Patients with Dilated Cardiomyopathy

JOHN LEMM *Rice University* *Class of 2004*

Sponsored by: Dr. Heinrich Taegtmeyer, MD, DPhil, Department of Cardiology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: lipotoxicity, heart failure, dilated cardiomyopathy, diabetes Mellitus Type 2

Lipotoxicity refers to the metabolic and functional consequences of deranged myocardial fatty acid metabolism. Recent studies have demonstrated that diabetes and obesity are associated with increased intramyocellular triglyceride accumulation (a marker of lipotoxicity), which may contribute to cardiac dysfunction. In order to evaluate the role of lipotoxicity in the diabetic and obese patients with dilated cardiomyopathy, we examined the clinical records and full-thickness myocardial biopsy samples of 27 patients with dilated cardiomyopathy referred to the Texas Heart Institute (n=10), and to the DeBakey Heart Center (n= 17) for heart transplantation, and compared them to three normal heart samples from accident victims. The patients' mean age was 59 years (range: 26-68). The mean ejection fraction was 19% (range: 10-28). The predominant co morbidity was diabetes mellitus type 2 (10 patients) and obesity (BMI > 30; 6 patients). The biopsy samples were prepared with Oil Red O stain for intramyocellular triglyceride deposits, after which digital microscopic photographs were taken for each slide. Geiss imaging software was then employed to provide relative counts of the Oil Red O staining in each sample. Among the patients with dilated cardiomyopathy and diabetes there is a 2.25 fold increase in intramyocellular triglyceride deposits ($p = 0.05$). Although there was a 1.5 fold increase in intramyocellular triglycerides among obese patients with dilated cardiomyopathy, the values were not statistically significant. Our results suggest that among diabetic or obese patients with dilated cardiomyopathy, lipotoxicity contributes to the pathogenesis of heart failure.

ABSTRACT

Role of RGS proteins in development of Dictyostelium Discoideum

BEATRISA LERMAN *University of Texas at Houston- Medical School* *Class of 2003*

Sponsored by: Dale Hereld, MD, PhD, Department of Microbiology and Molecular Genetics
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Dictyostelium Discoideum, G-proteins, RGS- proteins

Dictyostelium is a soil amoeba which feeds on bacteria. Upon starvation, up to 10^5 amoebae aggregate to form a multicellular organism and undergo cell differentiation and morphogenesis to form a fruiting body consisting of a mass of spores held up by a slender stalk.

G protein heterotrimers mediate a broad spectrum of physiological processes in eukaryotes. G protein-coupled receptors activate G proteins by catalyzing the exchange of bound GDP for GTP. On the other hand, Regulators of G protein Signaling, or RGS proteins, catalyze G protein inactivation. RGS proteins share a conserved ~120-amino acid RGS domain which binds directly to the activated Gα subunit, stimulates GTP hydrolysis, and returns the G protein to its inactive state.

Six RGS genes, containing seven RGS domains, have been identified in *Dictyostelium*'s genome. We took two approaches to determine their functions: overexpression of the RGS domains in *Dictyostelium* cells, and disruption of the genes. For overexpression, we constructed plasmids to express each RGS domain tagged with yellow fluorescent protein (YFP) and a Myc epitope for co-immunoprecipitation and detection by western blotting. We transformed the constructs into cells and confirmed expression of RGS1, RGS2, RGS3, RGS4C, and RGS6 by fluorescence microscopy and western blotting. RGS4N and RGS5 expression was undetectable. To assess the expressed proteins' effects on development, each cell line was starved and observed over a 24-hour period. Compared to wild type cells, RGS1, RGS4N, and RGS6 exhibited several possible developmental phenotype. However, more research must be done to reach confident conclusions about the role of RGS proteins in *Dictyostelium* development.

ABSTRACT

Design and Implementation of a Particle Image Selection Program

ANGIE LI *University of Texas at Austin* *Class of 2004*
Sponsored by: Z. Hong Zhou, Ph.D., Department of Pathology and Laboratory Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: electron cryomicroscopy; particle reconstruction; particle selection; high resolution

Electron cryomicroscopy (cryoEM) is an emerging technique in structural biology that is suitable for determining the structures of viruses and large molecular complexes in their native, non-crystalline forms. In cryoEM, images of macromolecules embedded in vitreous ice are recorded on photographic film and digitized using a high-resolution microdensitometer. Subsequently, individual particle images of interest are selected interactively from large cryoEM micrographs by using a graphical image selection program. However, many high resolution micrographs are more than 0.5 Gigabytes in file size, consuming a substantial portion of a modern computer's physical memory and causing applications to be sluggish or halt. The focus of my research was to design a user-friendly and interactive program with a graphical user interface for selecting individual particles from such large images that could be used for common platforms, such as Windows-based platforms. Using Borland C++ Builder, the particle image selection program was implemented with a trackbar to continuously adjust the zoom of an image and the ability to pan using mouse drags on the image within its window or through a separate navigation panel. For very large images, the user may interactively select any part of the entire image to load into memory by dragging over the image shown at a small size. These essential features will provide the image processor with an application that allows for convenient determination of structures. Further directions include an automatic particle image selection feature.

ABSTRACT

Fortilin inhibits p53 activity

BENJAMIN T. LI *The College of New Jersey* *Class of 2004*

Sponsored by: Kenichi Fujise, MD; Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: P53, fortilin, Bax, p21

P53 has been found to be an important tumor suppressor. It functions as a transcription factor for both Bax, a pro-apoptotic protein, and p21, a cell-cycle inhibitor protein. Another protein fortilin has been found to have an anti-apoptotic function and to suppress cell cycle progression in vascular smooth muscle cells. To determine whether fortilin's anti-p53 functions may be attributed to its binding to p53, thus inactivating p53 and decreasing the transcription of Bax and p21, a plasmid was constructed in which Bax and p21 genes are inserted adjacent to a luciferase gene. Transfection of cells with this plasmid followed by p53 induction via UV radiation will allow luciferase assay to be performed. If native fortilin in cells bind to p53, less Bax and p21 would be transcribed, thus decreasing luciferase expression.

ABSTRACT

The Effects of wt Rho B and NET1ΔN on EGFR Trafficking

JESSICA LIAO *University of Pennsylvania* *Class of 2005*

Sponsored by: Jeffrey A. Frost, PhD, Department of Integrative Biology and Pharmacology
Supported by: The University of Texas HSC at Houston-Medical School – Summer Research Program
Key Words: EGFR, RhoB, NET1ΔN, Endocytic Trafficking

Rho family proteins are small G-proteins that play a role in metastatic tumor formation. However, for tumor formation to occur, upstream regulators are needed. The oncogene NET1ΔN is an upstream regulator that activates Rho proteins by converting inactive Rho_{GDP} to activated Rho_{GTP}. RhoB, which is a member of the Rho family proteins, regulates the trafficking of cell surface receptors, such as Epidermal Growth Factor Receptor (EGFR). In EGFR trafficking, the ligand binds to the receptor and stimulates the internalization of the EGF-EGFR complex, which eventually sorts to lysosomes where it is degraded. The trafficking of the ligand-receptor complex to the lysosomes is slowed by the activated RhoB. Previous experiments have shown that NET1ΔN can activate RhoB *in vitro*; however, the effects of NET1ΔN *in vivo* have not been explored. To understand the effects of NET1ΔN on RhoB *in vivo*, HeLa cells were transfected with EGFR, EGFR+RhoB, or EGFR+NET1ΔN. The cells were stimulated with EGF for different periods of time, stained for the expression of the transfected proteins, and analyzed under a fluorescent microscope. These assays showed that the number of cells with EGFR localized on the plasma membrane was significantly higher in the cells transfected with NET1ΔN and RhoB. This suggests that NET1ΔN may have activated RhoB and caused a delay in receptor trafficking. Further quantification of EGFR protein levels by Western blotting demonstrated that the normal degradation of EGFR was decreased by expression of NET1ΔN or RhoB. These results indicate that NET1ΔN may control EGFR trafficking through RhoB.

