



UTHealth™

Medical School

**The University of Texas
Health Science Center at Houston**



**2011 SUMMER RESEARCH PROGRAM
STUDENT ABSTRACTS**

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Preface

The University of Texas Medical School at Houston (UTMSH) Summer Research Program provides intensive, hands-on laboratory research training for MS-1 medical students and undergraduate college students under the direct supervision of experienced faculty researchers and educators. 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 conducted by the students.

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 analysis, interpreting data and summarizing results. The results are presented as an abstract and are written in the trainees' own words that convey an impressive degree of understanding of the complex projects in which they were involved.

To date, nearly 1,800 medical, college, and international medical students have gained research experience through the UTMSH 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.

UTMSH student research training is supported by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Neurological Disorders and Stroke (NINDS), and/or by financial support from the Dean and the departments and faculty of the medical school.

Biomedical science education remains a vital and integral part of our nation's interests. The UTMSH Summer Research Program, and the dedication of our faculty and administration exemplify the institution's commitment to training and educating the future leaders in our biomedical scientific communities.



Gary C. Rosenfeld, Ph.D.

Director, Summer Research Program
Assistant Dean for Educational Programs

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Acknowledgements

This publication marks the completion of the twenty-fifth year of The University of Texas Medical School at Houston (UTMSH) 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 the medical school.

Indicative of this support is the administrative assistance and financial support for the Program's college and medical students provided by UTMSH. Sincere appreciation is expressed to Dean Giuseppe Colasurdo M.D. and Patricia M. Butler, M.D., Associate Dean, Office of Educational Programs who continue to ensure the yearly success of the Summer Research Program.

Major financial assistance for medical students has also been provided through short term research grants by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK; 5 T32 DK007676) and the National Institute for Neurological Disorders and Stroke (NINDS; 5 T35 NS064931).

Negotiated cooperative agreements with several international medical schools have been set up to offer tailored research programs at UTMSH for selected foreign medical students who interact fully with the other students in the Summer Research Program.

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

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Lab Research Ownership

Publication and/or Disclosure

Each student participating in this program is required to read, agree to, and sign this disclosure form. The original signed copy is on file in the Summer Research Program office; the student and their faculty mentors are each furnished with a copy.

“In reference to the laboratory research you will perform this coming summer through The University of Texas Medical School at Houston’s Summer Research Program, you are required to comply with the standard restrictions regarding participation in the Summer Research Program:

“All of your laboratory research is *CONFIDENTIAL* and although your abstract will be available through our website, you cannot independently disclose or publish any research findings or data in any form (including at meetings or conferences) without the express prior written approval of The University of Texas Medical School at Houston. If you wish to submit your abstract to any third party, you must first contact your faculty mentor no less than three (3) weeks prior to any deadlines in order to obtain the necessary written approvals.

“Because your research was generated from ideas and funds that originated with your faculty mentor and The University of Texas Medical School at Houston, ownership of any data generated by you during the Summer Research Program belongs to The University of Texas Medical School at Houston or the Principle Investigator (PI).”

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Medical Students

ABSTRACT

The Specificity of the Serum Antibody Response to the Epstein Barr Virus is altered in Multiple Sclerosis

WASEEM ANSARI

The University of Texas Medical School at Houston Class of 2014

Sponsored by: John W. Lindsey, MD. Dept of Neurology

Supported by: Foundation of the Consortium of Multiple Sclerosis Centers and in part by the Clayton Foundation for Research

Key Words: Epstein-Barr, Multiple Sclerosis

Epstein-Barr virus (EBV) has been shown to play a role in the pathogenesis of multiple sclerosis (MS). The specific role has not been revealed by previous experimental studies. A current hypothesis assumes that persons with MS may have an abnormal immune response to a latent EBV infection, leading to development of MS. To test this hypothesis, Western blots of EBV antigens were reacted with viral antigens with the sera of 75 patients. Of multiple bands, 12 were selected for analysis by lab imaging software. The antibody response to most of bands was higher in MS, with the most significant increases for the 77 kD ($p=0.006$), 12 kD ($p=0.014$), and 360 kD bands ($p=0.014$). This strengthens the theory that Epstein Barr antibodies could be linked to the development or exacerbations of multiple sclerosis.

ABSTRACT

Atheroma Macrophage Targeting by Rational Liposomal Design

TYE ARNETT

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Drs. Patrick Kee and Delia Danila

Supported by:

Key Words: Atherosclerosis, atheroma, macrophage, liposome

Macrophage in atheroma plays an important role in destabilizing the plaque. Development of a non-invasive molecular imaging technique targeted to inflammatory components of plaque formation may offer a more robust test for staging atheroma development versus the current anatomic-based techniques of luminal stenotic measurement. The objective of this study is to target macrophage by use of rational liposomal shell designs with the view of incorporating contrast agent into the liposomes for more precise imaging of atheroma formation. Phosphatidylserine (PS) and 1-palmitoyl-2-oxoaleroyl-sn-glycero-3-phosphorylcholine (POVPC), which are known to interact with macrophages, were incorporated into the liposomal shell to mimic the surface markers present in senescent erythrocytes and oxidized low density lipoproteins, respectively. Rhodamine-phosphatidylcholine and lipophilic near infrared (NIR) dye were also incorporated into the liposomal shell to facilitate the visualization of liposomes by fluorescence microscopy and ex vivo NIR imaging. Physicochemical characteristics such as average liposome size and particle homogeneity. In vitro uptake and toxicity profiles in the presence of mouse macrophage-like monocytes, in vivo organ distribution as assessed by near-Infrared (nIR) imaging and histological analysis were compared among the different liposome formulations. Fluorescent microscopy of liposome formulations containing 8.5% PS and 8.5% POVPC showed excellent uptake by cultured macrophages after two hours of incubation. Formulations containing higher and lower molar percentage of PS showed much less affinity for uptake by cultured macrophages. Cell proliferation assays with XTT reagent demonstrated a minimal toxicity profile to cultured macrophages after 24 hours of incubation. In vivo injection of liposomes containing PS or POVPC into Western Diet-fed apoE deficient mice confirmed localized uptake of liposomes in aortic atheroma by fluorescent microscopy. Ex vivo NIR imaging confirmed the anticipated high level uptake by the liver and spleen. However, NIR dye-labeled liposomes containing PS or POVPC were also detected in aortic atheroma in the aortic arch and proximal descending aorta in apoE deficient mice, confirming the optimal formulations were readily taken up by resident macrophages in the atheroma. In conclusion, rational modifications of the liposomal shell may represent an attractive and biocompatible approach for developing new theranostic agents for targeting atherosclerosis.

ABSTRACT

Long-Circulating Liposome-Encapsulated Computed Tomographic (CT) Contrast Agent

DAVID M. CASSEL *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Patrick Kee, MD, PhD, Department of Cardiology
Delia Danila, PhD, Department of Cardiology

Supported by: *The University of Texas Medical School at Houston - Patrick Kee, MD, PhD*

Key Words: Computed Tomography (CT), Contrast, Liposomes, Long-Circulating

Rapid renal clearance of computed tomographic (CT) contrast agents necessitates large bolus injection of contrast agent, which may result in irreversible renal toxicity. The objective of this study is to prepare a liposome-encapsulated CT contrast agent for prolonged intravascular enhancement for CT imaging and improved toxicity profile of the contrast agent. Conventional iodine-containing contrast agents, Iohexol and Visipaque, were encapsulated in liposomes containing dipalmitoylphosphatidylcholine (DPPC), cholesterol, and a polyethylene glycol (PEG)-lipid - a coupled spacer to inhibit uptake by the reticuloendothelial system. Five techniques for separating unencapsulated from liposome-encapsulated contrast agents were compared for their abilities to maintain average liposome size, particle homogeneity, structural integrity, and percent encapsulation of contrast agents. Various CT contrast preparations were studied for their uptake and toxicity profiles in the presence of mouse macrophage-like monocytes, in vivo vascular opacification as assessed by CT imaging and organ biodistribution. Among the separation techniques, treatments with Amicon centrifugal units and Ficoll gradient ultracentrifugation resulted in excellent recovery and separation of encapsulated payload while maintaining a homogeneous liposome size distribution and structural integrity. Size exclusion chromatography and dialysis were reasonable alternatives for separation but the dilution of the end-product was unfavorable for in vivo administration. In contrast, spin column centrifugation resulted in unacceptable aggregation of liposomes, which was confirmed by electron microscopy and Dynamic Light Scattering. Fluorescent microscopy uptake studies confirmed that the inclusion of PEG in the liposomal shell led to minimal uptake of fluorescein isothiocyanate [FITC] labeled liposomes by mouse macrophage-like monocytes at 2 hours of incubation. Cell proliferation assays with XTT reagent demonstrated reduced cellular toxicity with exposure to liposome-encapsulated Visipaque versus free Visipaque. Finally, microCT of the vascular system was performed in mice by comparing separated, contrast-encapsulated liposomes over 60 minutes with free Visipaque over 30 minutes. Signal intensity, measured in Hounsfield Units, for the Amicon centrifuge-separated, Iohexol-encapsulated liposomes remained higher in the vascular system at every corresponding time point versus the clinically used free Visipaque. This confirms an improved intravascular retention profile for liposome-

encapsulated CT contrast agent. In conclusion, liposome-encapsulated CT contrast agents can be optimally prepared by separation techniques with the potential to reduce cellular toxicity and prolonged intravascular CT enhancement.

ABSTRACT

Dynamics of tCREB2 After 5-HT Treatment In Sensory Neurons of Aplysia

ALEX DALKE

The University of Texas Medical School at Houston Class of 2014

Sponsored by: John Byrne, PhD, Department of Neurobiology

Supported by: Dr. John Byrne

Key Words: Aplysia, long-term synaptic facilitation(LTF), 5-HT, CREB2, sensory neurons.

Long-term memory and plasticity, including long-term synaptic facilitation (LTF) of the Aplysia sensorimotor synapse, depend on the activation of transcription factors that regulate genes necessary for synaptic plasticity. In the previous study we found that treatment with 5-HT and behavioral training produce dynamic changes in the expression of total CREB2, a transcriptional repressor, in ganglia. Similar changes also presented in isolated sensory neurons. We detected an immediate increase of CREB2 followed by a decrease at 12 h time point by immunofluorescence. Present study is to examine the changes of CREB2 in 5-HT-treated presynaptic sensory neurons at other time points (eg 1, 2, 5 and 24 h post 5-HT). Examining the regulation of CREB2 after 5-HT treatment will allow us to define the temporal contribution of CREB2 to consolidation of LTF.

ABSTRACT

Case-Control Study of Renal Disease Patients on Dialysis for Pesticide Exposure & Biomarkers of Renal Damage

VIPAL DURKAL

The University of Texas Medical School at Houston Class of 2014

Sponsored by: The University of Texas Medical School at Houston Summer Research Program

Supported by: Dr. Donald Molony

Key Words: Pesticide, nephrotoxicity, dialysis

The intention of our study is to evaluate current dialysis patients (cases) at UTH and Memorial Hermann Hospital for prior exposure to pesticides. Pesticides have been demonstrated to show nephrotoxicity after chronic exposure. The study will survey renal dialysis patients for prior exposure to pesticides, based on an online survey instrument. The eventual goal of our study is to enroll one-hundred dialysis patients with prior pesticide exposure as the case group. The survey includes distractor questions to control for recall bias. The survey evaluates exposure to chlorinated pesticides as well as household exposures to ammonia and other chemicals. Our goal is to match three-hundred controls, based on demographic factors including socioeconomic status and geographic location of residence, to those controls using a survey instrument by telephone. The numbers of cases and controls demonstrates appropriate statistical power based on statistical analysis. Our intention is to evaluate whether there is a statistical significance (p value < 0.05) that dialysis patients were exposed to pesticides on a chronic basis compared to controls. In addition, our goal is to take serum collections from 30 controls and 30 cases to screen for a set of known biomarkers of renal damage at a local dialysis center. The study is currently being conducted.

ABSTRACT

Comparison of pCREB1 Levels in *Aplysia* Sensory Neurons Following 5-HT Treatment Using a Standard and an Enhanced Protocol

ALEXANDER FROLOV *The University of Texas Medical School at Houston* Class of 2014

Sponsored by: Dr. John H. Byrne, PhD

Supported by: Dr. John H. Byrne, PhD

Key Words: *Aplysia*, 5-HT, long-term facilitation, training protocol, CREB1

It is known that several learning trials with breaks between each produce long term memory that is more persistent than one long learning trial massed together. However, it is not known what the optimal spacing of these trials may be. Traditionally, in learning trials using serotonin and cultured *Aplysia* sensory neurons, the protocol employed has been five 5-minute bursts of serotonin with 15-minute breaks in between each. It is postulated that two biochemical cascades are specifically activated by serotonin in order to phosphorylate CREB1, one of which mediates the activation of protein kinase A (PKA), and the other which activates the extracellular signalregulated kinase (ERK). When the interaction between these kinases is maximized, levels of pCREB1, and thus of long-term facilitation, are postulated to be maximal. To this end, a computer model has identified a new training protocol (the "Enhanced" protocol) that maximizes PKA and ERK interactions and thus can induce long-lasting memory (Zhang et al *accepted*). Indeed, both immediately after treatment as well as 18 hours post-treatment, this "Enhanced" protocol shows significant elevation of phosphorylation of the transcription factor cAMP response element (CRE)-binding protein 1 (CREB1) in the treated sensory neurons, over both control levels *and* the "Standard" protocol levels as described above (Liu et al 2008). The current project focuses on the time point two hours after treatment with serotonin, in an attempt to examine pCREB1 levels following "Enhanced" and "Standard" protocols. Previous data has demonstrated that pCREB1 levels are increased over control levels at 2 hours posttreatment using the "Standard" protocol, and thus it is hypothesized that the "Enhanced" protocol will show a concomitant rise in pCREB1 levels to an even higher degree (Liu et al 2008). This, then, will further prove that the "Enhanced" protocol is more efficient at maximizing PKA and ERK interactions, thus augmenting pCREB1 levels and long-term facilitation.

ABSTRACT

Comparing hemodynamics of pulsatile or continuous flow of a left ventricular assist device using a computational model

MITCHELL J GEORGE *The University of Texas Medical School at Houston* *Class of 2015*

Sponsored by: Richard W. Smalling, MD, PhD, FACC, Division of Cardiology

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
5 T32 DK007676-19

Key Words: Left-ventricular-assist-device (LVAD), pulsatile flow, computational model

Debate continues with regards to describing optimal flow characteristics for left ventricular assist devices (LVAD), and currently no computational model exists that is capable of simulating and accurately comparing ventricular support from a synchronized pulsatile pump with a continuous-flow pump. The purpose of this investigation was to build an appropriate computational model to test the hypothesis that pulsatile left ventricular assist devices potentially deliver superior circulatory support compared to continuous-flow left ventricular assist devices at the same level of ventricular assist device flow. A computational model predicting physiology of the human heart and cardiovascular system in a failing and control state was built in MatLab, a commercially available mathematical computing software package. The model simulates support from either a continuous-flow or a synchronous pulsatile-flow LVAD. Hemodynamic measurements were collected in the control and failing state with left ventricular device assistance from both devices individually. This data was validated by comparison to similar in-vivo porcine experiments. Both the computational model and its in-vivo counterpart predict the pulsatile-flow LVAD to provide superior cardiac output, cardiac unloading, cardiac pulsatility and improved aortic valve flow compared to the continuous flow model for an identical pump output. The computational model presented in this investigation accurately predicts similar hemodynamics of the human cardiovascular system with a healthy or failing heart.

ABSTRACT

Age Related Changes in the Trabecular Meshwork

MARK GOLD

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Robert M. Feldman, M.D., Richard S. Ruiz, MD Department of
Ophthalmology and Visual Science

Supported by: Richard S. Ruiz, MD Department of Ophthalmology and Visual Science &
National Eye Institute Vision Core Grant P30EY10608 and the Hermann Eye
Fund, Houston, TX

Key Words: Trabecular Meshwork, Glaucoma

The Trabecular Meshwork (TM) is the primary drainage system of aqueous and is intimately related to the pathophysiology of glaucoma. Because changes to this structure and function can often have detrimental effects on the eye, this topic has been a source of interest for many decades. However, with the recent development of the Casia SS-1000 (Tomey, Nagoya, Japan) Swept Source Fourier Domain Anterior Segment Optical Coherence Tomography (FD-ASOCT) system, the anatomy of the eye's anterior segment, including the TM, can finally be identified and quantified in living eyes. This purpose of this study was to examine the relationship between age and characteristics of the trabecular meshwork in living, non-glaucomatous eyes. This measurement can be used as a future diagnostic tool in eyes with abnormal trabecular meshwork.

ABSTRACT

A Retrospective Analysis of HIV/AIDS Hospice Patients and Survival

MICHAEL A. HANSEN *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Philip Johnson, MD; Gus Krucke, MD, Department of Internal Medicine

Supported by: Regan Ryan Summer Medical Stipend

Key Words: HIV, AIDS, Hospice, Palliative Care, Recovery, Survival, Population Study

Bering Omega Hospice (BOH) was created with the intent of caring for the terminally ill HIV/AIDS patients in the city of Houston. With the advent and improvement of Highly Active Antiretroviral Therapy (HAART) the terminal outcome for individuals affected by Acquired Immunodeficiency Syndrome (AIDS), as well as the associated comorbid diseases, has been significantly impacted. We performed a retrospective analysis based on chart reviews of previous residents of BOH. Our study goals were to compare 1) characteristics between patients who left BOH with a positive outcome to those who died, 2) the effect of HAART before and during a patient's stay at BOH, and 3) the significance of comorbid complications on patient outcome. A total of 370 de-identified patient charts of residents at BOH between the years 2005-2011 were reviewed. Criteria considered were the following: population factors (age, race, gender, etc) along with medical comorbidities and interventional factors (HAART status, length of stay). Early analytical results show several significant differences between bereavement planning, psychological history, and status of HAART therapy while a patient at BOH. However, correlations between comorbidities were found to be insignificant. These results show specific areas of care that indicate a need for further study in order to better treat and plan for the severely ill HIV/AIDS population. As the terminally ill prognosis of HIV continues to change, so must the clinician's attention to risk factors as well as areas of care that may provide for the greatest chance of improvement.

ABSTRACT

Can Thromboelastography Predict Rapid Clinical Improvement or Hemorrhagic Transformation After tPA Treatment of Acute Ischemic Stroke?

AMANDA A. HASSLER *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Dr. James C. Grotta MD Neurology

Supported by: Department of Neurology and The University of Texas Medical School at Houston

Key Words: Thromboelastography, Ischemic stroke, hemorrhagic transformation

Background: A weight adjusted dose of Tissue Plasminogen Activator (tPA) is the only approved treatment to improve outcome after acute ischemic stroke (AIS). However, tPA often fails to achieve clot lysis and involves a 6% chance of hemorrhagic transformation. Thromboelastography (TEG) is a test performed on whole blood samples to determine the speed (R, delta, K and α angle) and strength of clot formation (MA and G) and lysis (LY30). Furthermore, clot subtype (fibrin-platelet rich “white” clot vs. thrombin generated “red” clot) can also be surmised from TEG G and delta. We tested whether TEG values of blood drawn post-tPA differed from pre-tPA values, and if the change in values from pre to post-tPA differed according to “subtype”, and could predict recanalization as evidenced by rapid clinical improvement in the NIHSS score (8 point decrease or reduction to total score of 0 or 1) or hemorrhagic transformation on brain imaging. **Methods:** Patients who received tPA within 4.5 hours of AIS onset were included. Blood for TEG was drawn prior to and 10 minutes after the tPA bolus. Data was collected on NIH stroke scale and presence of any hemorrhagic transformation shown on CT or MRI 24-48 hours after tPA treatment. Samples with pre tPA G values >11 were considered white clots. The remainder with delta <0.7 were considered red clots and all others were mixed clots. A Wilcoxon signed rank test was used to compare pre- to post-tPA TEG, Wilcoxon Mann-Whitney U test for the association between TEG and rapid clinical improvement or hemorrhagic transformation, Fisher exact test to assess the association between clot type and clinical improvement and hemorrhagic transformation, and Kruskal Wallis to test association between clot subtype and change in TEG. **Results:** 40 patients were enrolled. Eight of those patients showed rapid clinical improvement, four patients developed hemorrhagic transformation, and one of those four hemorrhagic transformations was symptomatic. Compared to pre-tPA, post tPA TEG showed a decrease in α angle, MA (maximum amplitude), and G, and an increase LY30 ($p < .0001$ for all). These changes indicate slower and decreased clot strengthening and substantial clot lysis after tPA. There was no association between post tPA TEG values or clot subtype and rapid clinical improvement or

hemorrhagic transformation. However, the variability in TEG was great after tPA (for instance, median LY30 = 94 (IQR 15-95)). **Conclusion:** After tPA treatment, TEG demonstrates clot lysis but with substantial variability. While we found no relationship between any TEG parameter or clot subtype and, rapid clinical improvement or hemorrhagic transformation, further study of larger numbers of patients is needed.

ABSTRACT

Why SCIP-based antibiotic prophylaxis is inadequate to prevent surgical site infections

RUSSELL HAWKINS *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Dr. KuoJen Tsao

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
5 T32 DK007676-19

Key Words: SCIP, prophylaxis, compliance, antibiotic, SSI

Purpose: The Surgical Care Improvement Project (SCIP) recommends appropriate spectrum and timing of antibiotic prophylaxis to prevent surgical site infections (SSIs). However, emerging data has demonstrated that despite increased compliance, SSIs are not decreasing. Furthermore, there is an all-or-none phenomenon associated with SCIP infection guidelines. We hypothesized that despite the routine administration of antibiotic prophylaxis in pediatric surgery patients, compliance with appropriate evidence-based practice does not occur in a majority of cases.

Methods: Data was prospectively collected, over a 10 week period, in randomly selected pediatric surgical cases occurring in operating rooms, neonatal and pediatric intensive care units. Emergent cases were excluded. Information was obtained from direct observation of cases and review of electronic medical records. Five aspects of antibiotic usage were evaluated for each case to determine compliance with evidence-based pediatric surgery service guidelines at a university-affiliated hospital including appropriate administration when indicated, type, weight-based dose, time between infusion and surgical incision, and redosing (if applicable).

Results: During this study, 143 cases were observed. In 141 cases (98.6%), antibiotics were given or withheld appropriately, in one case unnecessary antibiotics were given, and in one case, indicated antibiotics were withheld. Of the 100 cases (69.9%) requiring antibiotic prophylaxis, only 48% of cases were compliant with all four guidelines (figure). The most common failures in compliance occurred because of dosing or timing errors.

Conclusions: There is significant room for improvement in the appropriate administration of prophylactic antibiotics to prevent SSIs. The perceived failure of increased compliance with SCIP infection guidelines may be linked to lack of attention to other important aspects of antibiotic prophylaxis. The importance of these components that are not addressed by SCIP on SSI rates remains to be determined.

ABSTRACT

The Incidence and Effects of Metabolic Bone Disease in Orthopaedic Trauma Patients: A Prospective Cohort Study

JACOB C. HOFFMANN The University of Texas Medical School at Houston Class of 2014

Sponsored by: Milan Sen, MD - Department of Orthopaedic Surgery
Catherine Ambrose, PhD- Department of Orthopaedic Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
5 T32 DK007676-19

Key Words: trauma, metabolic bone disease, bone mineral density

In traumatic fractures, having functioning hormonal and mineral balance is essential for proper healing of the bone. Unaccounted endocrine and metabolic abnormalities can lead to malunion and nonunion of the fracture site. We propose that endocrine and metabolic abnormalities are prevalent within the general orthopaedic trauma population leading to increase malunion and nonunion rates. Adult orthopaedic trauma patients will be recruited and informed consent obtained in the hospital setting by the investigators, and will have base line labs drawn, quantitative ultrasound (QUS) performed, and will complete a fracture assessment questionnaire (FRAX). Patients will then be expected to follow the standard of care for fracture follow up and return for clinical assessment at 3 months, 6 months and 12 months post-operatively. In addition to standard clinical follow up, the QUS and FRAX will be repeated at 6 months and 12 months. The metabolic and endocrine panels obtained from all orthopaedic trauma patients include: comprehensive metabolic panel (CMP), serum levels of 25-OHD, 1,25-hydroxyvitamin D (1,25-OHD), serum magnesium, phosphate, osteocalcin, bone-specific alkaline phosphatase, thyroid hormones (TSH, T3, and T4), parathyroid hormone, and hormones related to the reproductive system. As a pilot study, we plan to collect the data for the first 100 patients and then run a power analysis to determine optimal sample size. Recent approval was granted by Memorial Hermann Hospital and The University of Texas Medical School at Houston IRB (approval #HSC-MS-11-0291). This study is currently in progress.

ABSTRACT

Oral Lactoferrin as a Therapeutic Regulator of LPS Induced Hypotensive Response and Pathology in Rats

HALEY HORTON

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Jeffrey Actor, PhD, Department of Pathology

Supported by: The University of Texas at Houston Medical School

Key Words: LPS, Lactoferrin, Hypotension

Objectives: Lactoferrin was tested as an oral modulator for development of LPS induced sepsis in rats. Sepsis is a deadly condition characterized by a systemic inflammatory state in response to infection. The progression of systemic inflammatory response syndrome (SIRS) to sepsis is due to the cellular damage and death caused by the acute inflammatory response of the immune system. Lactoferrin (LF) is an iron binding glycoprotein that has demonstrated a role in mediation of this immune response, including the burst of pro-inflammatory cytokine production. Lipopolysaccharide (LPS), or endotoxin, can be used to mimic bacterial sepsis in animal models.

Methods: Rats were divided into five groups: sham, LF alone, LPS alone, LF given orally at one hour prior to LPS administration (-1), and LF given orally at 18 hours prior to LPS administration (-18). Heart rate and blood pressure were measured post administration of LPS. Blood was collected at various times post LPS administration, and serum was analyzed for levels of the pro-inflammatory mediators TNF- α , IL-1, IL-6, and TGF- β . Animals were sacrificed 24 hours following LPS administration. Proximal duodenum was harvested and subjected to histo-pathological analysis.

Results: Following LF administration alone, heart rate decreased at all points as compared to the sham rats. Heart rate for (-18) LF and LPS was also decreased as compared with heart rate of rats given LPS alone. In addition, the (-1) LF and LPS rats showed a decrease in production of IL-6 at the 1 and 3 hour time points. Furthermore, LF was able to confer histo-pathological protection of intestinal tissue post LPS administration.

Conclusions: These studies indicate that lactoferrin may be a novel therapeutic for the treatment of sepsis and septic like pathology, and may be useful in infectious diseases to reduce immune-mediated tissue damage.

ABSTRACT

Use of Thrombelastograph (TEG) to evaluate coagulation in patients with end stage liver disease

CASSANDRA HOWELL *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Evan Pivalizza, MD, The Department of Anesthesiology

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

Key Words: TEG, thrombelastograph, cirrhosis, coagulation

In anesthesia and critical care medicine, there is an increasing use of the TEG™ as a point-of-care monitor of blood coagulation. This test measures the dynamics of coagulation from the initiation of the clot, clot strengthening, and eventual clot degradation. The purpose of this study is to document blood coagulation, with the TEG™, in patients with end stage liver disease who may be presenting for other surgeries or interventions in addition to liver transplantation. The TEG™ uses a small volume (1ml) of whole blood (as opposed to plasma based laboratory tests) to assess the full range of blood coagulation. Parameters measured include: 1) R time (measured in minutes- time from initiation of sample to a set point of fibrin formation), 2) K time (measured in minutes- reflects clot strengthening with interaction of fibrin and platelets), 3) alpha angle (measured in degrees- the angle at which the clot strengthens, same parameters as K time), 4) MA maximum amplitude (measured in millimeters- reflects the greatest clot strength, a reflection of platelet function as opposed to platelet count which may not reflect platelet function), 5) G (measure in dynes/sec- a measure of shear strength derived from the MA data with platelets contribute significantly to shear strength, preventing premature clot breakdown), and 6) percentage fibrinolysis (percent- a measure of the rapidity of clot breakdown). The study is still ongoing. Thirty-six patients were enrolled throughout the study. In this heterogeneous group of patients with liver disease and documented derangements in isolated laboratory plasma-based coagulation indices and thrombocytopenia, whole blood based TEG assay revealed all indices within accepted normal limits, including time to fibrin formation (R time), clot strengthening (K time and angle) and clot strength incorporating platelet function and fibrinogen levels (MA, G). Of great interest was an apparent defect in platelet function, inferred from poor responses to traditional platelet agonist (arachadonic acid and ADP). Although this test of platelet response was developed to detect residual inhibition to aspirin and clopidogrel therapy, it is remarkable that in this cohort without any exposure to these platelet inhibitor drugs, platelet response to these agonists was so retarded. The study is ongoing and will be complete for submission to a prominent anesthesiology meeting in 2012.

ABSTRACT

Evaluation of Sepsis Screening Tool in Trauma Patients

ALEXANDRA IACOB *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Dr. Laura J Moore, MD

Supported by: The University of Texas Health Science Center at Houston - The Center for Translational Injury Research (CeTIR)

Key Words: sepsis, screening, trauma, validation, patients

The purpose of this prospective, observational study is to validate a screening tool for the early identification of sepsis in trauma patients (pts). 5,485 screens were completed on 587 trauma pts admitted to a Level 1 Trauma Center over a 10 week period. A score of ≥ 4 was categorized as a positive screening score. Chart review was conducted on all pts to determine if sepsis was present. Pts were categorized into one of four groups: True Positives (46), True Negatives (479), False Positives (43), & False Negatives (1). A 2x2 table was utilized to statistically validate the tool. The sepsis screening tool had a sensitivity of 97.9%, specificity of 91.8%, positive predictive value of 51% and negative predictive value of 99.8%. These results indicate that the screening tool is a valid method for the early identification of sepsis in trauma patients.

ABSTRACT

Possible Association of Lower Rate of Postherpetic Neuralgia in Patients on Anti-Tumor Necrosis Factor α .

SABA JAVED

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Stephen K. Tyring, MD, PhD, Department of Dermatology

Supported by: The University of Texas Medical School at Houston

Key Words: Herpes Zoster, Postherpetic Neuralgia, TNF- α inhibitor

Postherpetic neuralgia is exceptionally drug-resistant neuropathic pain making it extremely challenging to manage, thereby leading to a significant physical, psychosocial and economic burden. Recently, a large scale study of patients with rheumatoid arthritis who developed herpes zoster while taking a TNF- α inhibitor reported a decreased incidence of postherpetic neuralgia.

The objective of this study was to investigate whether patients on TNF- α inhibitors who developed herpes zoster have a lower incidence of subsequent development of postherpetic neuralgia.

A retrospective review of herpes zoster patients on TNF- α inhibitors (infliximab, etanercept, or adalimumab) was conducted in 12 dermatology clinics. Medical records of such patients were reviewed thoroughly to confirm herpes zoster and TNF- α inhibitors and any subsequent development of postherpetic neuralgia (pain score ≥ 3 out of 10 after 90 days of shingles onset) was noted.

A total of 206 cases were reviewed, of which only 2 cases (1.0%) developed postherpetic neuralgia, a considerably lower incidence rate than noted in the literature. Increasing age is a known risk factor in the development of postherpetic neuralgia. However, of the 58 (28.1%) cases ≥ 70 years of age, only 1 patient (1.7%) developed neuralgia compared to approximately 50% of patients who develop postherpetic neuralgia in this age group as reported in the literature.

Treatment with TNF- α inhibitors may be associated with a lower incidence of postherpetic neuralgia but further prospective large scale studies are needed to confirm this data.

ABSTRACT

Testing Missense Variations of the Grainyhead-like3 Gene for Association with Myelomeningocele in Humans

SARAH JECHOW

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Hope Northrup, M.D., Division of Medical Genetics, Department of Pediatrics

Supported by: Division of Medical Genetics, Department of Pediatrics

Key Words:

Spina bifida myelomeningocele (MM), an opening in the vertebral column through which meninges and neural tissue protrude, is the most common neural tube defect seen in humans that is compatible with survival. This defect occurs with a frequency of approximately 1 in 2000 live births and places a significant financial burden upon health care systems. Up to 70% of neural tube defects are preventable by peri-conceptual supplementation with folate, but the remaining 30% are unalleviated. The curly-tail mouse, an established animal model for folate-resistant neural tube defects, is known to be a hypomorph for expression of the grainyhead-like 3 gene (*Grhl3*). Previous work in our lab indicated the possibility of association between genetic variants in the coding region of *GRHL3* and the MM phenotype in humans. Our objective was to examine 6 missense variants, in 4 exons of the *Grhl3* gene, to confirm this association. We used a restriction enzyme length polymorphism (RFLP) approach to genotype the 5 variants in the amplified exons 2, 4, 11, and 12 from 838 affected subjects. RFLP variants were differentiated using the ABS3100 Genetic Analyzer. Variants identified in affected subjects were then confirmed by Sanger sequencing. One variant contained in exon 12 was examined by the Taqman protocol due the apparent lack of a suitable restriction enzyme site. Gene frequencies among our patient cohort as confirmed by sequencing were compared to those reported in public databases using a chi square test with a p value <0.05. Our results show a statistically significant association between the both the variant of interest in exon 2 and the development of MM in the Caucasian population. A similarly increased frequency was seen with the second variant in exon 11. No significant association has been found among the other variants.

ABSTRACT

Assessing the use of Circulating Tumor Cells in the Management of Hormone Naive Prostate Cancer Patients

BRETT T. JENSEN

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Robert Amato, DO, Department of Oncology

Supported by: Robert Amato, DO, Department of Oncology

Key Words: circulating tumor cells, hormone naive, prostate cancer, PSA

The Veridex CellSearch system has been approved by the U.S. Food and Drug Administration for the detection of circulating tumor cells (CTCs) in cases of metastatic prostate cancer. This study evaluates sensitivity of the FDA approved CTC detection method's ability to detect circulating tumor cell numbers that accurately reflect hormone naive prostate cancer patients disease burden based on PSA levels and clinical presentation. Patients were selected with biopsy proven prostate carcinoma that had non-castrate levels of serum testosterone (>50) on 1 or more of the days they had CTC levels measured. Patient information was collected from the patients' electronic medical records. Much of the data collection was focused on the dates that CTC levels were collected. Of the eligible patients 52 had received surgery as a primary treatment, 9 had undergone radiation, 8 had no primary therapy but had been placed on chemotherapy, and 4 had no primary therapy and were had been monitored with watchful waiting. In the hormone naive patient population 7 patients had significant levels of CTCs (≥ 5), 9 had <5 CTCs and 57 had 0 CTCs isolated. 15 of the men had increases in PSA of >50% however only 2 of the men had CTC levels which increased as their disease showed signs of progression. Both of these men had received no primary local therapy and had just received chemotherapy. In this patient population (prostates intact receiving chemotherapy) 4 of the 8 men had significant CTC measurements (≥ 5) and accounted for 4 of the 7 total significant measurements. The Avg. PSA in significant CTC measurements was 338.54 compared to 2.71 in CTCs <5 and 1.48 in 0 CTCs. It appears the current methods available to test for CTC levels in prostate cancer are not sufficiently sensitive to isolate CTCs in hormone naive patients. Only 7 (10%) of the patients had CTC levels considered to be significant. It appears that primarily patients with very extensive disease (Avg. PSA 338.54) have significant levels of CTCs recovered with the CellSearch system. Many patients have no CTCs recovered even when based on their clinical presentation it would be expected that some CTCs would be present.