ABSTRACT

The Effectiveness of Education as a Tool for Preventing Heart Disease

JAMES R. LLOYD *Rice University* *Class of 2006*

Sponsored by: Francisco Fuentes, MD, Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: heart disease, cardiovascular, prevention, education

Cardiovascular disease (CVD) is an epidemic that kills over 17 million people each year worldwide (World Heart Federation). Given that increased knowledge of cardiovascular disease risk factors has been linked to decreased cardiac mortality rates, this study was developed to measure the effectiveness of an educational tool aimed at reducing CVD risk factors in underserved populations.

For this study, a new program was developed that included an educational tool that provided a succinct and easily understood overview of the causes, risk factors, and risk reduction of CVD. A key feature of the educational tool was its ability to serve as a "general overview" thereby increasing its functionality, clarity, and organization.

Of 63 patients initially interviewed, 32 underwent a complete screening and were tested before and after studying the educational tool for their knowledge of CVD, including risk factor reduction. Patients who studied the materials showed a marked increase in knowledge of CVD. Eighty-eight percent of the patients tested increased their knowledge of CVD and how to lower the risk of CVD. Their knowledge of cholesterol increased dramatically with only 16% correctly identifying the types of cholesterol before studying the materials and 78% correctly after studying the materials.

Results of CVD Test (Before and After Educational Tool)

Type of Question	% Answered Correctly	
	Before	After
Death Rate of Heart Disease	25	63
Blood Pressure Levels	81	100
Types of Cholesterol (HDL vs. LDL)	16	78
Cardiopulmonary System	9	56
Normal Cholesterol Levels	75	81
Overall (Total Correct)	65.65	86

Based on the study results, the educational tool developed in our laboratory has a profound impact on patients' knowledge of CVD risk factors and can play an important role in reducing cardiovascular mortality.

ABSTRACT

Primary Failure of Eruption

MATT MAYER *Baylor University* *Class of 2005*

Sponsored by: Rena D'Souza, DDS, MS, PhD, Department of Orthodontics
Supported by: The University of Texas HSC at Houston–Dental School & Summer Research Program
Key Words: primary failure of eruption

This study proposes to collect and analyze data on individuals and/or families affected with primary failure of eruption (PFE) and to further design molecular tools that can be applied to studies aimed at elucidating the genetic basis of this disorder of dentition. Preliminary efforts have revealed that several cases of PFE are being currently treated in the local dental community. My fundamental hypothesis is that the molecular pathogenesis of PFE involves a basic defect in the dental follicle signaling of osteoclasts to form the eruptive pathway. The following aims will directly test the working hypothesis that PFE is an inheritable condition, affects both primary and permanent dentitions and occurs at a higher rate than previously reported in the general population.

Aim 1: To develop inclusion and exclusion criteria for a database of individuals/families affected with PFE.

Aim 2: To delineate by phenotypic and segregation analyses of affected individuals, whether PFE occurs as an isolated or familial condition.

Aim 3: To design the molecular probes against prime candidate genes that can be used for genetic analysis aimed at determining the pathogenesis of PFE.

The significance of this project is that PFE continues to be a challenge for dental professionals to diagnose properly. The treatment outcomes are generally inadequate, and the financial, emotional and esthetic burden for patients is phenomenal. Ultimately, knowledge about PFE and other syndromes associated with failure of eruption will lead to a greater understanding of normal tooth eruptive processes.

ABSTRACT

Quantitating Expression Levels of Wnt/Frizzled mRNA in Endometrium of Post-Menopausal Women Following Estrogen Replacement Therapy

CHRISTOPHER M. MCGRAW *Rice University* *Class of 2004*

Sponsored by: David Loose-Mitchell, PhD, Department of Integrated Biology and Pharmacology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: estrogen replacement therapy (ERT), frizzled, wnt, quantitative PCR (QPCR)

An interaction that is common to several developmental pathways in diverse organisms involves wnt signaling molecules activating frizzled membrane receptors to initiate a signal transduction pathway responsible for certain feats of cell-cell regulation. The role that wnts/frizzleds play in the normal functioning of adult tissue (if any) is currently unknown, however, it has been shown that certain secreted frizzled-related proteins (sFRPs), a wnt antagonist, demonstrate transcript up-regulation in the epithelial cells of the endometrium in post-menopausal women having undergone estrogen replacement therapy (ERT) with either Premarin or conjugated equilin and estrone (CEE). We proposed that wnts and frizzleds are important to the endocrinology and normal function of the adult

ABSTRACT

Bronchodilator Stimulated Phosphorylation of the Beta 2 Adrenergic Receptor

BENJAMIN M. MULLOY *The University of Texas at Austin* *Class of 2005*

Sponsored by: Richard Clark, PhD, Department of Integrative Biology and Pharmacology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: β_2 Adrenergic Receptor, GRK Desensitization, Formoterol, Salmeterol

Agonist activation of the β_2 Adrenergic Receptor (β_2AR) causes relaxation of tracheal smooth muscle and bronchodilation. Following activation, the β_2AR is desensitized by GRK and PKA mediated phosphorylation. Understanding the role of G-protein coupled receptor kinase (GRK) and protein kinase A (PKA) phosphorylation of the β_2AR in response to agonists used in the treatment of asthma and cardiovascular disease is important in treating and understanding the diseases. The purpose of this study was to determine the effects of chronic exposure of different β_2AR agonists on the phosphorylation of serines 355 and 356. The study used a human embryonic kidney cell line (HEK293) with an over expression of the β_2AR. The cells were grown to confluency and incubated with β_2AR agonist from 30 minutes to 24 hours. The agonists used were formoterol and salmeterol, two long-acting asthma drugs. As a control we also used epinephrine, whose half life for stimulation is very short. After treatments the cells were then lysed and the receptor was solubilized in detergent. The samples were run on a SDS-PAGE and transferred to a nitrocellulose membrane in preparation for a Western analysis. The β_2AR GRK site phosphorylation was quantitated by its reactivity with an anti-phosphoserine specific antibody against pS 355 and pS 356. Each of the bronchodilators showed an initial increase in GRK phosphorylation at the S355, S356 sites. However, after 30 minute treatment epinephrine and salmeterol both showed a gradual decrease in the phosphorylation of S355 and S356 from 4-24hrs treatment. Formoterol did not show a significant decrease in the phosphorylation of S355 and S356, although there was a shift in the major phosphorylation species from ≈ 48Kd to 46Kd. These data show a remarkable effect of formoterol to prolong GRK site phosphorylation. Determining the mechanism of this effect may help shed light on the clinical efficacy of this drug producing long-term bronchodilation.