ABSTRACT

Differences in Social Interactions in 6-Month-Old Infants Based on Later Autistic Spectrum Disorder (ASD) Classification: A Potential Screening Tool for ASD

KATHERINE M. JOHNS The University of Texas Medical School at Houston Class of 2014

Sponsored by: Pauline A. Filipek, MD, Department of Pediatrics – Children’s Learning Institute and Division of Child and Adolescent Neurology

Supported by: The Children and Families Commission of Orange County and The Larry & Helen Hoag Foundation

Key Words: ASD, autism, infants, social interactions

Autistic spectrum disorders (ASDs) include deficits in social interaction and verbal and nonverbal communication with restricted/repetitive behaviors and interests. Early behavioral intervention can greatly improve the prognosis for children with ASD, but early intervention is contingent upon early identification. Current research reports that atypical development cannot be identified until 12 months of age. This study is among the first to evaluate social interactions in 6-month old infants as potential screening tools for ASD. Differences in social interactions between infants later classified with ASD ($n = 11$) and those not later classified with ASD (non-spectrum; N/S; $n = 16$) were explored. An infant-parent social interaction was divided into three consecutive periods: infant-directed speech (90 seconds), still-face paradigm (20 seconds), and re-initiation of infant-directed speech (90 seconds). Infant smiles and vocalizations were measured from videos of these interactions, and ASD classification was assessed at 12-20 months of age with the ADOS-Toddler module. Significant differences between the ASD and N/S groups were observed for directed smiles (smiles with direct eye contact) and directed vocalizations. If replicated, these findings may lead to the development of a screening tool for ASD that allows infants to be identified several months earlier than they would be with the tests that are currently available.

ABSTRACT

Electro-corticographic Correlates of Face and Place Recognition

CIHAN MEHMET KADIPASAOGLU *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Nitin Tandon, MD
Vivian L. Smith Department of Neurosurgery

Supported by: NIH Center for Clinical and Translational Sciences. Grant #KL2RR0224149

Key Words: ECoG, Ventral Temporal Lobe, Category Specific Regions

Purpose: To explore the differences between recognition of faces and places using intracranial EEG recorded from the basal temporal language area.

Method: Seven patients diagnosed with intractable temporal lobe epilepsy were scheduled for implantation of subdural electrodes (SDEs) for clinical localization of seizure focus sites. Subjects were presented images of famous faces and places during concurrent collection of electrocorticography (ECoG) from lingual, fusiform, inferior temporal, and parahippocampal gyri. ECoG data were decomposed into seven frequency bands: delta (0-4Hz), theta (4-8), alpha (8-13), beta (13-30), low gamma (30-60), mid gamma (60-120) and high gamma (120-240). Percent change during task performance was calculated over prestimulus baseline.

Summary: In all SDEs, power increases in the gamma frequency bands were most strongly locked to task performance. Right hemisphere electrodes showed greater increases in gamma power during face naming tasks than place naming tasks, while left hemisphere SDEs had greater activation during place naming. The most consistent gamma activation was seen in the right fusiform gyrus during face naming, and in the left fusiform gyrus during place naming.

Conclusions: Similar patterns of activity during the naming of places and faces were noted across the seven individuals. The right fusiform gyrus was selective for face recognition tasks, as compared to the left fusiform gyrus, which was selective for place recognition.

ABSTRACT

Immortalized Human Pancreatic Stellate Cells as an *in vitro* Model for the Study of Bone Morphogenetic Proteins' Anti-fibrogenic Role in the Pancreas

MOHAMMED ASAD KHALID *The University of Texas Medical School at Houston* Class of 2014

Sponsored by: Tien C. Ko, Department of Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
5 T32 DK007676-19

Key Words: Pancreatic Stellate Cell, Pancreatic fibrosis, Bone Morphogenetic Protein

Background. Pancreatic stellate cell (PSC) activation is a key step in the development of pancreatic fibrosis. Transforming growth factor (TGF)- β is a key fibrogenic cytokine that activates PSCs. Bone morphogenetic protein 2 (BMP2), a member of the TGF- β superfamily, has been shown to have anti-fibrogenic properties in the kidneys, liver, and lungs. While we have shown BMP2 to suppress TGF- β induced PSC activation and extracellular protein expression in primary human PSCs, this ability has not been confirmed in immortalized human PSCs.

Methods. Immortalized human PSCs were treated with vehicle, TGF- β , BMP2, and a combination of TGF- β and BMP2. The cells were treated with vehicle, TGF- β (1 ng/ml) combined with BMP-2 at 0, 25, 50, 100, 200, 250 ng/ml. **Conclusions.** Immunofluorescence staining for GFAP and α -SMA and oil-red O staining were performed. **Conclusions.** Immortalized hPSCs are mesenchymal cells, and maintain low activation demonstrated by 4.9% α -SMA staining.

BMP2 decreases TGF- β -induced α -SMA and GFAP expression in immortalized hPSCs at 24 hrs and at doses \geq 100 ng/ml. BMP2 effectively blocks activation of the immortalized PSCs by TGF- β as seen previously in our lab with primary hPSCs. Immortalized hPSCs offer a reliable, practical *in vitro* model for the study of BMP's role in pancreatic fibrosis

ABSTRACT

Stabilizing Distal Radioulnar Joint Dislocations Using the Arthrex TightRope® Fixation System

ANDREW M. KHOURY *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Milan K. Sen, MD, Department of Orthopaedic Surgery

Supported by: Department of Orthopaedic Surgery, The University of Texas Health Science Center at Houston

Key Words: Distal radioulnar joint, dislocation, biomechanics, Arthrex®, TightRope

The distal radioulnar joint (DRUJ) is an essential component of the upper extremity, allowing the wrist to rotate independently from flexion and extension. A biomechanical study was designed to compare the application of a suture anchor by Arthrex® to current reduction methods, which entails the use of stainless steel Kirschner wires. At this time, testing is ongoing in determining the advantages of using the Arthrex TightRope® system to conventional K-wires. A retrospective study of three patients was also conducted as part of the project. These patients were identified to have dislocations of their distal radioulnar joints, which were subsequently reduced in full supination using the Arthrex TightRope® fixation system. Preliminary results have shown to be promising in patients' ability to regain close to full pronation and supination of their forearms, with only one out of the three patients requiring further surgery to remove the implant. Further studies include gathering follow-up data, and comparing these reduction methods to revised techniques.

ABSTRACT

Perceptions and Opinions on Sports Related Concussion Management in High School Athletes by Healthcare Providers and the General Community

MELISSA Y. KWAN

The University of Texas Medical School at Houston Class of 2014

Sponsored by: William Mosi Jones, MD, Department of Orthopaedic Surgery

Supported by: National Institute of Neurological Disorders and Stroke 5 T35NS064931 02

Key Words: Concussion, Epidemiology, Sports

Introduction: Concussions are the most common form of mild traumatic brain injury in sports. There have been recent changes to concussion management and return to play guidelines. An IRB approved study was designed to assess the awareness of and compliance with current concussion management and return to play guidelines among healthcare provider populations that commonly treat concussions. We hypothesize that not all healthcare providers treating high school athletes for sports-related concussions follow the most recent guidelines.

Methods: An online questionnaire was distributed to over 600 physicians, athletic trainers, and physical therapists in the Greater Houston area. Data is still being collected. Currently there are 69 responses to the questionnaire (14 physicians, 48 athletic trainers, 7 physical therapists).

Results: Fifty-seven percent of the participants have been in practice for greater than 10 years. Most participants in all disciplines felt either moderately comfortable or comfortable with treating sports-related concussions (64%). The most common concussion guidelines used by the participants are their own personal return to play guidelines (26%), as opposed to the current published guidelines. Most participants would not allow a concussed athlete to return to the same game or practice (94%). Though most healthcare providers are aware of computerized neuropsychological testing (80%), only half use it in clinical practice (48%). Most of the respondents (86%) are aware of recent Texas legislation stating that an athlete suspected of having a concussion must be withheld from all athletic activities for at least 24 hours and can return to play only with proper medical clearance. The majority agree with this law (96%).

Conclusions: Although this is early promising data, further analysis and final conclusions will be performed once more data is collected.

ABSTRACT

Examining the Role of the *RELN*, *ABAT*, *GRIK2*, and *GRIN2A* Genes in Modifying the Neurologic Phenotypes of Tuberous Sclerosis Complex

DAKOTA R. LANE *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Hope Northrup, MD, Pediatric Genetics
 Kit-Sing Au, PhD, Pediatric Genetics

Supported by: National Institute of Neurological Disorders and Stroke 5 T35NS064931 02

Key Words: Tuberous sclerosis complex, modifier genes, TSC2, GRIK2, ABAT

Tuberous sclerosis complex (TSC) is a neurocutaneous disorder characterized by neurologic and dermatologic symptoms such as seizures and intellectual disability. The symptoms of the disease result from the proliferation of benign tumors in multiple organ systems. TSC is an autosomal dominant single gene disorder that can be caused by a mutation in either the *TSC1* or *TSC2* genes. The clinical manifestation of the disease can vary widely, even among individuals in the same family with the same mutation. A study was designed to determine if the expression of TSC is influenced by the presence of single nucleotide polymorphisms in potential “modifier genes” that have shown associations with non-syndromic intellectual disability, seizures, and autism spectrum disorder. Discovering the cause of the differences in gene expression would allow patients better prognostic information and improved treatment options for themselves and their children. One family of multiple affected individuals with varying phenotypes was selected and tested for SNPs in the genes *RELN*, *ABAT*, *GRIK2*, and *GRIN2A* using PCR and sequencing. In the selected family, the *GRIK2* and *RELN* genes demonstrated little to no variation from the normal sequence. The *ABAT* and *GRIK2* polymorphisms were present in several family members and could show promising results in a statistically powerful study with a greater number of enrolled individuals.

ABSTRACT

The molecular mechanisms underlying the function of the apical complex protein, Pals1, during cortical development.

ZHENHAO LIU

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Seonhee Kim

Supported by: National Institute of Neurological Disorders and Stroke 5 T35NS064931 02

Key Words: pals1, in situ hybridization, cortical development

The apical complex protein, Pals1, has been shown to have critical importance on the cell fate and survival of neural progenitors in the developing cerebral cortex. Loss of Pals1 leads to the premature withdrawal of these neuroepithelial progenitors from the cell cycle followed by massive apoptotic cell death. Consequently, the Pals1-CKO mice display a near complete loss of their cerebral cortex, while heterozygotes exhibit an intermediate, partial loss. Past studies have linked Pals1 to the PatJ-Pals1-Crbs and Par6-Par3-aPKC complexes in the establishment of polarity and cell fate of mammalian epithelium; however the exact underlying molecular mechanisms remain largely undefined. In this study, we 1) selected 13 candidate genes that showed significant upregulation/downregulation in Pals1-CKO mice from a microarray analysis, 2) synthesized digoxigenin-labeled RNA probes for the candidate genes, and 3) performed in situ hybridization with the probes to demonstrate gene expression on cryo-sectioned WT, Het, and Pals1-CKO mice at E14.5. Some candidate genes showed the expected upregulation (Casp1, Ccl4, Fgf13, Phlda3, and Rin2) or the expected downregulation (Bop1 and Loxl1) in the mice samples, while other candidate genes (Bach2, Cav1, Hap1, Ifitm2, Ltbp3, and Mef2c) showed inadequate staining or staining contrary to expectation.

ABSTRACT

Is the cAMP-PKA pathway in nociceptors involved in the maintenance of chronic pain following spinal cord injury?

MAURA LIVENGOOD *The University of Texas Medical School at Houston* Class of 2014

Sponsored by: Edgar T. Walters, Ph.D. and Carmen W. Dessauer, Ph.D., Department of Integrative Biology and Pharmacology

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) 5 T32 DK007676-19

Key Words: Spinal cord injury, chronic pain, dorsal root ganglion, cyclic AMP

Spinal cord injury (SCI) often results in the induction of chronic neuropathic pain, which greatly diminishes patient quality of life. Previous research demonstrates SCI induces a hyperexcitable spontaneously active (HSA) state in small, nociceptive dorsal root ganglion (DRG) neurons (Bedi et al 2010). Spontaneously active DRG neurons are likely to drive pain pathways and their resulting sensitization. The mechanism behind the development of this chronic hyperexcitable state is unknown; however, previous pharmacological studies on compression injury of the DRG indicated the maintenance of a hyperexcitable state required increased activity of the cAMP-PKA pathway in DRG nociceptors (Zheng et al 2007). I hypothesized the hyperexcitable state following SCI was due to increased activity of the cAMP-PKA pathway. I examined upregulation of multiple pathway components including Adenylyl Cyclase (AC) isoforms 1-9, EP4, TrpV1, Nav1.8, GRK2, PKA RII β , Yotiao, and AKAP150 through RT-PCR and Western Blots. I determined naïve rat DRGs express AC2, 3, 5, 8, and 9. Western Blots demonstrate increased expression of TrpV1 and decreased GRK2 3 months post-SCI. Blots from 9 months post-SCI indicate decreased expression of Nav1.8, TrpV1, Yotiao, AKAP150 and no apparent change in GRK2 and PKA RII β . The difference in expression of TrpV1 between 3 months and 9 months post-SCI poses an interesting possibility about how SCI changes overtime; however, this change could be attributable to the aging process or protein degradation in the 9 month samples. The involvement of the cAMP-PKA pathway in the development of chronic pain has yet to be elucidated and should be the subject of further research.

ABSTRACT

Chronic hyperinsulinemia sensitizes myocytes to hyperglycemia-induced cell death

GENNA LUBRANO

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Heinrich Taegtmeier, MD, DPhil, Department of Internal Medicine

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
5 T32 DK007676-19

Key Words: Heart, insulin resistance, hyperglycemia, apoptosis

Background. Patients with diabetes demonstrate alarmingly high incidence and mortality rate from heart failure. Because systemic insulin resistance (and the ensuing hyperglycemia), are associated with coronary artery disease and hypertension, current therapeutic strategies aim to reverse hyperglycemia at any cost. However, knowledge of the metabolic changes affecting the heart in diabetes is still incomplete. This hinders the effectiveness of broad therapeutic approaches. The most striking example is the recent report from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, showing that *intensive insulin therapy in type 2 diabetic patients paradoxically increases death from cardiovascular causes*. **Hypothesis.** We speculated that (besides its beneficial effects on systemic metabolism), intensive insulin therapy sensitizes cardiac myocytes to glucotoxicity. **Methodology.** Rat L6 myoblasts were differentiated into myocytes, and were then treated every 24 hours with 10 or 100 nM insulin. After 5 days of treatment, the rates of glucose uptake were measured using [2-³H]-deoxyglucose as a tracer, and the expression of the glucose transporters GLUT1 and GLUT4 quantified by western blotting. Another set of cells was incubated for 24 hours in hyperglycemic conditions (30 mM glucose) and the activity of the proapoptotic caspase-3 measured by a spectrophotometric assay. **Results.** The differentiation of L6 myoblasts was confirmed by the expression of the myogenic differentiation markers Myf5 and Myogenin, and by the appearance of the myocyte-specific proteins Troponin I and fast myosin heavy chain. Compared to non-treated cells, chronic treatment with 10 nM and 100 nM insulin increased the rates of glucose uptake by 50% and 135%, respectively. This increase, which was associated to higher protein levels of both GLUT1 and GLUT4, could not be further potentiated by acute insulin stimulation. In addition, the cells chronically treated with insulin also exhibited an increase in caspase-3 activity when incubated with high glucose concentrations. **Conclusions.** Chronic hyperinsulinemia upregulates glucose transporters in myocytes. The resulting increase in glucose uptake is associated with a sensitization of the cells to hyperglycemia-induced cell death. *This work provides the first evidence for toxic effects of increased glucose metabolism in muscle cells.*

ABSTRACT

Early Onset and Recurrence of Schwannomas in Patients with Schwannomatosis

WILLIAM METCALF-DOETSCH The University of Texas Medical School at Houston Class of 2014

Sponsored by: Dina Chelouche-Lev, M.D., MD Anderson Cancer Center

Supported by: Sarcoma Research Center, MD Anderson Cancer Center

Key Words: Schwannoma, Schwannomatosis, INI1

Schwannomas are nonmalignant nerve sheath tumors arising from Schwann cells, occurring sporadically or as part of a larger tumor syndrome. A database of patients with schwannomas was compiled from MD Anderson medical records, and the incidence, treatment, and recurrence of sporadic schwannomas as well schwannomas in the setting of schwannomatosis were analyzed and compared. It was found that patients with schwannomatosis have a greater amount of tumors at an earlier age of onset, and that these tumors were more likely to recur after surgical resection. Further goals of this study will be to expand the database and construct a tissue microarray of schwannoma specimens to stain for expression of INI1.

ABSTRACT

The impact of prehospital care on trauma patient outcomes

BRIAN L. MILLER

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Bryan A. Cotton, M.D., M.P.H. Department of Surgery

Supported by: Center for Translational Injury Research (CeTIR)

The University of Texas Medical School at Houston – Office of the Dean

Key Words: Prehospital, gunshot wound, air transport, ambulance transport

Background: While the majority of patients sustaining GSWs receive prehospital care prior to arrival in the ED, no consensus exists to whether there is demonstrated benefit to prehospital care compared to the risk of increased time to definitive care. This study sought to correlate the prehospital care of GSW patients with patient outcomes. We hypothesized that prolonged on-scene times are associated with increased 24-hour and 30-day mortality in GSW patients.

Methods: Upon IRB approval, the Memorial Hermann Hospital trauma registry was queried for patients meeting the inclusion criteria of (1) admitted between 01/01/06 and 12/31/10 and (2) more than 18 years of age. We excluded patients who were (1) less than 18 years of age, (2) pregnant, (3) prisoners, (4) transferred from an outside hospital, or (5) readmissions or follow-ups. The primary outcome evaluated was 30-day survival for air transport, ground transport (ambulance), and private vehicle transport. Secondary outcomes included immediate transfers from ED to OR, hospital length of stay, and discharge status. Univariate analysis was performed for demographics and study outcomes. A multivariate logistic regression model was developed to evaluate whether transport method was associated with increased mortality.

Results: 1069 patients met study criteria (508 arriving by air transport (helicopter), 561 arriving by ground transport (ambulance), and 28 arriving by private vehicle). Compared to ground transport patients, air transport patients were more likely to be white (56% vs. 28%), have a higher injury severity score, ISS (median 16 vs. 9), and have more severe individual head, chest and abdominal injuries, all $p < 0.001$. Air transports were also more likely to be intubated in the field (29.7% vs. 5.3%), pronounced dead on arrival (8.5% vs. 2.0%), and less likely to be discharged to home (58% vs. 80%), all $p < 0.001$. Interestingly, there was no difference between air and ground patients in requiring immediate transfer from ED to the operating room (34.5% v. 34.8%. $p = 0.706$). While Univariate analysis demonstrated a lower survival among those transported by air (72% vs. 88%, $p < 0.001$), this did not remain on multivariate analysis. Multiple logistic regression identified higher arrival GCS (odds ratio 2.43, $p < 0.001$), heart rate (odds ratio 1.02, $p = 0.013$), and systolic blood pressure (odds ratio 1.01, $p = 0.005$) as independent predictors of improved 30-day survival. However, increased severity of head (odds ratio 0.42, $p < 0.001$) and abdominal (odds ratio 0.59, $p = 0.021$) injuries and white race (odds ratio 0.17, $p = 0.002$) were predictive of lower 30-day survival.

For ground vs. private vehicle (POV) transport, POV patients were more likely to be male

(88 vs. 82%, $p=0.005$), Black (68% vs. 42%, $p<0.001$), and less severely injured by ISS. POV patients were less likely to go immediately to the OR from the ED (14.3% vs. 35.8%, $p=0.019$) and had shorter hospital stays (1 day vs. 3 days, $p=0.012$). After controlling for age and injury severity, arrival by POV was not associated with improved survival (odds ratio 1.39, $p=0.717$), nor was it associated with lower survival.

Conclusion: Compared to ground transport, air transport was not associated with improved survival even after controlling for injury severity and arrival vital signs. A well-designed prospective trial is warranted to determine the true benefit of air versus ground transport, with close inspection to the procedures employed in the prehospital setting.

ABSTRACT

Factors predicting fascial closure after damage control laparotomy: The impact of hypertonic saline

MARK M. MIMS

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Bryan A. Cotton

Supported by: Center for Translational Injury Research (CeTIR)

Key Words: Damage control laparotomy, hypertonic saline

Background: The damage control laparotomy (DCL) is a vital tool in treating patients with severe abdominal trauma. However, it carries many possible risks to the patient, especially in the setting of an open abdomen. The purpose of this study was to determine if patients receiving hypertonic saline within twenty-four (24) hours post-operatively achieve higher rates of primary fascial closure within seven (7) days. Additionally, patients' temperature, acid-base balance, coagulation status, and in-hospital fluid and blood product use were also measured.

Methods: Retrospective cohort study of all adult patients undergoing immediate DCL at a Level I trauma center between January 2010 and July 2011.

Results: A total of 67 patients were included in this study. Of these, 53 (79%) received no hypertonic saline and 14 (21%) received hypertonic saline post-operatively. Both groups were similar in demographics, ISS, MOI, blood product use, temperature, and coagulation status. Patients in the hypertonic saline group were more acidotic in the ED (pH 7.12 vs. 7.25, $p=0.006$) and the OR (BE -10 vs. -7, $p=0.012$). Fluid use between groups was similar in the ED and OR but hypertonic saline patients received less crystalloids in the ICU over 24 hours (3.1 vs. 9.0, $p<0.001$) and 48 hours (5.6 vs. 12.0, $p<0.001$). Primary fascial closure at 7 days was different between groups, but did not achieve statistical significance (93% vs. 73%, $p=0.111$).

Conclusion: The use of hypertonic saline in DCL patients was shown in this study to significantly reduce the amount of crystalloid use necessary in the ICU, a risk factor for prolonged open abdomen status. While early primary fascial closure did not reach statistical significance, this may be the result of a Type II error due to small sample size. Future studies will include a larger sample size and the development of a randomized, controlled trial.

ABSTRACT

Admission Rapid Thromboelastography (r-TEG) Predicts Development of Pulmonary Embolism in Trauma Patients

KRISTIN MINEI

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Center for Translational Injury Research

Supported by: Bryan Cotton, M.D. M.P.H.

Key Words: Coagulation, trauma, thromboelastography, pulmonary embolism

Injury leads to dramatic disturbances in coagulation with increased risk of bleeding followed by a hypercoagulable state. A comprehensive assessment of these coagulation abnormalities can be measured and described by thromboelastography. The purpose of this study was to identify if admission Rapid-TEG (r-TEG) could identify patients at risk of developing pulmonary embolism (PE) during their hospital stay. Patients admitted between 09/09-02/11 who met criteria for our highest-level trauma activation and were transported directly from the scene were included in the study. PE defined as clinically suspected and CT-angiography confirmed pulmonary emboli. We evaluated r-TEG values with particular attention to the maximal amplitude (mA) parameter that is indicative of overall clot strength. Demographics, vital signs, injury severity and rTEG values were then evaluated. In addition to rTEG values, gender and ISS were chosen a priori for developing a multiple logistic regression model predicting development of PE. rTEG was obtained on 2070 consecutive trauma activations. Of these, 2.5% (53) developed PE, 97.5% (2017) did not develop PE. Patients in the PE group were older (median age of 41 vs. 33, $p=0.012$) and more likely to be white (69% vs. 54%, $p=0.036$). None of the patients in the PE group sustained penetrating injury (0% vs. 25% in the no-PE group, <0.001). The PE group also had admission higher mA values (66 vs. 63, $p=0.050$) and higher ISS (median 31 vs. 19, $p=0.002$). When controlling for gender, race, age and ISS, elevated mA at admission was an independent predictor of PE with an odds ratio of 3.5 for $\text{mA}>65$ and 5.8 for $\text{mA}>72$. Admission r-TEG mA values can identify patients with an increased risk of in-hospital PE. Further studies are needed to determine if alternative anticoagulation strategies should be employed for these high-risk patients.

ABSTRACT

Surgical Complications in the Treatment of Pediatric Melanoma

PAUL E PALMER, III *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Mary T. Austin, MD MPH, Pediatric Surgical Oncology
Andrea Hayes-Jordan, MD, Pediatric Surgical Oncology

Supported by: The University of Texas Health Science Center at Houston, Department of
Pediatric Surgery

Key Words: pediatric, melanoma, surgery, complication

Objective: Our objective was to characterize the complications associated with the surgical treatment of melanoma in pediatric patients.

Methods: All pediatric melanoma patients (ages <18 yr) treated with surgical intervention at M.D. Anderson Cancer Center between 1992 and 2011 were reviewed. Patients were categorized into one of three treatment groups: Wide Local Excision only (WLE), WLE and Sentinel Lymph Node Biopsy (SLNB), and WLE and Completion Lymph Node Dissection (CLND). Complications examined included lymphedema, wound infection, skin graft failures and other wound-related complications. Groups were compared using a two-tailed Fisher's Exact Probability Test.

Results: 126 patients were identified: 37 patients received WLE only, 48 patients received WLE and SLNB, and 41 patients had WLE and CLND. Surgical complications were significantly increased in the CLND group (31.9%) compared to patients in the SLNB (10.4%) and WLE (18.9%) groups ($p=0.038$). Lymphedema was the most prevalent complication and had a significantly higher incidence in the CLND group compared to the SLNB (28.6% vs. 2.8%, $p=0.01$). Patients who received either SLNB or CLND were more likely to have complications if their procedure was performed in the inguinal region compared to the axillary region (50% vs. 15.8%, $p=0.041$). There were no surgical complications identified in either SLNB or CLND of the neck.

Conclusion: A significantly greater risk of surgical complications was found in patients treated with WLE + CLND compared to treatment with WLE only and WLE + SLNB. Lymphedema was the most prevalent complication overall and occurred more commonly in the patients undergoing CLND in the inguinal region. There was an overall increase in complications associated with inguinal lymph node dissection.

ABSTRACT

Acute Kidney Injury After Acute Type B Aortic Dissection

SAURABH C. PATEL *The University of Texas Medical School at Houston Class of 2014*

Sponsored by: Dr. Anthony Estrera, MD

Supported by: Dept. of Cardiothoracic and Vascular Surgery

Key Words: Acute Type B Aortic Dissection, Acute Kidney Injury

Background: Acute aortic dissection occurs when the media of the aortic wall separates and divides, extending along the aorta for a variable length. Once the “false” lumen becomes pressurized, the compromised “true” lumen may lead to decreased perfusion to any critical vessels arising from the aorta. Acute type B aortic dissections (ATBAD) occur in the descending and/or thoracoabdominal aorta. Acute kidney injury (AKI) may occur after ATBAD, but little is known about the affect of AKI on early and late outcomes after ATBAD.

Methods: Between January 2001 and June 2011, 355 patients presented with ATBAD and were entered into a prospectively collected database. Seven patients (2%) were on dialysis prior to presentation and were excluded from analysis. Clinical variables were obtained, allowing comparison between patients who developed AKI (AKI group: 21%, 73/348) and those that did not (No AKI group: 79%, 275/348). Missing data was obtained from review of patient charts and direct patient contact. Kaplan-Meier was used for survival plots.

Results: The AKI group experienced greater early mortality than the no AKI group, 27% (20/73) vs. 12% (33/275), $p < 0.002$. In addition, the AKI group experienced longer ICU and hospital length of stays (14 ± 12 days vs. 5 ± 4 days, $p < 0.001$, and 19 ± 16 days vs. 12 ± 9 days, $p < 0.001$, respectively). Forty-four percent (32/73) of the AKI group required in-hospital dialysis which was associated with an early mortality of 50% (16/32). Of survivors, only 25% (4/16) required permanent dialysis, and 75% (12/16) were free of dialysis by 4 months. One, 5, and 10 year survival was 50%, 46%, and 46% for the AKI with dialysis group and 87%, 70%, and 65% for the no AKI group, $p < 0.024$.

Conclusion: Acute kidney injury conveys a poor early and late prognosis for patients with ATBAD. A better understanding about the mechanism of AKI is required in order to ultimately provide treatment and possible prevention of the devastating complication during ATBAD.

ABSTRACT

Cytotoxicity of ActiCoat silver dressing on human osteoblasts *in vitro*: A suitable treatment for diabetic ulcers?

ERIK T. PETERSEN *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Catherine Ambrose, PhD, Department of Orthopaedic Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
5 T32 DK007676-19

Key Words: Diabetic ulcer, ActiCoat silver, bone/osteoblasts

Diabetic ulcers are a common, disabling, and potentially fatal complication of diabetes. Antibiotics alone are not sufficient to treat the infections, but a promising new therapy involves the use of continuous-release silver dressings such as ActiCoat. ActiCoat is able to eliminate *Staphylococcus aureus* grown in a biofilm, and anecdotal reports from hospitals have shown promise, but its effects on different types of human tissue have not been well characterized in a lab setting. Previous studies have looked at fibroblasts and keratinocytes, but diabetic ulcers can involve other cell types as well, particularly human osteoblasts (HOBs). A study was designed to 1) establish a cytotoxic profile for HOBs exposed to silver, 2) confirm ability of HOBs to produce mineral matrix post-exposure, and 3) determine whether a dose of silver exists that will eliminate a biofilm of *S. aureus* while remaining inert towards HOBs. HOBs were cultured in lab in osteoblast growth media until 70% confluent, and then incubated with varying amounts of ActiCoat for 24 hours. A resazurin assay was performed to evaluate cell viability, and alkaline phosphatase and total protein assays were performed to evaluate cell functionality. All assays were interpreted on a plate reader to provide quantitative data. A second group of cells was grown in mineralization media and exposed to ActiCoat to determine if the mineral matrix offered any protection against the effects of silver, and a final group of cells was exposed to ActiCoat first and then grown in mineralization media to determine if matrix production occurs post-exposure. Our initial findings are as follows: ActiCoat in excess of 4mg/mL is lethal to HOBs, with the LD50 being approximately 2 mg/mL. Mineral matrix offers no additional protection against ActiCoat, and initial exposure to ActiCoat does not prevent later production of mineral matrix. Quantitative data for the mineralization studies is still being compiled, and we are currently developing a cytotoxic profile for ActiCoat in *S. Aureus* biofilms. We hope to reveal a range of ActiCoat that will spare bone while completely eliminating a biofilm. The experiments should be complete in the near future.

ABSTRACT

Characterization of *MYH11* R247C double-knock in mice

JOHN PHAM

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Dianna Milewicz, MD, PhD, Department of Internal Medicine

Supported by: The University of Texas Medical School at Houston

Key Words: Myosin heavy chain mutation, TAAD, double-knockin mice, SMC

Missense mutations in *MYH11*, which encodes the smooth muscle myosin heavy chain important in the cyclic interaction between thin and thick contractile filaments that contract in response to pulse pressures, have been found enriched in disease cohorts including thoracic aortic dissections, intracranial aneurysms, strokes and other vascular diseases. The most frequent recurrent alteration in *MYH11* was *R247C*. Our data indicates knockin mice harboring this mutation have decreased expression of contractile genes when using a qPCR assay, including *ACTA2*, *CNN*, and *MYH11*. These results were confirmed with a western blot using standard protocol. We confirmed the phenotype of the smooth muscle cells using IF techniques with alpha-actin as a primary antibody. Our results demonstrate that despite the decrease in alpha actin mRNA expression, the actin cytoskeleton architecture was intact. Furthermore, this mutation is found in vascular occlusive disease; it is believed that proliferation may play a pathological role. Explanted cells were treated with BrdU reagent for 24 hours and BrdU incorporation during DNA replication was measured using an ELISA assay. We confirmed that cells homozygous for the *R247C* mutation were more proliferative. Finally, we investigated possible pathways that could be driving SMC proliferation and it appears to be independent of PDGFRb but could involve the MRTF axis and focal adhesion rearrangement.

ABSTRACT

Impact of Morbid Obesity on Therapeutic Outcomes in a Lymphedema Management Program

MELANIE M. PICKETT *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Adelaide A. Hebert, MD, Department of Dermatology

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases 5 T35
DK007676-19

Key Words: Lymphedema, obesity, BMI

Lymphedema develops due to a failure of the lymphatic system to drain protein-rich interstitial fluid during normal capillary filtration. Manual lymphedema drainage (MLD) is a manual massage technique aimed at increasing lymphatic flow and decreasing lymphedema in the extremities. MLD therapeutic success has shown to be impacted by patient body weight, but no BMI has been identified past which MLD will be ineffective. In this retrospective study a correlation between the upper levels of BMI and the outcome of MLD therapy was evaluated, with the goal of identifying the relationship between the two.

Five hundred and nine cases of lower limb lymphedema were reviewed in which patients were treated with MLD between the dates of 2003 and April 2011. Of these, seventy-seven subjects met the criteria for this retrospective analysis, having available data on ethnicity, height, weight, and beginning and ending volumes of the affected limb. Data was charted and analyzed to determine whether a correlation between upper limits of BMI and outcome of treatment existed. Successful treatment was defined as treatment that resulted in a 20% reduction in affected limb volume.

Pearson correlation analysis showed elevated BMI states not to be a significant predictor of MLD success. A strong correlation was found ($C=0.923$; $P<0.0001$) between beginning volume of the affected limb and the change in volume after MLD therapy, however. This result indicates that at higher limb volumes there exists a more positive response to MLD therapy. The relationship between beginning volume of the affected limb and percent reduction in limb volume was also found to be significant. ($C=0.638$; $P <0.0001$). Additionally, results from the logistic regression model reveal that treatment was five times more likely to be ineffective in Caucasian patients compared to non-Caucasian patients, with effectiveness defined as a 20% decrease in affected limb volume.

This data suggests that patient response to MLD therapy is dictated by the severity of fluid accumulation in the limb, rather than patient BMI. While BMI may be an important indicator of success for other therapies, comprehensive evaluations of beginning limb volume rather than BMI are more likely to determine MLD treatment outcomes.

ABSTRACT

Quantification of Anti-Epstein-Barr Virus Antibodies in the CSF of Patients with Multiple Sclerosis

THOMAS POWELL *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: J William Lindsey, MD

Supported by: The Foundation for the Consortium of Multiple Sclerosis Centers

Key Words: Multiple Sclerosis, Epstein-Barr virus

Experimental evidence suggests that the Epstein-Barr virus (EBV) plays some role in the pathogenesis of multiple sclerosis (MS), although the exact role has yet to be elucidated. One hypothesis is that persons affected with MS may have an abnormal immune response to latent EBV infection, which leads to disease. In order to test this idea, Western blots run with EBV antigens were reacted with the CSF of 60 persons, 30 with and 30 without MS. Anti-EBV antibodies in patients' CSF bound to the EBV antigens were then detected using a rabbit anti-human IgG antibody. The relative intensities of signals generated for 14 different bands were then compared and analyzed using KODAK 1D software. In the CSF of patients with MS, there appears to be an increased antibody response to the EBV antigens of molecular weights 360kD ($p=0.029$), 235kD ($p=0.056$), 130kD ($p=0.054$), 77kD ($p=0.069$), and 45kD ($p=0.063$). However, not all of these are statistically significant, and we may need future tests to increase the power of our study and determine whether the antibody responses in MS patients are truly elevated to these antigens. Further studies are also needed to sequence and definitively identify these antigens. When the data from CSF are combined with data from similar experiments done in the serum of patients with and without MS, the results indicate that the immune response to EBV is likely altered in patients with MS.