ABSTRACT

Localization of GSK-3β in Hormonally-Treated Rat Brain Tissue

HARRY PAPASOZOMENOS *Rice University* *Class of 2006*

Sponsored by: Diane Bick, PhD, Department of Pathology and Laboratory Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Alzheimer's disease, GSK-3β, immunohistochemistry, testosterone

It has previously been shown that testosterone prevents the hyperphosphorylation of tau protein by inhibiting the overactivation of glycogen synthase kinase-3β (GSK-3β. Heat shock-induced hyperphosphorylation of tau protein is estrogen independent and similar to Alzheimer's disease. This investigation sought to examine the mechanism by which testosterone inhibits GSK-3β by studying the light and electron microscopic localizations of GSK-3 and other proteins so we could better understand how testosterone could be used in the preventative treatment of Alzheimer's disease. Forty-five ovariectomized Sprague-Dawley rats received daily injections of either 250 μg testosterone propionate (TP), 10 μg estradiol benzoate (EB), both, or sesame oil vehicle for three to seven weeks. Sham operated rats received sesame oil. Forebrain tissue, fixed by perfusion, was obtained either immediately following heat shock (42°C) or six hours later. The control rats were not heat shocked. TP and EB concentrations in blood serum obtained midcourse and just before perfusion were measured using the appropriate immunoassay kits. Vibratome brain sections were immunostained with nine different antibodies using the peroxidase-antiperoxidase technique in order to localize the desired proteins. Some of the antibodies used were against GSK-3β phosphorylated at Ser9 (inhibited) or Tyr216 (activated), heat shock proteins, HSTF-1, or activated protein kinase B. The sections were then prepared for both light and flat-embedding electron microscopy. Brain tissue samples from each heat-shocked group were also obtained in order to run SDS-PAGE immunoblotting and immunoprecipitation kinase assays. Evaluation of the tissue samples stained for light and electron microscopy is ongoing.

ABSTRACT

The Sensory Gating in Aplysia

HYUN PARK *The University of Texas at Austin* *Class of 2005*

Sponsored by: John Byrne, PhD, Department of Neurobiology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: sensory gating, *Aplysia,* B21

To generate adaptive behavior, all animals face the problem of integrating motivation, past experiences and the current sensory input. Due to its large neurons, the marine mollusc *Aplysia* lends itself to study of learning and memory, generation of behavior and sensory processing. The well-studied neural circuitry responsible for the generation of *Aplysia*'s feeding behavior is not only malleable to learning, it also exhibits sensory-motor integration at various levels. The mechanosensory neuron, B21, in *Aplysia* can transmit a sensory signal from the periphery if its soma is depolarized or block that signal if its soma is at the resting potential. The target neurons of B21 include crucial motor neurons. Thus, the neural mechanism affecting the membrane potential in B21 are important case study for the neurobiology of sensory motor integration and its relevance for the generation of adaptive behavior. To examine further the processing of sensory information by B21, a computational model was constructed using SNNAP (Simulator for Neural Networks and Action Potentials) based on electrophysiological data from B21. The gating mechanism was reproduced in this model, and, in the future, neighboring neuron B4/5 will be added for further investigation.

ABSTRACT

20S Proteasome Isolation

KIRAN PRAVIN PATEL *University of Alabama at Birmingham* *Class of 2006*
Sponsored by: Sudha Veeraraghavan, PhD, Biochemistry and Molecular Biology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: proteasome, angiogenesis

The proteasome is one of two major ways to recycle proteins in a cell. It is a multi-protein protease complex that digests proteins that have been marked for degradation. The proteasome is found in the cytosol and the nucleus; it is capable of unfolding and hydrolyzing most proteins. These properties make the proteasome a significant regulator of cell cycle and cell stress, in addition to other cellular functions. Recent studies show that proteasomes are important for angiogenesis, the process of creating blood vessels. Angiogenesis occurs by the stimulation of hypoxia-inducible factor (HIF-1α). HIF-1α regulates genes such as VEGF which are crucial in the development of new blood vessels. Proline and arginine rich peptides called PR39 and PR11 (a truncated form of PR39) inhibit the proteasome from degrading HIF-1α. This inhibition results in increased vascular growth. However, little is known about how PR11 binds to the proteasome complex and inhibits it. An understanding of the structural basis of PR11/PR39-proteasome interaction is quintessential to delineating this angiogenic pathway. Proteasome isolated from *Saccharomyces cerevesiae* using methodologies I established during the summer will be used to prepare crystals of proteasome-PR11 complex and used to obtain its three-dimensional structure by x-ray crystallography.

ABSTRACT

Gene Polymorphisms that Predispose to Infectious Diarrhea

LAUREN E. PATTERSON *Duke University* *Class of 2004*

Sponsored by: Philip C. Johnson, MD, Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
The Ragan Ryan Stipend
Key Words: travelers' diarrhea, genetic factors, pro-inflammatory cytokines,

The primary cause of travelers' diarrhea is enteric bacteria, which usually occurs through ingestion of contaminated food. Preliminary studies comparing infection rates of travelers' diarrhea suggest that genetic factors have a significant role in susceptibility and illness severity in response to infection. One hypothesis is that subjects with wild type genes for pro-inflammatory cytokines (such as IL-1β, IL-6, TNFα, IL-8), cytokine receptors and/or specific enteropathogen receptors (such as guanylate cyclase) are more likely to develop diarrhea than those with polymorphisms in these genes. To understand these mechanisms, a study commenced involving male and female subjects over sixteen years of age, traveling to Central and South America this summer as part of the Amigos de las Americas program. Blood samples were collected from each of the participants before departure to identify genetic markers of each subject. If the subject acquires travelers' diarrhea during their travels in Latin America, he or she will also send us a stool sample to be analyzed. The study will conclude at the end of the summer. To date, the number of subjects who sought medical attention for travelers' diarrhea is 3 of 44 subjects (6.81%). In prior studies approximately 11% of travelers' who acquire diarrhea see a physician. Therefore we can predict that around 27 of our subjects (61%) will have experienced travelers' diarrhea by the end of the summer. More conclusive data will be obtained once all samples and travel diaries have been received.