ABSTRACT

Efficacy of Electroencephalography Neuromonitoring During Carotid Endarterectomy.

MUJTABA A. RAHMAN *The University of Texas Medical School at Houston Class of 2014*

Sponsored by: Kristofer Charlton-Ouw, MD, Department of Cardiothoracic & Vascular Surgery

Supported by: Department of Cardiothoracic & Vascular Surgery

Key Words: Carotid endarterectomy (CEA), electroencephalography (EEG), stroke, shunt

Specific Aims: The objective of this study was to retrospectively assess the outcomes of carotid endarterectomy (CEA) using selective shunting based on electroencephalography (EEG) neuromonitoring versus routine shunting.

Background: The current standard for hemodynamically significant atherosclerotic carotid artery stenosis is CEA for stroke prevention and treatment. EEG is one of several accepted intra-operative neuromonitoring techniques used to determine the presence of brain ischemia during carotid artery clamping. If the EEG shows ischemic changes after carotid clamping, a shunt can be placed (selective shunting). Advocates of routine shunting generally do not require intra-operative neuromonitoring. We assessed the rate of perioperative stroke based on routine or selective shunting.

Methods: The medical records of 100 patients who had CEA were retrospectively reviewed. Group A consisted of 50 patients whose CEA was performed from 1999-2001 using selective shunting based on EEG monitoring. Group B consisted of 50 patients whose CEA was performed from 2008-2011 using routine shunting without intra-operative monitoring. Cox proportional analysis was used to determine the risk factors for perioperative complications.

Results: The total cohort consisted of 52 men and 48 women with a median age of 73.5 (range 42-92). 54% of patients presented with a stroke or TIA. 30-day perioperative complications for Group A included 8% stroke, 0% MI, 14% cranial nerve deficit, 6% hematoma, 4% wound infection, and 0% death. 30-day postoperative complications for Group B included 2% stroke, 2% MI, 6% cranial nerve deficit, 2% hematoma, 2% wound infection and 0% death. There was a difference ($p=0.02$) in perioperative stroke with selective shunting versus routine shunting.

Conclusion: Routine shunting appeared to be protective of perioperative stroke compared to selective shunting with EEG neuromonitoring. Larger studies are needed to confirm these results.

ABSTRACT

Prevalence of Vitamin D deficiency in Patients who Have Undergone Total Hip Arthroplasty- A Retrospective Chart Review.

HEATHER RAYMOND The University of Texas Medical School at Houston Class of 2014

Sponsored by: Ken Mathis

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
5 T32 DK007676-19

Key Words: Vitamin D Deficiency, total hip arthroplasty

Background:

Vitamin D deficiency is becoming more apparent in the general population. At the same time, more information is being obtained as to the various roles of vitamin D in human health and disease. More research is needed in order to clearly define the role and effects of vitamin D on humans. Bone health can possibly be used as an indicator for metabolic vitamin D adequacy and deficiency. In addition, looking at the effects on patients treated for vitamin D deficiency will determine if vitamin D supplementation is an easy, inexpensive method to prevent complications after orthopedic procedures.

Methods:

This will be a retrospective study reviewing patients who have undergone total hip arthroplasty from January 2000 to the present. Blood tests have already been drawn and tested for 25-hydroxyvitamin D levels. The prevalence rate of vitamin D deficiency in patients undergoing total hip arthroplasty will be examined. Patients will be divided based on their underlying disease state leading to total hip arthroplasty, including fracture, osteoarthritis, or rheumatoid arthritis. Information collected includes age, sex, surgery date, disease state, vitamin D level, and any associated complications. Data will be analyzed using Chi-square analysis.

ABSTRACT

Deletion of Astroglial Bone Morphogenetic Protein Receptor Ia After Ischemic Stroke Reduces Gliosis and Worsens Neurological Outcomes

RANIER G. REYES

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Qilin Cao, MD, The Vivian L. Smith Department of Neurosurgery

Supported by: NIH R01 NS0619751 (Q.L.C), and TIRR foundation through Mission Connect (Q.L.C).

Key Words: gliosis, BMPRIa, stroke recovery

Reactive gliosis, which is characterized by the hypertrophy and hyperplasia of astrocytes, is a common reaction to neurological insults such as trauma and stroke. However, the functions of astrogliosis and the mechanisms by which it is regulated are poorly understood; the process has demonstrated both harmful and beneficial effects for recovery after injury. This study will look at the functions of astroglial bone morphogenetic protein receptor Ia (BMPRIa) signaling in gliosis and the consequential neurological outcomes after ischemic stroke.

We used the Cre recombinase-loxP system under the regulation of the human GFAP promoter to conditionally delete BMPRIa from astrocytes and compared these subjects against wild-type control subjects. Both groups received a transient middle cerebral artery occlusion for 45 minutes. Subjects were tested for neurological function at days 1, 3, 5, and 7 post-operatively using the Neurological Deficit Score and the Rotarod Performance Test. Additionally, specimens were collected for histological and immunohistochemistry staining on day 7 and analyzed for infarct volume, BMPRIa expression, and immune cell proliferation.

Our results show that the knockout mice demonstrated (1) a down-regulation, but not complete absence, of BMPRIa receptors on astrocytes, (2) a decreased level of hypertrophy and hyperplasia, (3) an excessive infiltration of inflammatory cells into the peri-infarcted areas, (4) a statistically significant increase in infarction volume, and (5) significantly lower scores in both the Neurological Deficit Score and Rotarod Performance Test.

This study concludes that BMPRIa signaling is an important regulator of reactive astrogliosis after ischemic stroke. These reactive astrocytes also play an important role in restricting the spread of inflammation cells into the peri-infarct tissue and in preserving neurological function acutely after stroke. Thus, BMPRIa signaling in the astrocytes proximal to the infarct core may prove to be an important target for stroke treatment and recovery.

ABSTRACT

An Evaluation of the Efficacy of Using a Non-Adherent Dressing to Achieve Hemostasis in Burn Surgery

MICHAEL J. ROKYTA *The University of Texas Medical School at Houston Class of 2014*

Sponsored by: David J. Wainwright, MD, Division of Plastic and Reconstructive Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
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Key Words: hemostasis, burns, non-adherent dressing, Telfa

BACKGROUND: Bleeding following burn wound excision or skin grafting can be severe, resulting in hemodynamic instability and the need for blood transfusions. Patients with diabetes are particularly prone to cardiovascular instability and compromised wound healing in these instances. This study evaluated a non-adherent topical dressing (Telfa) in achieving hemostasis. Our hypothesis was that Telfa's non-adherent properties would reduce blood loss.

METHODS: Patient data included age, sex, injury type, days post injury, and procedure type. Either a skin graft donor or burn excision wound site was created. A Telfa pad immersed in a thrombin-epinephrine (T/E) solution was placed over one side of the site while an adjacent area was covered with a T/E soaked laparotomy sponge. After 10 minutes the dressings were removed and a series of photographs taken at defined intervals. Photographs were evaluated by three blinded observers for differences in degree of bleeding between the two sites.

RESULTS: Six patients with 21 sites were evaluated. Under Telfa, 12 (57%) were judged to have less bleeding. When sorted on degree of bleeding (minimal, moderate, extensive), 10/11 sites with moderate bleeding showed reduced blood loss with Telfa. When there was minimal (1/6) or extensive (1/4) bleeding, Telfa demonstrated less of an improvement. No differences were seen when bleeding was evaluated based on age, sex, procedure type, or days post injury.

CONCLUSION: There was no difference in severity of bleeding when Telfa was used in this study. However, when subpopulations were evaluated certain factors appeared to influence the results, indicating there may be certain subgroups or circumstances where Telfa may produce a positive response. To elucidate this difference the study is ongoing to increase the sample size.

ABSTRACT

Effects of Low Testosterone on Fracture Healing

ANDREW M. RYON

The University of Texas Medical School at Houston

Class of 2014

Sponsored by: Catherine Ambrose, PhD, Department of Orthopaedics

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
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Key Words: testosterone, fracture, hypogonadism

Fractures are responsible for hospitalizations, disability, and loss of independence. It is critical to provide the most appropriate therapy to ensure a quality union of bone to prevent these adverse outcomes. However, low testosterone has been shown to contribute to a lower bone density and maybe even alter fracture healing. The goal of this study is to evaluate the effects that low testosterone have on fracture healing by first setting up an animal model. 10 male Sprague Dawley rats, that were evenly separated into a control group and a castrated group, underwent surgery to place intramedullary K wire into the right femur. After the rod placement, a fracture device was used to create a mid-shaft, transverse fracture. 3 Weeks later, the rats were sacrificed and at that time a blood sample, X ray, and DEXA scan were taken to confirm the low testosterone and evaluate the callus formation of the femur. The blood sample and DEXA confirmed that the rat model was an appropriate model because low testosterone rats in fact had a significantly lower bone mineral density. However, X rays showed they every rat did not have a fracture. This may have been due to the slightly bigger rats used in the study compared to other published studies or a flawed design in the fracture device used in our study. Taken what was learned in this study, future adjustments are going to be made to the device and the study will be repeated. In conclusion, the model is an appropriate model to represent a hypogonadal rat, but the fracture device needs to be adjusted for further testing.

ABSTRACT

Glutamine Mitigates Injury in the Postischemic Gut

ARITRA SEN

The University of Texas Medical School at Houston Class of 2014

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

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases R01 GM077282

Key Words: Syndecan-1, glutamine, ischemia/reperfusion

INTRODUCTION: Syndecan-1 is the primary trans membrane proteoglycan on intestinal epithelial cells and is crucial to maintaining an intact intestinal barrier. We have shown clinically and in the laboratory that enteral glutamine is protective to the post ischemic gut by protecting the intestinal barrier. **We therefore hypothesized that enteral glutamine would mitigate damage in the post ischemic gut via syndecan-1.**

METHODS: A well characterized model of intestinal ischemia/reperfusion (I/R), superior mesenteric artery occlusion, was applied to syndecan-1 knockout (KO) and wild type (WT) mice. Both WT and KO mice underwent intestinal ischemia for one hour ± glutamine (60 mM via enteral sac), and compared to shams. After six hours of reperfusion, tissue was harvested for the following assays: Intestinal injury was measured by placing Alexafluor 680 dye into an intestinal sac and calculating clearance using the In Vivo Imaging System (IVIS). FD4 permeability, one indices of gut barrier function, was assessed using the everted sac technique to calculate the mucosal to serosal clearance. Finally, myeloperoxidase (MPO) activity was measured to assess intestinal polymorphonuclear leukocyte (PMN), an index of inflammation. Results are presented as mean ± SEM and analyzed by ANOVA with post hoc Tukey, n=3-4/group, p<0.05 significant.

RESULTS: As shown in Table 1, intestinal injury, permeability, and inflammation were significantly increased after gut I/R in WT mice but further worsened in syndecan-1 KO mice. Glutamine attenuated these parameters of intestinal damage in WT, but not KO mice.

CONCLUSION: These data suggest that syndecan-1 plays an important role in glutamine's protection of the post ischemic gut. As this is the first report of an association between glutamine and syndecan-1, the mechanism of protection is unclear. Current microarray studies are in progress to begin to investigate this important and novel observation.

Groups	Permeability (ng/cm ² /min)	MPO (mU/ml)	Fluorescence Intensity
WT sham	28.3 ± 1.6 a	0.24 ± 0.01 a	1.9x10 ⁸ ± 2.2x10 ⁷ a
KO sham	33.8 ± 3.4 a	0.27 ± 0.01 a	1.7x10 ⁸ ± 3.0x10 ⁷ a
WT IR	87.8 ± 2.5 b	1.25 ± 0.12 b	3.2x10 ⁸ ± 1.4x10 ⁷ b
KO IR	119.8 ± 9.0 c	1.83 ± 0.13 c	4.8x10 ⁸ ± 4.3x10 ⁷ c
WT IR glut	59.2 ± 9.03 d	0.77 ± 0.06 d	2.6x10 ⁸ ± 4.6x10 ⁷ d
KO IR glut	116.8 ± 9.92 c	1.54 ± 0.13 c	4.6x10 ⁸ ± 5.1x10 ⁷ c

ABSTRACT

Assessment of the Implementation of a Surgical Preoperative Checklist

CASEY E. SENTER *The University of Texas Medical School at Houston Class of 2014*

Sponsored by: KuoJen Tsao, MD, Department of Pediatric Surgery

Supported by: The University of Texas Health Science Center at Houston, Department of Pediatric Surgery

Key Words: Surgical timeout, surgical safety checklist, compliance

Introduction: Peri-operative checklists are mandated by many hospitals based on the reduction in morbidity and mortality seen with utilization of the World Health Organization's (WHO) "Surgical Safety Checklist." Although an adapted peri-operative checklist was implemented within our hospital system without formal system-wide training, compliance with the checklist is reported to be 100%. We hypothesize that compliance does not measure fidelity of implementation, in that all items on the checklist are not performed as intended. **Methods:** Over a 10 week period, a prospective study was performed evaluating the completion of the 12 pre-incision components of the surgical checklist. Pediatric surgical operations were randomly selected for direct observation. Emergent cases were excluded. The evaluated checkpoints include essential parties present, team members identified, patient name/procedure verified, incision site confirmed, team member concerns addressed, administration of appropriate antibiotics, essential imaging displayed, anticipated case length stated, anticipated risk of blood loss stated, and sterility indicator confirmed. **Results:** 142 pediatric surgical cases were observed. Hospital data demonstrated 100% compliance with the pre-incision phase of the checklist for these cases. Our observation revealed that in 3.5% of cases the checklist was not performed at all. None of the cases completely executed all items on the checklist, and the average number of checklist items performed in the observed cases was five. The most commonly performed checkpoints were the confirmation of patient name and procedure (99.3%) and administration of antibiotics (88.1%). The rest of the checkpoints were performed in less than 60% of cases. **Conclusions:** These data show that despite the 100% documented completion of the pre-incision phase of the checklist, most of the individual checkpoints are not routinely performed. These findings demonstrate lack of fidelity in implementing the checklist, which may be a reflection of the poor strategy in disseminating and implementing this patient safety practice. Failure of the system to measure the appropriate implementation metrics and to fully adopt the evidence-based intervention could lead to failure to achieve the intended outcomes.

ABSTRACT

Evaluating the Efficacy of Using Circulating Tumor Cells to Monitor Disease Progression in Castrated Males with Prostate Cancer

PARTH K. SHAH

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Robert J. Amato, DO, Department of Oncology

Supported by: Robert J. Amato, DO, Department of Oncology

Key Words: Prostate cancer, circulating tumor cells, hormone sensitive

Purpose

Prostate cancer is the most frequent non dermatologic cancer among U.S. males. A new approach, the CellSearch system, based on the detection of circulating tumor cells (CTCs) as a marker for disease progression, has been approved recently by the Food and Drug Administration. The primary objective of this study was to correlate CTCs to clinical progression of castrated prostate cancer patients based on PSA levels and metastasis.

Methods

A total of 62 men still responsive to hormone ablation therapy, indicated by testosterone levels < 50 ng/dl were identified retrospectively via chart. Baseline data along with number of CTC's (number per 7.5 mL) was documented, as well as pertinent laboratory and radiologic studies done at the time of CTC collection.

Summary of the results

The mean CTC count of patients that had undergone surgery, surgery + XRT, or XRT was 0.13, 1.56, and 22, respectively. OS was longer in patients with combination therapy, 8.78 yrs, compared to surgery, 7.13 yrs and XRT, 7.07 yrs. Patients with Gleason score 8 had greater CTC levels, 125.57 compared to those with Gleason score 10, who had CTC levels of 16. Lower CTC levels, 10.67 vs 33, were present in patients with multiple metastatic sites, compared to those with only bone metastasis.

Conclusion

Patients in whom CTC levels should be highest, for example those with multiple metastasis sites and those with high Gleason actually have lower CTC levels than those patients with less advanced disease. Interestingly, the patients who have undergone combination primary treatment of surgery and radiation show both a lower mean CTC count and also increase in overall survival, thus suggesting the increased efficacy of combination therapy over single therapy.

ABSTRACT

Prolonged cocaine use and its association with early repolarization and severe bradycardia

DANIEL SHOHAM *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: F. Gerard Moeller, MD, Department of Psychiatry
 Anne H. Dougherty, MD, Department of Cardiology
 Jyoti Sharma, MD, Department of Cardiology

Supported by: Saltzberg Summer Research Fellowship

Key Words: bradycardia, early repolarization, cocaine

Introduction: Cocaine is an abused drug that is associated with cardiovascular diseases such as myocardial infarction and stroke. What is currently unknown is cocaine's effect on the conduction pathway of the heart. This study focused on determining a relationship between the years of cocaine use and cardiovascular conduction measures. Methods: 244 subjects (mean [S.D.] age 42.24 [8.49]) participated in this study, and were evaluated via electrocardiogram (EKG) reading, comprehensive physical, and self-report surveys that determined their personal drug use. Results: 52.0% of the subjects had bradycardia (Heart Rate < 60 bpm). 21.7% of the subjects had early repolarization readings from their EKG. This compares to previous studies where overall prevalence of early repolarization was 0.9%, with 4.4% in African-American males the highest subset prevalence. Baseline heart rate correlated negatively with number of years of cocaine use, but was insignificant after adjusting for age. 26.4% of subjects with early repolarization had severe bradycardia (HR <50 bpm) compared to the 11.0% without early repolarization ($p = .005$). Subjects with the greatest longevity of cocaine use had both early repolarization and severe bradycardia with declining years of use for only severe bradycardia, only early repolarization, and neither respectively. Conclusion: The results suggest that there is a trend for bradycardia and early repolarization with increased longevity of cocaine use. Further analysis should be done to see if the conduction issues resolve with cocaine abstinence.