ABSTRACT

Cross-Sensitization to Amphetamine following Repeated Exposure to Methylphenidate in Female Spontaneously Hypertensive/Hyperactive Rat

ELIZABETH S. PIENKOS *Rice University* *Class of 2005*

Sponsored by: Nachum Dafny, PhD, Department of Neurobiology and Anatomy
Alan C. Swann, MD, Department of Psychiatry and Behavioral Sciences

Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program

Key Words: cross-sensitization, methylphenidate (Ritalin), amphetamine, drug addiction

Current research has shown that repeated use of psychostimulants such as cocaine, amphetamine, and methamphetamine results in behavioral sensitization. Behavioral sensitization refers to the progressive increase of behavioral response to a psychostimulant, which can be an indication of drug addiction. A related phenomenon is cross-sensitization, whereby repeated exposure to one psychostimulant produces sensitization to another, thus increasing its potential for addiction. Previous studies have revealed cross-sensitization with such psychostimulants as cocaine and amphetamine, but there is little literature regarding the role of psychostimulant methylphenidate (MPD, Ritalin®) in this phenomenon. The present study used two groups of female spontaneously hyperactive/hypertensive rat (SHR) to ascertain whether repeated exposure to MPD elicits cross-sensitization to amphetamine (Amph). Group I was pre-treated with MPD during adolescence and adulthood, and group II was treated with MPD only in adulthood. Each group consisted of 3 treatment subgroups so that rats received intraperitoneal injections of 0.6 (n=12) (low dose), 2.5 (n=12) (moderate dose), or 10.0 mg/kg MPD (n=12) (moderate to high dose) for 6 consecutive days as adults only or as youths and adults. An additional control group (n=12) received saline throughout the experiment. All rats were given 0.6 mg/kg Amph after the last day of MPD injection. Results revealed that groups receiving moderate and high doses, but not the lower dose, of MPD exhibited cross-sensitization to Amph. Furthermore, within the same dose, SHR pre-treated with MPD during adolescence displayed a more intense locomotor response to Amph than did SHR treated with MPD only during adulthood. This study showed that repeated administration of MPD can elicit cross-sensitization to Amph in rats and can be modulated by exposure to MPD during adolescence, which may have clinical significance in enhancing current understanding of the pharmacokinetic effects of MPD.

ABSTRACT

Physiologic FDG Uptake in the Atrial Appendage in a Patient Population: Potential Causes

JESSE M. PROETT *University of Houston* *Class of 2004*

Sponsored by: Bruce J. Barron, MD, MHA, Department of Radiology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: PET, FDG, atrial appendage

Positron Emission Tomography (PET) detects electron/positron annihilation events, where positrons come from the decay of ^{18}F nuclei in fluorodeoxyglucose (FDG). FDG acts much like glucose and collects in areas of high metabolic activity allowing us to image these active areas. Areas with considerable FDG uptake are the brain, kidney, bladder, and heart where the latter shows a great deal of variability. Many factors affect FDG uptake in the heart such as diet, glucose level, heart disease, or various cancer treatments. Occasionally we will see uptake in the right atrium, which could be mistaken as a metastasis in the mediastinum. The goal of this study is to document the appearance of the right atrial appendage.

Patients with known malignancies were injected with 15 to 20 mCi F-18-FDG intravenously and images were obtained approximately sixty minutes later. PET scans were reviewed by one of three nuclear medicine physicians and cardiac abnormalities were recorded.

Of ~490 patients only 18 showed significant evidence of an atrial appendage. 12/18 patients received some kind of radiation therapy. 4/12 that received radiation therapy had multiple PET scans before and after radiation therapy. All four cases showed no evidence of an atrial appendage until after radiation therapy.

Uptake in the atrial appendage is very rare and the fact that two thirds of the documented cases had received radiation therapy leads us to believe that there could be a possible connection. This finding should not be construed with malignancy.

ABSTRACT

Role of Somatostatin Receptor Phosphorylation in Desensitization

MADEEHA SAEED *Houston Baptist University* *Class of 2004*

Sponsored by: Agnes Schonbrunn, PhD, Department of Integrative Biology and Pharmacology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Somatostatin, ERK1, ERK2, SSTR2

Somatostatin (SST), a 14 amino acid peptide, signals via a family of G-protein coupled receptors (GPCR). There are five human somatostatin receptor (SSTR) subtypes, SSTR1-5. Effects of SST include modulation of hormone and exocrine secretion, neurotransmission, smooth muscle contraction, cell proliferation, and inhibition of hormone responsive tumors. GPCRs are known to regulate their responsiveness through desensitization. The G-proteins linked to the SSTR activate multiple pathways upon ligand binding in various cell types. One of the pathways leads to activation of Mitogen-Activated Protein Kinases (MAP kinases) which are a superfamily of proline-targeted serine/threonine kinases. The MAP kinase superfamily includes extracellularly regulated kinase 1 (ERK1) and ERK 2. In the SSTR2 subtype, the cytoplasmic serine and threonine residues serve as phosphorylation sites that are hypothesized to lead to agonist-induced desensitization when phosphorylated. The purpose of our study was to determine the requirement for receptor phosphorylation in SSTR2 desensitization by measuring the duration of ERK1 and ERK2 activation after SST treatment. For this experiment, both wild type receptor and a phosphorylation-defective mutant receptor (serine and threonine residues in the intracellular loop 3 and carboxyl terminus converted to alanines) were generated and over expressed in CHO-K1 cells. The time course after somatostatin stimulation of the wild type SSTR2 showed a peak in ERK1/2 activation at 10 minutes and a quick decrease to background activity thereafter. In contrast, the phosphorylation-defective mutant receptor, showed sustained ERK1/2 activation well beyond the 10-minute time point following stimulation with 100 nM SST. This finding indicates that SSTR2 phosphorylation upon ligand binding is required for desensitization.

ABSTRACT

Deletional Analysis of the Regulatory Region of the Protective Antigen Gene in *Bacillus anthracis*

AARON L. SCHNELL University of Texas – Austin Class of 2004

Sponsored by: Theresa M. Koehler, PhD, Department of Microbiology and Molecular Genetics
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Bacillus anthracis, toxin, regulation

Bacillus anthracis, the causative agent of anthrax, secretes a tripartite toxin comprised of protective antigen (PA), lethal factor, and edema factor. Protective antigen (PA) is an antigenic protein that confers immunity against anthrax. PA is the major component of the human vaccine for anthrax (AVA). AVA is derived from *B. anthracis* culture supernates. It has been shown previously that several factors affect transcription the PA gene (*pagA*): (1) expression is highest during growth in elevated CO_2 (5% or greater), (2) a *trans*-acting regulator *atxA* is required for transcription from the major promoter, and (3) *pagA* is co-transcribed with and weakly repressed by *pagR*, an autogenous regulator of the *pag* operon. The purpose of this study was to determine the minimal upstream region required for *pagA* transcription. Varying lengths of the DNA region upstream of the *pagA* coding sequence were cloned into a vector in order to make transcriptional fusions to the β-galactosidase gene l*acZ*. The constructs were electroporated into *B. anthracis*. Strains were grown in appropriate media in a 5% CO_2 atmosphere and assayed for β-galactosidase activity. A clone harboring 100 nucleotides upstream of the major *pagA* transcription start site produced high levels of enzymatic activity. Reporter gene expression was 50- to 80-fold lower in a clone harboring only 77 nucleotides upstream of the transcription start site. The findings suggest that nucleotides between -100 and -77, relative to the major transcriptional start site, are required for high level *pagA* expression.