ABSTRACT

A Tablet Based Stimulus and Response System for Cognitive and Behavioral Experiments

YUJAN SHRESTHA *The University of Texas Medical School at Houston* Class of

Sponsored by: Anne Sereno, PhD

Supported by: The University of Texas Medical School at Houston

Key Words: iPad, Autism, TBI, Screening, Diagnostics

Reaction times (RT) and error rates (ER) on simple behavioral tasks have been shown to be valuable diagnostic tools. The iPad and other tablets offer a portable tool which could be used to gather diagnostic data from a wide variety of patient populations (e.g. Autism, TBI) in many different situations. However, these portable devices are typically unable to record data with the temporal resolution of other less portable devices thus they may not be appropriate for the detection of subtle differences in behavior that are often diagnostically relevant. An iPad based tablet was used to create a mobile response time measuring platform complete with simple behavioral tasks and collection of behavioral measures (e.g. RT & ER). Using special signal processing techniques, a temporal resolution on the order of 0.2 ms was achieved, comparable to expensive data acquisition systems. Acoustic and optical techniques were employed to methodically crosscheck and verify timing data extracted from the iPad. With simple alterations to the iPad it was found that accurate and precise reaction times could be collected. The utility of such a portable and user friendly diagnostic device in contexts such as football games or classrooms has exciting implications for rapid and universally accessible screening and diagnostic tools.

ABSTRACT

Selection of a Thioaptamer Targeted to Human IgE

ANGELA R. SUNG

The University of Texas Medical School at Houston Class of 2014

Sponsored by: David Gorenstein, Ph.D.
Department of NanoMedicine and Biomedical Engineering

Supported by: David Gorenstein, Ph.D.
Department of NanoMedicine and Biomedical Engineering

Key Words: Thioaptamer, immunoglobulin E, allergy

Immunoglobulin E (IgE) plays a major role in type I hypersensitivity allergic reactions. IgE binds to FcεRI receptors on the surface of mast cells. Binding of an allergen to surface IgE leads to mast cell degranulation, which cause the typical symptoms of allergies. One way to treat allergies is to target IgE and prevent its binding to FcεRI, disrupting the pathway for mast cell degranulation. Aptamers are short oligonucleotides specially selected to bind a target with high affinity and specificity. Thioaptamers are aptamers with sulfur groups inserted in the DNA backbone that are particularly resistant to nuclease degradation, making them ideal for inhibiting the IgE-FcεRI interaction.

The purpose of this project was to select a thioaptamer from a random library that binds with high affinity to IgE. The initial library consisted of about 10^{17} random single-stranded DNA sequences. Each sequence consisted of a central 30 bp random region flanked on both sides by constant 20 bp primer regions for replication. The library was PCR amplified using dATP(αS) instead of dATP to create the thioaptamers. The thioaptamers were then incubated with the IgE target protein and those that bound to IgE were collected and reamplified. The selection cycle was repeated five times using successively higher DNA:protein concentration ratios to identify the sequences with the highest IgE binding affinities.

The selected aptamers were sequenced, but no common patterns or motifs were identified after five cycles. Further selection will be performed until a thioaptamer with optimal binding has been identified. Binding studies will then be performed to determine the binding constant. The ability of the thioaptamer to inhibit the IgE-FcεRI interaction will also be analyzed.

ABSTRACT

Properties of spontaneous oscillations in nociceptors that may drive chronic pain after spinal cord injury

AARON J. THOMAS *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Edgar Walters, Ph.D., Department of Integrative Biology and Pharmacology

Supported by: The University of Texas Medical School at Houston

Key Words: SCI, nociceptors, spontaneous oscillations

Spinal cord injury (SCI) causes chronic, intractable pain in many patients. It was discovered recently that this pain is associated with the spontaneous generation of action potentials (spontaneous activity or SA) in the cell bodies of nociceptors (sensory neurons that detect injury and/or inflammation) (Bedi et al., *J Neurosci* 30:14870, 2010). SA in nociceptors may therefore be a promising therapeutic target for treating chronic neuropathic pain, but the mechanisms underlying the generation of SA in nociceptors are unknown. We hypothesize that in nociceptors, as previously described in low threshold mechanosensory neurons (Amir et al., *J Neurosci* 19:8589,1999), SA is generated by spontaneous oscillations of resting membrane potential (RMP). To begin to test this hypothesis, I have defined basic properties of subthreshold spontaneous oscillations (SOs) recorded with whole-cell patch methods from presumptive nociceptors (small dorsal root ganglion neurons) 1 day after dissociation performed 1 to 5 months after SCI or control procedures (sham surgery or no treatment) in adult male rats. I found that the amplitude of SOs was significantly larger in neurons exhibiting SA than in silent neurons. SO amplitude was significantly correlated with resting membrane potential (RMP) -- increasing with depolarization -- and SA neurons had significantly depolarized RMP compared to silent neurons. After controlling for RMP, SO amplitudes were not significantly different in neurons from SCI and control animals. These data indicate that SCI increases SO amplitude in nociceptors (thereby increasing SA), not by a direct action on SOs, but instead by chronically depolarizing a population of nociceptors that exhibit voltage-sensitive SOs. This suggests that drugs that selectively hyperpolarize nociceptors might be a useful treatment for chronic neuropathic pain produced by SCI and perhaps other conditions.

ABSTRACT

Modulation of Microglia by Multipotent Adult Progenitor Cells after Traumatic Brain Injury

CHELSEA THOMAS *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Charles S. Cox Jr., Department of Pediatric Surgery

Supported by: National Institute of Neurological Disorders and Stroke
grant # 5 T35NS064931 02

Key Words: TBI, MAPC, microglia, M1, M2, CD86, CD206

Traumatic brain injury (TBI) results in inflammation and cell death. As a result, TBI can cause cognitive, physical and behavioral deficits that are dependent on the severity and location of the injury. Immune responses are key regulators of TBI-induced alterations in the central nervous system. One key component of the immune response is microglia. In these experiments, we are investigating interactions of multipotent adult progenitor cells [MAPC (Athersys, Inc)] and splenocytes to attenuate the immune response of microglia (pro to anti-inflammatory: M1 to M2) after TBI. Specifically, antibodies to CD86 and CD206 were used to assess the ratio of M1 and M2 phenotypes respectively using flow cytometry and immunohistochemistry. For the *in vivo* experiments, MAPC treatment was administered 2 and 24 hr after injury. Microglia harvested 48 and 120 hr after injury showed a significant increase in the M2:M1 phenotype when compared to microglia from untreated animals. For the *in vitro* experiments, isolated microglia were stimulated with Lipopolysaccharide (LPS). They were then incubated with supernatant derived from MAPC in direct contact with stimulated splenocytes for 72 hr. There was a significant increase in the M2:M1 phenotype of MAPC media cultured microglia when compared with LPS stimulated microglia alone when analyzed with flow cytometry. Interestingly, immunostaining of the cells showed a significant decrease in cells dually labeled for M1 and M2 and a significant increase in the cells labeled for M2 alone after treatment with supernatant derived from MAPCs in direct contact with splenocytes.

These results suggests that there is a secreted soluble factor(s) due to the interactions between the spleen and MAPC that modulates the microglia phenotype from pro to anti-inflammatory. MAPC, a primitive form of bone marrow derived progenitor cells modulate the systemic inflammatory response [via the spleen (Walker 2011)] that significantly alters the resident microglia/macrophage populations from M1 to M2. Delineating the mechanisms that modulate the pro to anti-inflammatory state of microglia with MAPC treatments is vital in attenuating the harmful effects of TBI. MAPC therapy, one day may be administered to patients immediately after TBI to help aid in the recovery process.

ABSTRACT

Utility of Urinary Biomarkers in Assessing Risk of Renal Failure in Subjects Occupationally Exposed to Petrochemicals

CLINTON J. THURBER *The University of Texas Medical School at Houston* Class of 2014

Sponsored by: Donald A. Molony, M.D., Dept of Internal Medicine

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
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Key Words: petrochemical, CKD, biomarker, occupational

Due to the prevalence of petrochemical-based energy use in Houston and elsewhere, there is a sizable workforce class necessarily exposed to significant levels of petrochemicals on a regular basis. Further, as petrochemical energy is utilized and consumed in a wide variety of settings, these compounds may expose nearby residents and laypeople. As chlorinated hydrocarbon exposure leads to chronic kidney injury, our purpose is to determine correlation between occupational petrochemical exposure and chronic kidney injury outcome using changes in baseline urinary biomarker levels over time and at various exposure levels as a primary measuring device. We will recruit 44 subjects occupationally exposed to petrochemicals and 44 age- and gender-matched control subjects from the same neighborhood as the employees. Subjects will fill out a pre-shift and post-shift survey detailing their exposure, and subjects will donate blood and urine samples before beginning a work shift and a urine sample at the conclusion of their shift at a nearby dialysis center. Samples will be analyzed for biomarker presence via ELISA/EIA assays. Relative to a non-exposed control group, we expect demonstration of group-specific risk will be evidenced by faster and more identifiable progression of biomarkers, with concurrent lower eGFR. We also expect that changes in biomarker level over time will be directly correlated with duration and intensity of exposure. Such progression may establish biomarker level progression as more sensitive than current conventional methods, may allow estimation of absolute risk associated with various biomarker levels, and may establish grounds for safety measures to be taken to decrease ensuing occupational exposure, thereby alleviating chronic renal injury.

ABSTRACT

Initial Experience with Radical Paraclavicular Thoracic Outlet Syndrome Decompression

MOHAMMAD A. TOLIYAT *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Ali Azizzadeh, MD, Department of Cardiothoracic and Vascular Surgery

Supported by: Ali Azizzadeh

Key Words: Thoracic Outlet Syndrome, decompression

Objective: Thoracic outlet syndrome (TOS) is a constellation of signs and symptoms caused by compression of the neurovascular structures in the thoracic outlet. These structures include the brachial plexus, the subclavian vein, and the subclavian artery resulting in neurogenic (N), venous (V), and arterial (A) types of TOS, respectively. The purpose of this study was to evaluate the outcomes of surgical decompression for TOS.

Methods: A retrospective review of medical records for patients who underwent surgical decompression for TOS at Memorial Hermann Hospital from 8/2004 to 6/2011 was performed. Primary outcomes were assessed according to Derkash's classification as excellent, good, fair, and poor. Secondary outcomes included complications and length of stay.

Results: 40 paraclavicular decompression operations were performed on 36 patients (16 males) with thoracic outlet syndrome. The mean age was 36.5 years (range 15 - 68). Bilateral decompression was performed on 4 patients. A previous history of trauma was present in 22.2%. Presenting symptoms were neurologic in 47.5% of cases, arterial in 12.5%, and venous in 40%. Two patients presented with recurrent symptoms after previous first rib resection at another institution. A paraclavicular approach was used for all decompression procedures, which includes complete anterior and middle scalenectomy, brachial plexus neurolysis, and partial (52.5%) or complete (35%) first rib removal. Mean follow-up was 10.3 months (range 0.2 - 57.1). Functional outcomes were excellent, good, fair, and poor in 74.4%, 15.4%, 10.3%, and 0% of cases, respectively. One patient was lost to follow up. Two patients with incomplete relief of symptoms after paraclavicular decompression underwent pectoralis minor decompression. No patients experienced injury to the long thoracic nerve or phrenic nerve. Four patients underwent hematoma evacuation and 1 patient experienced a lymph leak postoperatively. The mean length of stay was 4.4 days after the operation.

Conclusions: In our experience, radical paraclavicular decompression can provide safe and effective relief of neurological, venous, and arterial TOS symptoms. Functional outcomes were excellent or good in 89.8% of patients with minimal complications.

ABSTRACT

Evaluating Circulating Tumors Cells and Current Markers of Prostate Cancer in a Castrate-Resistant Prostate Cancer Population

KAREN TORRES

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Robert Amato, DO, Department of Oncology

Supported by: Robert Amato, DO, Department of Oncology

Key Words:

Background: Prostate cancer is the second leading cause of cancer death in men in the United States. It is estimated that in 2011 240,890 new cases of prostate cancer will be detected and 33,720 deaths will occur from prostate cancer.¹ The men who die from prostate cancer succumb to a progressive disease despite hormone treatments, and are thus determined to have castration-resistant prostate cancer. (CRPC). CRPC can remain hormone-driven despite androgen deprivation.² A contemporary laboratory method used to trace circulating tumor cells (CTCs), cells from solid tumors shed into the blood stream, may provide a way to better evaluate tumor progression, long-term prognosis, and aid in the identification of therapies most likely to reduce the risk of recurrence in individual patients.³ This study was designed to identify associations between CTCs and currently used indicators of CRPC. Such indicators include PSA, Gleason score, and radiographic evidence of disease in a castrate-resistant population. We predict that the patients with more advanced castrate-resistant disease involving more metastatic sites will demonstrate more CTCs retrieved. By profiling CTCs in conjunction with other indicators in subsets of CRPC patients we will be able to further understand the use of CTCs as a marker for cancer progression.

Methods: 68 men were identified as castration-resistance prostate cancer patients as they had previously been treated with androgen ablation therapy and subsequently presented with progressive prostate cancer before recovery testosterone levels. Progressive prostate cancer was defined as having a rising PSA or radiographic findings of metastatic disease in soft tissue or bone. Data was collected from the patients' electronic medical record correlating to the dates of their CTC collection.

Results: Of the 68 castrate-resistant were divided by the initial therapy received. The average overall survival for these initial therapy subgroups were 22.80 months, 19.13 months, 18.84 months for initial surgery, radiation, and chemotherapy, respectively. All men had undergone a variable amount of cytotoxic therapies, with 50% of the men undergoing at least a 3rd line therapy. In addition, among the 34 men who presented with metastatic disease in lymph nodes, bone and other soft tissue sites, only 17 (50%) had ≥ 5 CTCs collected (see Table 1). During the time of CTC collection 16 men who underwent surgery, 9 who underwent radiation, and 13 who had no initial treatment had PSA elevations; however, only 7 (44%), 5 (56%), and 6 (46%)

men in the surgery, radiation, and no initial therapy subgroups, respectively, had ≥ 5 CTCs retrieved (see Table 2).

Conclusion: Currently CTCs appear to have certain limitations in CRPC as those men with rising PSAs or metastatic disease were hypothesized to have more collections of CTCs. However, this research model is limited due to a relatively small patient sample. More sophisticated and accurate models are needed to draw any correlations from this data. Thus, further study in the utilization of CTCs is needed.

ABSTRACT

Outcomes of Treatments for Acute Critical Limb Ischemia

ASMI TRIVEDI

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Dr. Kristofer Charlton-Ouw

Supported by: Dept. of Cardiothoracic and Vascular Surgery

Key Words: Acute Critical Limb Ischemia, Thrombectomy, Thrombolysis

Background: Acute Critical Limb Ischemia (ACLI) is a critical condition in which the blood flow to a limb suddenly decreases, affecting its viability. In this study we compared two treatment options: catheter-directed thrombolysis and open surgical thrombectomy. Ancillary procedures, such as leg fasciotomies, are often necessary. We identified risk factors for decreased limb function after treatment for ACLI.

Methods: We retrospectively reviewed ACLI patients in our department from 1999 to 2011. Patients were classified according to viability at presentation into Rutherford Class I, IIa, IIb, or III. Class I and II represents patients with potentially salvageable limbs. Based on the severity of ischemia, patients were offered either percutaneous catheter directed thrombolysis or surgical thrombectomy. Class III limbs were considered non-viable and were offered primary amputation.

Results: Of the 59 patients treated for limb ischemia during the study period, 56% were male and 44% were female. 12.5% were Class I, 10.7% were Class IIA, 33.9% were Class IIb, and 42.8% were Class III on admission. The overall in-hospital mortality was 4% and was not significantly different between groups. The limb salvage rate was 89%. Adjunctive procedures were required in 21% of which 58% were fasciotomies. 64% of patients were able to walk without assistance upon discharge ($p < .043$). Mean length of stay was 10.3 days. Limb salvage was 86% in the thrombolysis group and 88% in the surgical thrombectomy group.

Conclusion: ACLI is a vascular emergency where high limb salvage rates can be achieved using a combination of open and endovascular therapies. Fasciotomies are frequently required to treat or prevent compartment syndrome.

ABSTRACT

Fractures at Diagnosis in Infants and Children with Osteogenesis Imperfecta; a single institution experience

MELANIE VETTIMATTAM *The University of Texas Medical School at Houston* Class of 2014

Sponsored by: Christopher Greeley, MD, Department of Pediatrics

Supported by: Department of Pediatrics

Key Words: Osteogenesis Imperfecta, child abuse, fractures

Infants and children with unexplained fractures are often evaluated for child physical abuse. During the evaluation process the possibility of Osteogenesis Imperfecta (OI) is commonly entertained. We sought to characterize the fracture patterns in infants and children with OI prior to diagnosis. We performed a retrospective chart review of a cohort of infants and children under 18 years of age who have the diagnosis of OI (any type).

We identified 68 infants and children with OI: 23 (33.8%) type 1, 1(1.5%) type 2, 17(25.0%) type 3, 24(35.3%) type 4 and 3(4.4%) unknown type. The range of age at diagnosis was from prenatal to 13 years old with 29(42.6%) being diagnosed prenatally or at delivery and 14(20.6%) being diagnosed after 4 years of age. Forty-nine (72.0%) were diagnosed solely on clinical grounds, without genetic or fibroblast confirmation. The number of fractures identified at diagnosis ranged from 1 to >37 fractures. Eighteen (26.5%) infants were diagnosed after 1 week of age but prior to 12 months of age. None of these infants had more than 2 fractures at diagnosis.

In infants with unexplained fractures between 1 month and 12 months who have either rib fractures or greater than 2 fractures OI would be an unexpected explanation. Additionally, the diagnosis of OI can reliably be made in the absence of genetic or fibroblast testing.