ABSTRACT

Chronic Hypoxia Induced Trophic Adaptation and Gene Expression Changes of the Right Ventricle

SHIRAJ SEN *The University of Texas at Austin* *Class of 2005*

Sponsored by: Heinrich Taegtmeyer, M.D., D.Phil., Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: PPARα, MHC iso-genes, hypoxia, quantitative RT-PCR

Background: Recently, acute hypoxia studies have revealed a short-term switch in energy substrate utilization from fatty acid to glucose as well as a switch in myosin heavy chain iso-gene expression in the heart. However, the transcriptional response to chronic hypoxia remains unknown.
Methods: Male Wistar rats were subjected to hypobaric hypoxia (11% oxygen) for time periods of one and two weeks and their total RNA was isolated from right ventricular cardiac tissue thereafter. Real-time quantitative PCR was then used to measure transcript levels of adult isoform myosin heavy chain α (MHCα), fetal isoform myosin heavy chain β (MHCβ), sarco endoplasmic reticulum calcium ATPase (SERCA 2a) , peroxisome proliferator-activated receptor α (PPARα), and PPARα-regulated genes such as pyruvate dehydrogenase kinase 4 (PDK4) and medium chain acyl-CoA dehydrogenase (MCAD).
Results: At one week, chronic hypoxia induced a 54 % increase of right ventriclular to left ventriclular weight. Hematocrit levels increased from 47.16 ± .34 % at baseline to 67.4 ± 0.69 % at one week and 73.4 ± 1.24 % at two weeks. In the right ventricle, transcript levels of PPARα and PPARα-regulated genes (e.g. MCAD) were downregulated at one week of hypoxia. MHCβ was also downregulated while MHCα and SERCA 2A did not change. Interestingly, at two weeks of hypoxia, PPARα and PPARα-regulated genes were upregulated in the right ventricle. Similarly, MHCα , MHCβ, and SERCA 2A had upregulated gene expression as well.
Conclusion: These findings suggest that chronic hypoxia induces a fluctuating transcriptional profile. We speculate that the observed changes in gene expression over time stem from a complex interaction between compensatory mechanisms that restore normoxia and trophic adaptations of the right ventricle in response to pressure overload.

ABSTRACT

Development of a Bacterial Two-Hybrid System Using GFP to Detect Protein-Protein Interaction in *Rhodobacter sphaeroides* 2.4.1

JENNIFER L. SHERRILL *University of Texas at Austin* *Class of 2003*

Sponsored by: Samuel Kaplan, PhD, Department of Microbiology and Molecular Genetics
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: *Rhodobacter sphaeroides,* fluorescence, GFP, protein fusion

In order to detect protein-protein interactions in the Gram-negative bacterium *Rhodobacter sphaeroides*, a bacterial two-hybrid system was constructed using the *Bacillus subtilis* protein DivIVA and the Green Fluorescent Protein (GFP) from *Aequorea victoria*, cloned in two different vectors. DivIVA localizes to the poles of *Escherichia coli* and other Gram-negative bacteria during cell division and remains at the poles after the completion of division. Due to the natural fluorescence of GFP, a DivIVA::GFP protein fusion allows visualization of DivIVA localization. The *divIVA*-containing construct has an insert composed of the downstream region of the *R. sphaeroides' pucBA* operon, encoding the B800-850 light-harvesting complex, from plasmid pJE389; *divIVA* lacking the stop codon, from plasmid pZD6, and a Multiple Cloning Site (MCS) in three reading frames, from plasmid pUI1156, created by combinatorial PCR. The insert was cloned into the pRK415 vector in both orientations. DNA sequencing confirmed the desired structure of the *pucdivIVA*MCS fragment. Similarly, GFP was cloned into a compatible plasmid with an option for amino- or carboxy-terminal fusions. Application of this two-hybrid system is intended to detect protein interactions by fusing a desired protein to GFP and a potential protein target of interaction to DivIVA, *or vice versa*. After conjugation of both compatible plasmids into *R. sphaeroides*, if an interaction occurs between the protein fused to GFP and the protein fused to DivIVA, the GFP-DivIVA fusion complex is expected to be taken to the cellular poles and fluorescence will reveal bipolar localization.

ABSTRACT

Report of a Preliminary Study on the Effects of a Quality Management Intervention for the Treatment of Community-Acquired Pneumonia (CAP) on the Interval from Triage Time to Antibiotic Administration (ABx) and Rate of Blood Culture (BC) Collection Before Antibiotic Administration

JESSICA CHAO-YING TSAI *The University of Texas at Austin* *Class of 2006*

Sponsored by: Richard N. Bradley; MD; Department of Emergency Medicine.
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: community-acquired pneumonia, antibiotic, blood cultures.

CAP (Community-Acquired Pneumonia) affects about 3 million people/year in the US and is responsible for 45,000 deaths. It is the leading infectious cause of mortality and the sixth most common cause of mortality in the US, and one of the most common reasons for adult hospitalization (25% of the diagnosed cases require hospitalization). A decrease in the interval from the time the patient arrives to the ED (Emergency Department) to ABx results in shorter length of stay, lower mortality, and less cost. In preparation for a before-and-after, interventional study on the interval from triage time to ABx and rate of BC collection before ABx, we conducted a CPHS-approved, retrospective study prior to research. Our study questions were: 1) What was the mean interval from triage time to ABx? 2) What percentage of the intervals were under 191 minutes? 3) What was the rate at which BC were obtained before ABx? Our preliminary research consisted in reviewing all adult ED with a diagnosis of CAP from June 2002. There were 25 patients diagnosed with CAP; we were able to locate 21 of their charts, but three of these were missing essential data. The median interval from triage time to ABx was 677 minutes with a 95% CI of 402 – 858 minutes. The interval was < 191 minutes in 0 of 19 cases. Fourteen of 19 cases (74%) had BC obtained before ABx, which is below our goal of 88%. We need to conduct a quality management intervention study for the treatment of CAP in the ED.

ABSTRACT

CAT Expression after GRP78-CAT Transfection in Rat Adenocarcinoma Cells

ANITA UDAYAMURTHY *The University of Texas at Austin* *Class of 2005*

Sponsored by: Joan M. C. Bull, MD, Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: glucose response proteins, hyperthermia, gene therapy, MTLn3 mammary tumor cell line

Glucose Response Proteins (GRPs) are induced by glucose starvation. Malignant tumors characteristically are glucose deprived. A plasmid with a GRP promoter can target tumor cells for gene therapy. Fever-range whole body hyperthermia (heat, 40°C, 6h) is used for cancer treatment: it evokes the body's immune system to fight off foreign or abnormal conditions and increases blood flow to the tumor. Tumor cells transfected with a plasmid containing a GRP promoter and exposed to heat and glucose starvation stress should show a greater expression of the plasmid than cells not exposed to stress.

GRP78-CAT, a plasmid containing a GRP promoter and the bacterial reporter gene chloramphenicol acetyltransferase (CAT) protein, was purified, then transfected (using Fugene 6) into rat mammary adenocarcinoma (MTLn3) cells *in vitro.* Two experiments were conducted with the transfected cells to determine the effect of glucose starvation and heat on CAT expression. CAT expression was measured using a CAT-ELISA.

MTLn3 cells were grown in α-MEM and transfected with GRP78-CAT. Half the samples were exposed to glucose starvation (using RPMI 1640 media without glucose). Although not statistically significant, compared to cells cultured with media containing glucose, cells exposed to glucose starvation and harvested one day post-transfection showed a mean 18.5% increase in the amount of CAT expression where as cells exposed to glucose starvation and harvested two days post-transfection showed a mean 24% decrease in CAT expression.

A second experiment involved MTLn3 cells that were exposed to glucose starvation and heat either before, during, or after transfection. Unexpectedly, there was no increase in CAT expression in cells exposed to glucose starvation as opposed to cells grown in media with glucose (α-MEM or RPMI 1640 media with glucose), regardless of heat timing. Additional studies will be important to determine why CAT expression did not increase during glucose-starved conditions.

ABSTRACT

Genetic Susceptibility to Diabetic Nephropathy

SARAH A. UDDEEN *The University of Texas at Austin* *Class of 2005*

Sponsored by: S.N. Rahman, MD, FACP, Department of Internal Medicine
Supported by: The University of Texas HSC at Houston- Medical School – Summer Research Program
Key Words: ESRD, Diabetic Nephropathy, Diabetes Mellitus

Diabetic Nephropathy (DN) leading to End Stage Renal Disease (ESRD) is a multi-factorial disease that occurs in 1/3rd of patients with diabetes mellitus (DM). The incidence of DM leading to ESRD is increasing at a rate of 7-9% per year in the USA, with an annual mortality of 20-25%. DM and ESRD cluster in families. Familial aggregation is a powerful predictor of whether an individual with DM will develop ESRD. The purpose of this trial is to find the gene which may cause DM and ESRD. In this trial, affected relative pairs concordant for DM and ESRD are recruited from various dialysis centers. Extensive family and medical histories are obtained from each patient and their first degree affected relatives. Blood is collected for DNA extraction from the lymphocytes and immortalized lymphoblast cell lines. Candidate genes and other markers are genotyped. Participants' confidentiality is protected. Data will be analyzed by current genetic and statistical methods at Case Western Reserve University in Ohio. We are recruiting patients and hope to complete the trial in next 12 to 24 months. We expect that this study will aid in predicting risk for ESRD in families with DM. There is no benefit to the ESRD patients; however, the study may help anticipate which patients with DM need to be closely monitored for development of ESRD. This will benefit individuals at risk who can utilize therapeutic interventions to anticipate or alleviate disease at an earlier stage.

ABSTRACT

Inhibition of Allergen Induced Cell Proliferation by Omalizumab

SHEETAL WADERA *Texas A&M University* *Class of 2006*

Sponsored by: Gailen D. Marshall, Jr., MD, PhD, Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Monoclonal anti-IgE antibody, omalizumab, allergen

Allergic reactions, caused by the production of allergen-specific IgE and the body's inability to distinguish between innocuous and harmful stimuli, create an imbalance in cell mediated vs. humoral immune responses. The humoral arm of the immune system, composed of T helper cells and B cells, is responsible for the symptoms seen during allergic reactions by production of TH2 cytokines which influence the production of IgE, the allergy antibody. We wanted to further study the role of T lymphocytes in allergy to determine the effect of a humanized monoclonal anti-IgE antibody (omalizumab) upon allergic disease. Omalizumab (OMA) binds to free IgE thereby blocking the sites normally responsive to allergens, hindering the allergic response. The primary objective was to establish an in vitro model to demonstrate the effect of omalizumab on inhibiting allergen-induced cell proliferation of human T cells. Blastogenesis was performed in 10% autologous serum and 10% HAB serum with a suboptimal dose of dust mite allergen (der P1) and varying concentrations of omalizumab. Results demonstrated a difference in proliferation depending upon the type of serum present. At the 0.1 μg/ml dose in 10% autologous serum, the median values (percent control) increased – (OMA50: 159.08, OMA5: 140.84, OMA0.5: 123.32, p=.0017 by Friedman's test). In contrast, median values in autologous serum decreased (OMA50: 108.9, OMA5: 98.9, OMA0.5 83.6, $p<.05$). The 0.5mg dose corresponds to that used clinically. These data suggest a role for OMA that involves inhibition of T cell proliferation by autologous IgE-mediated allergen presentation.

ABSTRACT

The Role of 53BP1 in the DNA Damage-Response Network

BENJAMIN A. WILSON *Texas A&M University* *Class of 2003*

Sponsored by: Phillip B. Carpenter, PhD, Department of Biochemistry and Molecular Biology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: 53BP1, double-stranded DNA breaks, cell surface marker

p53-binding protein 1 (53BP1) is phosphorylated in response to DNA damage. It has been shown to interact with various factors implicated in maintaining genomic stability, such as ATR, p53, H2AX, BRCA1, and Chk2. 53BP1-deficient mice (*m53BP1*$^{tr/tr}$) display growth retardation, impeded B and T cell development, and hypersensitivity to ionized radiation (γ-IR). This hypersensitivity to γ-IR is characteristic of mice with defects in double-stranded break repair. To further investigate the role of 53BP1 in double-stranded break repair we employed Pulsed Field Gel Electrophoresis. If 53BP1 is involved in double-stranded break repair then genomic DNA from *m53BP1*$^{tr/tr}$ will be more fragmented than that of its wild-type counterpart upon exposure to γ-IR and will therefore migrate further into the agarose gel. In performing this experiment we treated wild type and *53BP1*$^{tr/tr}$ cells with varying amounts of γ-IR and allowed them to recover and repair their DNA for varying amounts of time. As a part of its role in double-stranded break repair 53BP1 assists in B cell development. Through the use of flow cytometry we detected fewer B cells in a mutant sample, as shown by the relative levels of cells displaying the B220 cell surface marker. Additionally, mutant B cells of a certain age remained in the pro-B stage of development longer and therefore did not display the IgM surface marker nearly as frequently as wild-type cells of the same age. This could suggest a role of 53BP1 in V(D)J recombination, a process requiring double-stranded break repair.

ABSTRACT

PEP-19 modulates specifically the C- Domain of Calmodulin

JOHN Y. WON *Columbia University* *Class of 2006*

Sponsored by: John Putkey, PhD, Department of Biochemistry and Molecular Biology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: Calmodulin, dissociation and association rate, C- domain, PEP-19

Calmodulin (CaM) is a signal transducer that mediates a great range of cellular functions. The mechanism behind CaM is that free CaM binds with Ca^{2+} forming Ca^{2+}/CaM which then binds to target proteins. CaM consists of an N- and C- domain with two Ca^{2+} binding sites in each domain. This laboratory recently discovered that a small neuronal protein, PEP-19, greatly accelerates the rates of association and dissociation of Ca^{2+} at the C-domain of CaM by 40-50 fold. PEP-19 alters the Ca^{2+} binding properties on the isolated C-domain affecting both the association and dissociation rates. There are two potential structural mechanisms for this effect. The PEP-19 may bind only to the C-domain independently or it may bind to both the N- and the C-domains, but affect Ca^{2+} binding only to the C- domain. To distinguish between these mechanisms, we first expressed and isolated recombinant C-domain of CaM (amino acid 77-148). Then we measured the effect of PEP-19 on the rates of Ca^{2+} association and dissociation to the C-domain using stopped-flow fluorescence. Quinn-2, a calcium sensitive dye, was used to measure dissociation of Ca^{2+} from CaM and intrinsic tyrosine was used to measure the Ca^{2+} association rate. The results show that both the association rate and the dissociation rates increased by 40-50 fold similar to that of the intact CaM with both the N- and C-domain. This proves that PEP-19 is a modulator exclusively to the C-domain on CaM and can function without the N-domain. The isolated C-domain provides a useful model system for structural characteristics of PEP-19/CaM interactions.