ABSTRACT

Thromboelastography, Clot Subtype, and Response to Therapy in Acute Ischemic Stroke

ERIC T. WARD

The University of Texas Medical School at Houston Class of 2014

Sponsored by: James Grotta, MD, Department of Neurology

Supported by: National Institute of Neurological Disorders and Stroke, 5T35NS064931-02

Key Words: Thromboelastography, fibrinolysis, hyperdense artery sign, blooming artifact

Introduction/Background: The treatment of acute ischemic stroke (AIS) is based on lysis of clots using tissue plasminogen activator (tPA), but tPA does not lyse all clots and little is known about what predicts therapeutic success. Thromboelastography (TEG) measures the clotting properties of venous blood, and previous studies using TEG have shown that some AIS patients are hypercoagulable in part based on the balance of thrombin generation and fibrin-platelet matrix strength of the clot. Imaging can distinguish between fibrin-platelet rich “white” clots and thrombin generated “red” clots which demonstrate hyperdense arteries on CT or “blooming artifact” on gradient echo MRI. To date, there has been no correlation between TEG obtained on venous blood and the composition of clots in AIS patients. In this study, we hypothesized that there is an association between TEG values (SP, R, Delta, K, Angle, MA, G, and LY30) measured prior to treatment with tPA and appearance of clot on radiographic imaging and stroke subtype. Furthermore, we looked for a relationship between TEG and response to tPA as measured by clinical improvement on the NIH Stroke Scale (NIHSS), arterial recanalization, and change in TEG values after tPA.

Methods: Patients presenting to the emergency department within 3 hours of symptom onset were enrolled. Blood was collected for TEG analysis upon arrival and 10 minutes after tPA bolus. CT and MRI results at admission and 36 hours were examined for the presence of a hyperdense artery sign or blooming artifact. Stroke subtype data were collected from an in-house registry. Recanalization was determined radiographically from CTA, MRA, or TCD results, and also clinically if the NIHSS score fell by 8 or more points or declined to 0 or 1 by 36 hours. Results for clot appearance and rapid clinical improvement were analyzed using a t-test, stroke subtype and arterial recanalization using ANOVA, and Δ TEG values using a Spearman correlation and Mann-Whitney U-test.

Results: 61 patients were included in the study, of whom 55 had complete pre-tPA TEG results. Stroke subtypes were classified as: cardioembolic (N=21), large artery atherosclerotic (N=8), small vessel occlusive (N=9), or other (N=23). Patients with either a hyperdense artery or blooming artifact were found to have significantly lower pre-tPA Delta values (0.47 vs. 0.71; $p=0.02$) consistent with greater thrombin generation (“red” clots) in such patients. However, we found no association between pre-tPA TEG and stroke subtype, or post-tPA arterial

recanalization or rapid clinical improvement. Additionally, we found no association between clot subtype, as measured by the pre-tPA G and Delta values, and the degree of fibrinolysis after tPA, as measured by the post-tPA LY30 value.

Conclusions: TEG from venous blood in AIS patients may help define the type of clot obstructing the cerebral artery but based on this small sample cannot predict clot lysis or clinical response to tPA. Further study of a larger patient sample is needed.

ABSTRACT

Outcomes for Hybrid Repair of Aortic Arch Aneurysms

S. TYLER WILLIAMS *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Ali Azizzadeh, MD, Department of Cardiothoracic and Vascular Surgery

Supported by:

Key Words: Aortic, Aneurysm, Hybrid, Endovascular

Background: Traditional treatment of aortic arch aneurysms involves open surgery, which includes a median sternotomy and cardiopulmonary bypass, to replace the diseased segment of the aorta. The alternative minimally invasive technique involves placement of a fabric-covered stent (stent-graft) from the groin. This device channels blood flow away from the aneurysm and prevents rupture. Open bypasses are performed to the arch vessels that require coverage prior to stent graft placement. The objective of this study was to review our institution's initial experience in treating aortic arch aneurysms using a hybrid repair (open bypass followed by endovascular stent-graft placement). **Methods:** A retrospective review of medical records was performed for all patients who underwent hybrid repair for aortic arch aneurysms. Patients were sub-divided into categories based on the number of arch vessels that required coverage. These included: left subclavian artery (zone 2), left subclavian and carotid arteries (zone 1), and left subclavian, left carotid and innominate arteries (zone 0). Primary endpoints were 30 day mortality and stroke. Secondary endpoints included complications and total hospital length of stay. **Results:** Between July 2005 and June 2011, a total of 18 patients (12 males, mean age 71.9 years, range 23-86 years) underwent hybrid repair. Patients required stent graft coverage for zone 0 (n=1), zone 1 (n=3), and zone 2 (n=14), respectively. The overall 30-day mortality and stroke rates were 5.6% and 11.1%. Postoperative complications occurred in 7 patients (38.9%). These included pulmonary complications (n=4, 22.2%), paraplegia (n=1, 5.6%), and cardiac complications (n=1, 5.6%). Mean hospital length of stay was 8.8 days (range 2-17) and average follow-up period was 2.7 months. **Conclusion:** Early results of hybrid repair for aortic arch aneurysms demonstrate that this is a safe and effective alternative to open repair for appropriately selected patients.

ABSTRACT

Severe Pulmonary Contusion is Associated with Coagulopathy and Mortality in Trauma Patients

ADAM P. WRIGHT

The University of Texas Medical School at Houston Class of 2014

Sponsored by: John Holcomb, MD, FACS, Department of Surgery

Supported by: 'Multicenter study evaluating the use of rapid thrombelastography in describing the acute coagulopathy of trauma.' Haemonetics Corporation.

Key Words: Pulmonary contusion, coagulopathy

Purpose: Exsanguination is the most common cause of preventable cause of early death following injury. Patients presenting with coagulopathy are 4 times more likely to die making early detection critical. We observed several patients presenting with severe pulmonary contusion (PC) on their admission CXR who were coagulopathic. We hypothesized that patients with a PC on initial chest X-ray (CXR) were more likely to be coagulopathic when compared to other trauma patients.

Methodology: This was an IRB approved, single center, retrospective cohort study of severely injured patients admitted between August 2009 - February 2011. Data were obtained from the trauma registry or medical records and included demographics, initial labs, injury scores, coagulation parameters, and PC severity based on diagnostic modality (CXR and CT). Patients on anticoagulants were excluded. Group 1 were those patients with PC diagnosed with initial CXR. Group 2 consisted of similarly injured patients including those with a PC diagnosed only by CT but not CXR and patients without a PC. Major outcome measures of coagulopathy were defined as $INR \geq 1.5$ and $PTT > 35$ seconds. Data was analyzed using a purposeful logistic regression model.

Results: Group 1 consisted of 189 patients and group 2 was 254. The incidence of coagulopathy was increased in group 1 vs 2, (27% vs 14%, $p < 0.001$). After adjusting for ISS, PC patients diagnosed by CXR were more likely to be coagulopathic by INR (OR = 1.793, $p = 0.017$) and PTT (OR=2.049, $p=0.013$) than controls and had a higher 24 hour and 30 day mortality rate ($p=0.04$).

Conclusion: Severe pulmonary contusion detected on initial CXR in trauma patients is associated with an increased incidence of coagulopathy and mortality.

ABSTRACT

The effect of extracorporeal photopheresis on Th1/Th2/Th17/T-reg cytokines and related genes in cutaneous T-cell lymphoma versus graft-versus host disease

BETTY YANG

The University of Texas Medical School at Houston Class of 2014

Sponsored by: Madeleine Duvic, MD, and Xiao Ni, MD, PhD

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
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Key Words: ECP, CTCL, GvHD, immunology

Extracorporeal photopheresis (ECP) has been shown to be an effective therapy for cutaneous T-cell lymphoma (CTCL) and graft-versus-host disease (GvHD). However, ECP is thought to mediate different immune responses in each disease. This project explores the effect of ECP on helper T cell cytokines and related genes.

Blood was collected from CTCL (n=6: 3 responders, 3 non-responders) and GvHD (n=3) patients pre-ECP and six months post-ECP. Normal donor (ND) samples were obtained from MDACC Department of Transfusion Medicine. Levels of mRNA were measured using PCR array and normalized to GAPDH. Fold regulation of each cytokine was calculated with respect to ND, and statistical analysis was performed (See Table).

Before ECP treatment, CTCL and GvHD patients had differing Th2 and T-reg profiles, but similar Th1 and Th17 profiles, except for IL-2. Th2 expression showed substantial upregulation in CTCL in IL-5 (1.60 ± 0.99), IL-13 (1.48 ± 0.90), IL7R (5.02 ± 3.66), and GATA3 (2.21 ± 3.75), and downregulation in GvHD patients (-0.27 ± 0.19, -2.16 ± 0.48, 0.82 ± 1.79, -2.91 ± 0.98, respectively). Overall, CTCL patients had high FOXP3 expression (14.25 ± 13.44), compared to lower levels in GvHD (-0.25 ± 2.01). Although most Th1 and Th17 cytokines did not show differences between the two diseases, IL-2 was substantially lower in GvHD (-3.45 ± 0.52) than CTCL (0.69 ± 1.39). CTCL patients who responded to ECP had higher IL-13 (2.41 ± 1.08), INFG (0.25 ± 2.60), and IL-17A (1.66 ± 0.32), than non-responders. After ECP treatment, responders showed increased IL-12A (2.08 ± 1.35) and IL-4 (2.21 ± 1.99), and decreased FOXP3 (-2.21 ± 1.49).

These results suggest that CTCL and GvHD have effects on Th1, Th2, Th17, and T-reg cytokines and related genes. CTCL patient who have higher IL-13, INFG, and IL-17A are more likely to respond to ECP, and successful ECP could increase IL-12A, IL-4, and FOXP3 expression in CTCL patients. More patient samples are needed to further confirm these findings.

Table. T helper subset Cytokines and Related Genes & Observed Expression Differences

T helper Subsets	Cytokines and Related Genes	CTCL vs GvHD Pre-ECP	CTCL R vs NR	
			Pre-ECP	Post-ECP
Th1	IFNG, IL-2, IL-12A, IL-12B, IL-18, IL-18-R1	↑IL-2	↑IFNG	↑IL-12A
Th2	IL-4, IL-5, IL-13, IL-7R, STAT6, GATA-3	↑(IL-5, IL-13, IL-7R, GATA3)	↑IL-13	↑IL-4
Th17	IL-17A, IL-6, IL-1A, STAT3		↑IL-17A	
T-reg	IL-10, TGF-β1, IRF4, FOXP3	↑FOXP3		↓FOXP3

Note: CTCL = cutaneous T-cell lymphoma, GvHD = graft-versus-host disease, ECP = extracorporeal photophoresis, R = responder to ECP treatment, NR = non-responder to ECP treatment, Th = T helper, IL = interleukin.



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ABSTRACT

Bactericidal Effects of Tranexamic Acid

MATTHEW YOUNG *The University of Texas Medical School at Houston* *Class of 2014*

Sponsored by: Audrey Wanger, PhD, Department of Microbiology

Supported by: Terry Clyburn, MD, Department of Orthopedic Surgery

Supported by: Cole Lewis, Department of Microbiology

Key Words: Tranexamic Acid, Bactericidal, Staph aureus, orthopedic surgery,

Tranexamic acid (TA) is an anti-fibrinolytic drug that competitively inhibits the activation of plasminogen to plasmin, thereby preventing the breakdown of fibrin clots. TA is commonly used by orthopedic surgeons to prevent excessive post-operative bleeding. The purpose of this study was to determine if TA had an additional benefit of killing (bactericidal) or inhibiting (bacteriostatic) bacteria and to determine if TA worked synergistically with different antibiotics. This was tested in two ways; 1) to determine if TA had any bactericidal effects, broth micro dilution(bmd) with Mueller Hinton broth was used with different concentrations of TA (50, 40, 30, 20, 10, and 5mg/ml). The following bacteria were tested; S. aureus (10), Methicillin resistant S. aureus (10), Staphylococcus species not aureus (SSNA) (4), Pseudomonas aeruginosa (PA) (12), E. coli (4), and Enterococcus(10). 2) to test TA's synergistic effects against the same organisms, Etest strips with various antibiotics were placed on Mueller Hinton plates with 15, 30 and 50 mg/ml concentrations of TA. For the gram positive bacteria the following antibiotics were tested; Vancomycin, Minocycline, Linezolid, Trimethoprim-sulfamethoxazole, and Moxifloxacin. To test the gram-negative bacteria Cefepime was used. The results of the above two methods showed that TA did not have any bacteriostatic or bactericidal effects. Furthermore, TA did not work synergistically with any of the antibiotics tested. Some signs of inhibition were seen using bmd, for PA and SSNA but they were not reproducible. In conclusions, TA doesn't seem to have any reproducible bactericidal effects towards killing the tested bacteria, however additional studies need to be done to rule any additional bactericidal/bacteriostatic applications for TA.

ABSTRACT

Determination of p-21 Activated Kinase (PAK) Subtype Involved in Edema-induced Intestinal Contraction Dysfunction

KATHY ZHANG-RUTLEDGE The University of Texas Medical School at Houston Class of 2014

Sponsored by: Karen Uray

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
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Key Words: Intestinal Edema, PAK expression

Surgery and trauma often result in intestinal edema formation due to perturbations in the hydrostatic and oncotic pressure differentials. Intestinal edema decreases intestinal contractile activity due to decreased myosin light chain phosphorylation. Intestinal edema leads to increased complications and morbidity and prolonged hospitalization for the patient.

Regulation of myosin light chain phosphorylation in edema-induced intestinal motility dysfunction involves a complex series of enzymes. Our laboratory has evidence that increased PAK activity causes myosin light chain (MLC) dephosphorylation by inhibiting MYPT1 phosphorylation, leading to decrease intestinal smooth muscle contraction. There are two groups of PAK: Group I and II. Preliminary data showed that a Group I PAK decreases myosin light chain phosphorylation. Group I consists of PAK 1-3. Since PAK3 is not expressed in the intestine, either PAK1 or PAK2 is likely to mediate the deleterious effects of edema on intestinal motility.

The goal of my summer research project was to determine which isoform of PAK mediates the MLC dephosphorylation. A cell model in which human intestinal smooth muscle cells are subjected to cyclical stretch was used to mimic edema development or control conditions in vivo. Using the cell model, I determined which PAK molecule is expressed in the intestinal smooth muscle by using siRNA to knockdown PAK and determined which isoform of PAK caused myosin light chain dephosphorylation. We achieved 90% knockdown using siRNA technique. PAK1 knockdown significantly decreased MLC and MYPT1P696 phosphorylation, but MYPT1P850 was not significantly affected. PAK2 knockdown did not affect MLC, MYPT1P696 or MYPT1P850 phosphorylation. This study reveals that PAK1 is responsible for inhibiting MYPT1 phosphorylation, which leads to intestinal smooth muscle contraction dysfunction.

ABSTRACT

Portal Venous Gas: Indicative of Increased Mortality in Infants with Necrotizing Enterocolitis Totalis

JANE Y. ZHAO

The University of Texas Medical School at Houston

Class of 2014

Sponsored by: Stacey D. Moore-Olufemi, MD, Department of Pediatric Surgery

Supported by: Stacey D. Moore-Olufemi, MD, Department of Pediatric Surgery

Key Words: Necrotizing Enterocolitis, Portal Venous Gas, Indications for Surgery

Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergency in preterm babies, with mortality rates $\geq 50\%$. Currently, indications for surgical intervention for babies with an aggressive variant of NEC, NEC totalis (NEC-T), remain to be determined.

Purpose: The objective of this study was to determine if portal venous gas (PVG) is a useful indicator for determining which NEC-T babies need surgical intervention.

Methods: A retrospective cohort study was conducted on all patients treated surgically for NEC at Children’s Memorial Hermann Hospital between 2004 and 2009. Infants born with gastrointestinal anomalies were excluded. Factors investigated included patient demographics, clinical presentations, surgical invention type, and morbidity and mortality.

Results:

	Portal Venous Gas (n=40)	No Portal Venous Gas (n=86)
Overall Mortality*	67.5%	37.0%
NEC-T**	58.5%	10.6%
Death within 24 Hrs***	50.0%	13.4%

*Odds ratio (OR) = 3.5 (95% CI 1.6-7.7) **OR = 11.9 (4.7-30.2) ***OR = 4.8 (1.8-12.7)

Conclusions: PVG was a strong predictor of overall mortality within 24 hours in NEC-T. PVG may be a useful clinical indicator for babies with NEC -T and help guide earlier surgical intervention and/or expectant management in this patient population.

ABSTRACT

Characterization of *Aplysia* adenylyl cyclase B using insect cell expression systems

CATHY ZHOU

The University of Texas Medical School at Houston Class of 2014

Sponsored by: John Byrne, PhD, Department of Neurobiology and Anatomy

Supported by: National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
5 T32 DK007676-19

Key Words: *Aplysia*, adenylyl cyclase, operant conditioning, insect cell culture

The *Aplysia californica* sea slug is capable of a variety of associative learning tasks and serve as a good model because of its small number of neurons, many of which are well-characterized. A behavioral protocol for reward operant conditioning of feeding behavior has been shown to correspond with cellular changes in the B51 neuron (Brembs 2002). Protein kinase C (PKC), protein kinase A (PKA) and adenylyl cyclase (AC) involvement has been substantiated in B51 operant conditioning. It has been proposed that AC and downstream PKA activity, part of the dopaminergic reinforcement pathway, could also be initiated with behaviorally induced increases in PKC activity.

To address this hypothesis, an AC isoform, ap1B, was expressed in two different insect cell lines (SF9 and TNI) via baculovirus vector. Enzymatic presence was confirmed with Western blot, and quantitative measurements in response to pharmacological treatments were measured using cAMP assays. Forskolin, which simulates dopamine activation, and phorbol, which increases PKC activity, were applied separately in increasing dosage. These results showed that although protein expression was robust, pharmacological responses were inconclusive. Further research into operant learning continues to be warranted given its implications in models of substance abuse and addiction.