ABSTRACT

Screening for Scattered Kinetochore Mutants in Fission Yeast

KELLY S. WU *Cornell University* *Class of 2005*

Sponsored by: Xiangwei He, PhD, Department of Biochemistry and Molecular Biology
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: ski mutants, kinetochore, spindle

During mitosis spindle microtubules instigate the separation of sister chromatids by attaching to the kinetochore of each chromosome. The interaction between kinetochores and spindle microtubules is believe to play a key role in the regulation of chromosome segregation. In order to better understand this mitotic process, fission yeast, Schizosacchromyces pombe, were screened for a specific type of mutation in which kinetochores show mis-localization. The scattered kinetochore (ski) mutants display a disturbance between the interaction of the spindle and kinetochore. An initial screening produced twelve thousand temperature sensitive mutants, which were subsequently screened for mutants of the ski phenotype. In total twelve ski mutants were isolated. Genetic analyses are currently being performed to reveal the nature of mutations responsible for producing this phenotype. Furthermore, library transformations will aide in the discovery of the mutated gene. The identification of mutated proteins will facilitate the search for specific proteins involved in preserving the spindle/kinetochore interface.

ABSTRACT

In Search of $GABA_A$

SESSUNU ZEMO *The University of Texas at Houston – Medical School* *Class of 2004*

Sponsored by: Donald Molony; MD; Department of Internal Medicine
Supported by: The University of Texas HSC at Houston–Medical School - Summer Research Program
Key Words: ST-1 cells, MDCK cells, $GABA_A$

Known antagonists to the $GABA_A$-Cl^- ionophore complex of the CNS cause apoptosis and functional impairment in the medullary thick ascending limb (mTAL) of the mammalian kidney. This apoptosis can also be demonstrated in ST-1 cells of mTAL origin, but not in MDCK cells of the proximal tubular origin. We hypothesize that apoptosis of ST-1 cells is mediated by a specific inhibition of a $GABA_A$-Cl^- like channel in the mTAL. The presence of the protein for a $GABA_A$-Cl^- channel, however, has not been demonstrated in the mTAL. The purpose of these experiments is to confirm the presence of a $GABA_A$ channel protein. Western blots were performed on cell membranes of ST-1 and MDCK cells. A titration of the 1^o anti-$GABA_A$ antibody and 2^o anti-rabbit antibody demonstrated that the optimal experimental concentrations are 1: 1,000 and 1: 25,000 respectively. Dog brain membranes served as the control source of $GABA_A$ protein. 65ug of membranes from ST-1 and MDCK cells, and 312.5ug of dog brain membranes were loaded into the wells of the gel. The gel was transferred over night onto a membrane, which was exposed to the 1^o anti-$GABA_A$ antibody and 2^o anti-rabbit antibody. Development of the Western blot by ECL, indicates that $GABA_A$ is present in ST-1 cells and not as abundant or may be absent from MDCK cells. These results support the hypothesis that specific inhibition of a $GABA_A$ Cl^- channel in the mTAL may lead to the apoptosis seen with GABA antagonists.

Faculty Mentors

Mentor	Page	Degree	Department
Actor,Jeffrey	15	Ph.D.	*Pathology*
Ali, Asra	14, 27	M.D.	*Dermatology*
Ambrose, Catherine	18, 46, 77	Ph.D.	*Orthopaedics*
Anderson, Kimberly	51	Ph.D.	*Surgery*
Barnett, Ben	65	M.D.	*Internal Medicine*
Barron, Bruce	42, 106	M.D.	*Radiology*
Bean, Andrew	82	Ph.D.	*Neurobiology*
Bick, Diane	38, 72, 101	Ph.D.	*Pathology*
Blackburn, Michael	78	Ph.D.	*Biochemistry*
Bradley, Richard	20, 90, 111	M.D.	*Emergency Medicine*
Bull, Joan	112	M.D.	*Internal Medicine*
Byrne, John	102	Ph.D.	*Neurobiology*
Carpenter, Philip	115	Ph.D.	*Biochemistry*
Carter-Dawson, Louvenia	57	Ph.D.	*Ophthalmology*
Cheung, Kim	84	M.D., Ph.D.	*Pediatrics*
Clark, Richard	100	Ph.D.	*Integrative Biology*
Clyburn, Terry	9	M.D.	*Orthopaedics*
Cox, Charles	41	M.D.	*Surgery*
D'Souza, Rena	98	Ph.D.	*Dental School*
Dafny, Nachum	89, 105	Ph.D.	*Neurobiology*
Dial, Elizabeth	86	Ph.D.	*Integrative Biology*
Doursout, Marie-Francoise	22	Ph.D.	*Anesthesiology*
DuPont, Herbert	17	M.D.	*Internal Medicine*
Duvic, Madeleine	34	M.D.	*Dermatology*
Eissa, Mona	24	M.D., Ph.D.	*Pediatrics*
Feldman, Robert	32	M.D.	*Ophthalmology*
Frost, Jeffrey	96	Ph.D.	*Integrative Biology*
Fuentes, Francisco	79, 97	M.D.	*Internal Medicine*
Fujise, Ken	95	M.D.	*Internal Medicine*
Geng, Yong	10, 28	M.D., Ph.D.	*Internal Medicine*
Gray, Lincoln	76	Ph.D.	*Neurobiology*
Grill, Raymond	40	Ph.D.	*Neurosurgery*
Groff, Janet	45	M.D., Ph.D.	*Family Practice*
Grotta, James	91	M.D.	*Neurology*
Hagberg, Carin	88	M.D.	*Anesthesiology*
He, Xiangwei	117	Ph.D.	*Biochemistry*
Hereld, Dale	93	M.D., Ph.D.	*Microbiology*
Jayaraman, Vasanthi	64	Ph.D.	*Integrative Biology*
Johnson, Philip	104	M.D.	*Internal Medicine*
Kao, Lillian	33	M.D.	*Surgery*

Mentor	Page	Degree	Department
Kaplan, Heidi	30, 83	Ph.D.	*Microbiology*
Kaplan, Samuel	67, 110	Ph.D.	*Microbiology*
Kiebzak, Gary	35	Ph.D.	*Orthopaedics*
Koehler, Theresa	108	Ph.D.	*Microbiology*
Koerner, Christine	31	M.D.	*Emergency Medicine*
Kozar, Rosemary	49, 53, 54	M.D., Ph.D.	*Surgery*
Kulkarni, Anil	47	Ph.D.	*Surgery*
Lamki, Lamk	26	M.D.	*Radiology*
Lichtenberger, Lenard	63	Ph.D.	*Integrative Biology*
Loose, David	99	Ph.D.	*Integrative Biology*
Loveland, Katherine	87	Ph.D.	*Psychiatry*
Maloney, Donald	118	M.D.	*Internal Medicine*
Marshall, Gailen	114	M.D., Ph.D.	*Internal Medicine*
Mayes, Maureen	61	M.D.	*Internal Medicine*
McDonald, Glenn	11, 19, 21	M.D.	*Internal Medicine*
McKinley, Bruce	12, 25	Ph.D.	*Surgery*
McMillin, Jeanie	71	Ph.D.	*Pathology*
Milewicz, Dianna	66	M.D., Ph.D.	*Internal Medicine*
Miller, Charles	13	Ph.D.	*Cardiothoracic & Vascular Surgery*
Moody, Frank	69, 74	M.D.	*Surgery*
Morano, Kevin	75	Ph.D.	*Microbiology*
Mullani, Nizar	58	B.S.	*Internal Medicine*
Murad, Ferid	59	M.D., Ph.D.	*Integrative Biology*
Narayana, Ponnada	81	Ph.D.	*Radiology*
Norris, Steven	80	Ph.D.	*Pathology*
Northrup, Hope	50	M.D.	*Pediatrics*
Patrick, Charles	44	Ph.D.	*Plastic Surgery*
Penczek, Pawel	85	Ph.D.	*Biochemistry*
Phelps, Cynthia	68	Ph.D.	*School/Health Information Sciences*
Porat, Eyal	36	M.D.	*Cardiothoracic & Vascular Surgery*
Putkey, John	116	Ph.D.	*Biochemistry*
Rahman, S.N.	113	M.D.	*Internal Medicine*
Schonbrunn, Agnes	107	Ph.D.	*Integrative Biology*
Scott, Allison	16, 37	M.D.	*Orthopaedics*
Sereno, Anne B.	70	Ph.D.	*Neurobiology*
Smith, Kevin	29	M.D.	*Otolaryngology*
Steinberg, Joel	43	Ph.D.	*Psychiatry*
Swann, Alan	62	M.D.	*Psychiatry*
Taegtmeyer, Heinrich	52, 92, 109	M.D., D.Phil	*Internal Medicine*
Veeraraghavan, Sudha	103	Ph.D.	*Biochemistry*
West, O. Clark	48	M.D.	*Radiology*
Wojner, Anne	39	Ph.D.	*Neurology*
Wright, Anthony	73	Ph.D.	*Neurobiology*
Yee, Richard	23	M.D.	*Ophthalmology*
Zhou, Z. Hong	60, 94	Ph.D.	*Pathology*

Departments & Faculty Mentors

Department	Mentor	*Degree*
Anesthesiology	Doursout, Marie-Francoise	Ph.D.
Anesthesiology	Hagberg, Carin	M.D.
Biochemistry	Blackburn, Michael	Ph.D.
Biochemistry	Carpenter, Philip	Ph.D.
Biochemistry	He, Xiangwei	Ph.D.
Biochemistry	Penczek, Pawel	Ph.D.
Biochemistry	Putkey, John	Ph.D.
Biochemistry	Veeraraghavan, Sudha	Ph.D.
Cardiothoracic & Vascular Surgery	Miller, Charles	Ph.D.
Cardiothoracic & Vascular Surgery	Porat, Eyal	M.D.
Dental School	D'Souza, Rena	Ph.D.
Dermatology	Ali, Asra	M.D.
Dermatology	Duvic, Madeleine	M.D.
Emergency Medicine	Bradley, Richard	M.D.
Emergency Medicine	Koerner, Christine	M.D.
Family Practice	Groff, Janet	M.D., Ph.D.
Integrative Biology	Clark, Richard	Ph.D.
Integrative Biology	Dial, Elizabeth	Ph.D.
Integrative Biology	Frost, Jeffrey	Ph.D.
Integrative Biology	Jayaraman, Vasanthi	Ph.D.
Integrative Biology	Lichtenberger, Lenard	Ph.D.
Integrative Biology	Loose, David	Ph.D.
Integrative Biology	Murad, Ferid	M.D., Ph.D.
Integrative Biology	Schonbrunn, Agnes	Ph.D.
Internal Medicine	Barnett, Ben	M.D.
Internal Medicine	Bull, Joan	M.D.
Internal Medicine	DuPont, Herbert	M.D.
Internal Medicine	Fuentes, Francisco	M.D.
Internal Medicine	Fujise, Ken	M.D.
Internal Medicine	Geng, Yong	M.D., Ph.D.
Internal Medicine	Johnson, Philip	M.D.
Internal Medicine	Maloney, Donald	M.D.
Internal Medicine	Marshall, Gailen	M.D., Ph.D.
Internal Medicine	Mayes, Maureen	M.D.
Internal Medicine	McDonald, Glenn	M.D.
Internal Medicine	Milewicz, Dianna	M.D., Ph.D.
Internal Medicine	Mullani, Nizar	B.S.
Internal Medicine	Rahman, S.N.	M.D.
Internal Medicine	Taegtmeyer, Heinrich	M.D., D. Phil
Microbiology	Hereld, Dale	M.D., Ph.D.
Microbiology	Kaplan, Heidi	Ph.D.

Department	Mentor	*Degree*
Microbiology	Kaplan, Samuel	Ph.D.
Microbiology	Koehler, Theresa	Ph.D.
Microbiology	Morano, Kevin	Ph.D.
Neurobiology	Bean, Andrew	Ph.D.
Neurobiology	Byrne, John	Ph.D.
Neurobiology	Dafny, Nachum	Ph.D.
Neurobiology	Gray, Lincoln	Ph.D.
Neurobiology	Sereno, Anne B.	Ph.D.
Neurobiology	Wright, Anthony	Ph.D.
Neurology	Grotta, James	M.D.
Neurology	Wojner, Anne	Ph.D.
Neurosurgery	Grill, Raymond	Ph.D.
Ophthalmology	Carter-Dawson, Louvenia	Ph.D.
Ophthalmology	Feldman, Robert	M.D.
Ophthalmology	Yee, Richard	M.D.
Orthopaedics	Ambrose, Catherine	Ph.D.
Orthopaedics	Clyburn, Terry	M.D.
Orthopaedics	Kiebzak, Gary	Ph.D.
Orthopaedics	Scott, Allison	M.D.
Otolaryngology	Smith, Kevin	M.D.
Pathology	Actor,Jeffrey	Ph.D.
Pathology	Bick, Diane	Ph.D.
Pathology	Hickson-Bick, Diane	Ph.D.
Pathology	McMillin, Jeanie	Ph.D.
Pathology	Norris, Steven	Ph.D.
Pathology	Zhou, Z. Hong	Ph.D.
Pediatrics	Cheung, Kim	M.D., Ph.D.
Pediatrics	Eissa, Mona	M.D., Ph.D.
Pediatrics	Northrup, Hope	M.D.
Plastic Surgery	Patrick, Charles	Ph.D.
Psychiatry	Carranza, Jose	M.D.
Psychiatry	Loveland, Katherine	Ph.D.
Psychiatry	Swann, Alan	M.D.
Radiology	Barron, Bruce	M.D.
Radiology	Lamki, Lamk	M.D.
Radiology	Narayana, Ponnada	Ph.D.
Radiology	West, O. Clark	M.D.
School of Health Information Science	Phelps, Cynthia	Ph.D.
Surgery	Anderson, Kimberly	Ph.D.
Surgery	Cox, Charles	M.D.
Surgery	Kao, Lillian	M.D.
Surgery	Kozar, Rosemary	M.D., Ph.D.
Surgery	Kulkarni, Anil	Ph.D.
Surgery	McKinley, Bruce	Ph.D.
Surgery	Moody, Frank	M.D.

2003 Summer Research Program undergraduate participants