Undergraduate Students

ABSTRACT

Mechanical characterization of polymers for dental fillings

PRATIMA ANUMOLU

University of Houston

Class of 2012

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

Supported by: NIDCR

Key Words: dental filling, mechanical testing, stress relaxation, cyclic loading.

The research presented aims at mechanical characterization of polymers to be used as dental fillings. Each specimen, with dimensions of about 1mm X 1mm X 7 mm, will be tested wet at 37 °C in three-point bending. Prior to testing, the dimensions of each specimen will be measured with digital calipers and will be used for calculating stress and strain. Viscoelastic testing will begin with stress relaxation and record it as function of time. A compressive strain of 5% nominal strain at a displacement of 10mm/sec will be applied to the specimen. The obtained data will be fitted to a Maxwell model to determine viscosity (η) and Young's Modulus. After 600s, small amplitude cyclical strain will be applied at a range of frequencies from 0.01Hz to 20Hz. The Bose DMA software will be used to calculate $\tan \delta$, storage modulus (E'), and loss modulus (E''). At the end of this testing, each specimen will be given at least 1 hour in 37 °C saline for recovery. Subsequently, each specimen will be cyclically loaded at 2 Hz using a stress value that is 50% the initial flexural strength (determined using 5 control samples of each material). To determine the fatigue properties, the number of cycles to failure will be reported for each specimen. At this time, we have created test methods on Instron Bluehill 2.0 software for stress relaxation, creep relaxation, and cyclic loading. Using these methods, we performed pilot testing on dry samples at room temperature. To be able to test specimen wet at 37 °C, we designed and built an environmental chamber. This is an ongoing study. The investigation of mechanical properties will be beneficial for development of new material for dental filling.

ABSTRACT

Simulation of Exocytosis at Ribbon Synapses in Bipolar Cells

KAITLYN BOLDUC

University of Connecticut

Class of 2012

Sponsored by: Ruth Heidelberger, MD, PhD, Department of Neurobiology and Anatomy

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

Key Words: Exocytosis at bipolar terminals, ribbon synapses

At the end of every neuron lies a synaptic terminal which houses thousands of prepackaged vesicles filled with neurotransmitters. These vesicles are waiting for the influx of calcium to provide the necessary stimulus for the vesicles to fuse with the membrane and release their contents. In certain sensory neurons, like the retinal bipolar cell, there is a need for more vesicles to be docked and primed for when calcium enters the terminal. This set up is known as a ribbon synapse; it allows for a faster transmission of sensory information. In these neurons there are distinctly different vesicle pools: the depot pool, the reserve pool, the ready to release pool, and the ultra fast pool. These pools refill each other until ultimately, they fuse with the terminal and exocytose to form the fused pool.

A program made using MATLAB 7.6 software was created to model vesicle fusion at the bipolar cell ribbon synapse. Values for calcium levels and vesicle pool refilling rates had been obtained from previous experiments performed on goldfish bipolar cell terminals. These values were inputted into the program and subsequent graphs displaying vesicle fusion vs. time were then analyzed.

By using different values of calcium at both the vesicle release site and the cytosolic levels of calcium, it was determined that vesicles cannot fuse in a linear fashion in high levels of calcium at the fusion site. At these higher levels, the fused pool increases to a plateau of 1500 vesicles occurring around $t = .002$ seconds. The value of 1500 vesicles is due to the complete depletion of the ultra fast pool, which is the pool that is primed for fusion before calcium enters the terminal. This pool is the first to fuse and release neurotransmitters into the terminal. Higher calcium levels cause this pool to have a faster depletion. The plateau will occur for shorter periods of time at higher calcium levels, but never disappears.

It has been found previously that calcium at the terminal reaches a maximum value of $325\mu\text{M}$. Both release and terminal calcium levels were lowered to determine the point where the fused pool changes from having a linear increase to incurring a plateau at 1500 vesicles. The change is very subtle, occurring after terminal calcium levels reach $10\mu\text{M}$, at low cytosolic levels of calcium. At higher cytosolic calcium levels, the change occurs slightly later, from between $12\mu\text{M}$ and $13\mu\text{M}$. These results demonstrate a role for calcium signaling in the switch from tonic to phasic neurotransmitter release.

ABSTRACT

Differentiating Bone Marrow Stem Cells into Bone-Forming Cartilage

AMSALE DERESE

University of Houston

Class of 2013

Sponsored by: Pauline J. Duke, Ph.D., Department of Orthodontics, School of Dentistry

Supported by: Texas Space Grant Consortium

Key Words: Tissue engineering, endochondral ossification, stem cells, cartilage, bone

For decades, patients with craniofacial bone defects have been treated with bone grafting. Allografts, autografts and xenografts have been used to repair the function and appearance of the face. Consequentially, bone grafting is a very common reconstructive procedure used in dentistry and oral surgery. However, in bone grafting, the limitation of suitable bone, risk of infection and immunologic rejection made researchers seek for a better alternative in repairing craniofacial bone defects. By using tissue engineering/ tissue regeneration, one can procure enough bone for a promising clinical outcome using highly proliferative and abundant adult stem cells. Previously, bone marrow stem cells were differentiated into bone-forming cartilage by manipulation of the gas environment during the initial adherence phase of culture. In this study, our laboratory characterized the pH changes that occur during this initial phase and their effects on the differentiation of mouse bone marrow stem cells into cartilage or neurons.

Mouse bone marrow stem cells (BMSCs) were isolated from tibias of two month old female mice (C57BL; Harlan Sprague Dawley). BMSCs were cultured for three weeks in Dulebecco's Modified Eagle Medium (DMEM) then removed from the surface and cultured in differentiation medium with or without 5% CO₂. Differentiation medium was BGJB FJM with 10% FBS, 150µg/ml ascorbic acid and 1% pen-strep. Cells cultured without CO₂ for the first four hours of incubation had the appearance of chondrocytes, and those in CO₂ for those hours had a neuronal-like appearance. The difference was attributed to the large pH change that occurred in the medium of cells cultured without CO₂-from 8.0 to 8.62. This change apparently caused activation of genes early in the cartilage differentiation pathway.

In the future, tissue engineering will allow patients to use their own bone marrow stem cells to overcome the scarcity of bone used for bone grafting, in a safe and practical approach.

ABSTRACT

Characterization of pH modification by *Candida albicans*

KELSEY E. DEVINE

Rice University

Class of 2014

Sponsored by: Michael C. Lorenz, PhD, Department of Microbiology and Molecular Genetics

Supported by Molecular Basis of Infectious Disease NIH sponsored training grant T32
AI055449-06

Key Words: Fungal pathogenesis, pH sensing, amino acid metabolism

Candida albicans is an opportunistic fungal pathogen that resides commensally in the gastrointestinal and genitourinary tracts of healthy individuals. However, in immunocompromised patients *C. albicans* can cause infections that are difficult to treat with anti-fungal therapies. This fungus exists in three forms with varied shapes: yeast cells, pseudohyphal cells and hyphal cells. It has been determined that the ability to alternate between these morphologies is necessary for virulence. *C. albicans* can promote development of its hyphal stage through raising extracellular pH. Mutations in the gene *STP2*, encoding a transcription factor responsible for regulating expression of amino acid permeases, hinder the ability of *C. albicans* to alter pH. To test the hypothesis that the *stp2* Δ phenotype is due to a lack of induction of amino acid permeases, I attempted to create constructs to express two General Amino Acid Permeases (GAPs) using the highly expressed *ACT1* promoter to bypass *STP2*. However, I was not successful at generating these constructs. The breakdown of arginine is involved in the ability of *C. albicans* to modify pH. Arginase enzymes convert arginine into urea and citrulline and *C. albicans* has three arginase genes. So far two of them have been deleted from a *C. albicans* strain with no phenotypic differences noticed. I was responsible for constructing a triple mutant in hopes that we would observe changes in the ability of *C. albicans* to alter pH. I have successfully deleted the first allele of *CAR1* in this diploid strain, and am in the process of deleting the second allele. Additionally, I tested a library of ~700 specifically generated *C. albicans* mutant strains for strains that lacked the ability to neutralize an acidic pH. Candidates that looked promising in the primary screen went on to a serial plate dilution test and a liquid aerated test. None of the mutants successfully passed all three tests.

ABSTRACT

Mechanisms of Granzyme B expression in HIV susceptible Memory CD4 T cells

MEGAN L. ESTEB

Texas A&M University

Class of 2013

Sponsored by: Dorothy E. Lewis, PhD, Department of Internal Medicine

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

Key Words: HIV, granzyme B, peptidoglycan, CXCR4, Toll-Like Receptor

During acute HIV infection, the epithelial lining of the gut is damaged, which is not repaired throughout the disease. As a result, microbial products that stimulate cells via Toll-Like Receptor (TLR) signals enter the body causing chronic immune activation. The mechanism for continued damage is not understood. One possible explanation is that granzyme B (GrB), a serine protease, cleaves proteins in tight junctions between epithelial cells. Previously, we showed that memory CD4 T cells, the immune cells at highest concentration in the gut, produce large amounts of GrB. To investigate whether TLRs could enhance GrB production, we stimulated memory CD4 T cells with TLR ligands and a T cell receptor activation signal (TCR) and measured activation markers and GrB (n=6). We discovered that activation, as indicated by CD69 and CD25 did not correlate with GrB inside the cell. Preliminary data indicate that memory CD4 T cells cultured with the bacterial cell wall component peptidoglycan (PGN) and a TCR activator release significantly larger amounts of granzyme B than cells cultured with a TCR signal alone. There is also a trend toward more GrB positive cells with PGN. To determine which HIV target CD4+ T cells made GrB, we examined CXCR4 (X4) and CCR5 (R5) expressing cells. We found PGN upregulated CXCR4 expression. In addition, GrB was expressed only in X4 and X4 R5 double positive cells. Because both types of cells are producing GrB, there may be multiple pathways by which PGN induces GrB production in HIV susceptible cells.

ABSTRACT

The Development of an Iridium pH Sensor for Dental Applications

AALIA FARUKHI

University of Houston

Class of 2014

Sponsored by: Francesco Contu, Ph.D, Ray Taylor, Ph.D, Department of Restorative Dentistry and Biomaterials, The University of Texas Health Science Center at Houston

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

Key Words: pH sensor, iridium, metal-metal oxide electrode

Introduction. The pH that develops within restricted environments of biofilms, dental restoration microgaps and material crevices can be significantly different than the bulk environment. Knowledge of the pH within these small spaces is very important for the prediction of the substrate dissolution kinetics. Iridium is a noble metal that is ideal to use as a micro-pH sensor. In fact, it behaves as a metal-metal oxide electrode that shows a linear relationship between its electric potential and the pH of the solution to which it is exposed. **Purpose.** Our research project aims to develop a miniaturizable iridium pH sensor that can be used to monitor pH within restricted environments. **Methodology.** Four iridium wires, 1 cm long x 0.5 mm in diameter were used to assess the precision, repeatability, response time, and accuracy of the iridium by measuring the pH as a function of surface pretreatments. These treatments included: as received (bare), anodic oxidation, and nafion coatings. Buffered solutions were used to assess the response of the iridium at pH 3.0, 6.0, and 9.0. The potential of the iridium wires was measured against a saturated calomel electrode (SCE) using a Solartron 1287 potentiostat. **Summary of results.** The bare wires showed low precision and slow response time, which was attributed to the lack of a stable oxide film on the iridium surface. The tests conducted with oxidized and coated iridium wires indicated that the surface treatments were necessary to obtain improvement in precision and response time of the sensors. However, when the accuracy of the coated wires was tested, readings of 3.6 and 6.0 were found for solutions of pH 4.0 and 7.0 respectively. **Conclusion.** Surface alteration of iridium either by oxidation, nafion coatings, or both will be required for optimum pH sensor behavior.

ABSTRACT

A Prospective Study of the Incidence and Effects of Metabolic Bone Disease in Orthopaedic Trauma Patients

VICTORIA GBENJO

Trinity University, San Antonio, Texas

Class of

Sponsored by: Catherine Ambrose, PhD – Department of Orthopaedic Surgery

Supported by:

Key Words:

Metabolic bone disease (MBD) is the generalized reaction of bone to a wide range of hormonal or metabolic disorders that deregulate bone remodeling. Recent research reveals correlations between metabolic bone diseases, longer durations for bone healing, increased fragility, and fracture risk within specific cohorts of orthopaedic trauma patients. We will determine the overlap between metabolic bone disease (MBD) and orthopaedic trauma patients that present one or more fractures, the correlation between MBD and bone mineral density (BMD), and the complication rate of orthopaedic trauma patients that have MBD, using four assessments. These assessments include a QUS, FRAX survey, clinical fracture assessments, and comprehensive metabolic panels. We will periodically follow up with all orthopaedic trauma patients and track their progress via these standards of care and research methods. Data collection has yet to be completed; however, it is assumed that there is a significant overlap between, and high incidence of, MBD in orthopaedic trauma patients. We hypothesize that those with MBD have lower BMD than orthopaedic trauma patients that lack the former, and that quality of life worsens more rapidly for those with MBD than for those without it. Furthermore, it is believed that the orthopaedic trauma population with MBD will show an increased rate of bone infection, delayed union, and nonunion of fractures, as compared to patients without metabolic abnormalities.

ABSTRACT

Identification of Type Three Secretory System (TTSS) Related Genes in Enteroaggregative *E. coli*.

DANIELA GOMEZ

Sam Houston State University

Class of 2011

Sponsored by: Pablo C. Okhuysen MD, FIDSA

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

Key Words: EAEC Adherence, Type Three Secretion System, Multiplex PCR

Background: Enteroaggregative *E.coli* (EAEC) is a common cause of acute and chronic diarrhea in children of developing countries and of traveler's diarrhea. The recently published whole genome sequence of the prototypic strain EAEC 042 identified genes with similarity to those described for TTSS in other *E. coli* pathotypes. The frequency of TTSS related genes in EAEC isolated from stools of travelers with acute diarrhea is unknown.

Hypothesis: We hypothesized that using PCR primers specific for intimin-like and IpaH genes from EAEC 042; we would identify a proportion of EAEC clinical isolates carrying TTSS related genes.

Methods: We determined the presence of intimin-like (Ec042-2220) and IpaH (Ec042-2094) genes in clinical isolates of typical (aat+) EAEC (n=56) and atypical (aat-) EAEC (n=101) that were isolated from short term US visitors to Mexico with travelers' diarrhea using a multiplex PCR reaction. EAEC were identified by their ability to cause aggregative adherence to Hep-2 cells. We compared the proportion of typical vs. atypical EAEC carrying specific genes by chi-square.

Results: The proportion of EAEC carrying IpaH was low (17 of 157 isolates or 11%) and was similar in typical and atypical EAEC. The proportion of EAEC carrying an intimin-like gene was higher (40 of 157 isolates or 25%). Of interest, the proportion of isolates carrying an intimin-like gene was significantly higher in typical EAEC (25 of 56 or 45%) than in atypical EAEC isolates (15 of 101 or 15%, $p < 0.001$).

Conclusions: The presence of TTSS encoding genes is relatively common in clinical isolates of EAEC. The higher proportion of strains carrying an intimin-like gene among typical EAEC suggests that TTSS may play a role in EAEC virulence. Additional studies that determine the role of TTSS and intimin subtypes in EAEC-related diarrhea are needed.

ABSTRACT

Ursodeoxycholic Acid as a Cytoprotective Agent Against NSAID-Induced Gastrointestinal Damage

MICHAEL HALISTA

Emory University

2013

Sponsored by: Dr. Lenard Lichtenberger

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

Key Words: COX-1, Thromboxane A₂, Bile Acid, NSAID, Primary Biliary Cirrhosis

The incidence of peptic acid ulcers, specifically duodenal ulcers, has been increasingly correlated with the use of non-steroidal anti-inflammatory drugs (NSAIDs). It is thought that this damage is largely caused by the NSAID inhibition of both cyclooxygenase-1 (COX-1) and Thromboxane A₂, which are related to gastrointestinal (GI) immune response. However, it has also been shown that endogenous bile acids released into the small intestine potentiate the damaging effect of the NSAIDs by a currently unknown mechanism. Ursodeoxycholic acid (URSO) is a secondary bile acid currently prescribed to nonsurgically treat patients with primary biliary cirrhosis. It acts by removing and replacing other bile acids from the bile acid pool, particularly chenodeoxycholic acid (CDCA) and cholic acid (CA). Interestingly, it has been found that the relatively hydrophilic nature of URSO also lends it a cytoprotective role in comparison to other bile acids. This study sought to use a liposome permeability test, coupled with MTT and LDH assays of intestinal cell-line 6 (IEC-6) cells, to examine and compare the injurious effects of CDCA and CA against those of URSO in the presence of Ibuprofen (IBU), a widely used NSAID, and phosphatidyl choline-associated Ibuprofen (PC-IBU), a relatively safe version of the original. The results of the liposome permeability tests showed that URSO caused a markedly reduced amount of membrane damage when combined with both IBU and PC-IBU, while CA induced intermediate liposome destruction and CDCA lysed all of the liposomes in almost every test. The MTT and LDH assays showed similar results, demonstrating that on a living system, URSO and CA cause a comparably small amount of damage while CDCA remains significantly cytotoxic. Additionally, the two cell-based assays taken together confirmed that the cell death was a direct result of membrane damage. Therefore, due to the reduced cytotoxicity of URSO on intestinal epithelial cells in the presence of IBU and PC-IBU and its ability to alter the bile acid pool composition, it presents itself as an effective preventative or treatment of NSAID-induced duodenal injury.

ABSTRACT

The Protective Effects of Lactoferrin against LPS-induced Hypothermia/Hypotension in Rats

LINH HOANG

University of Saint Thomas

Class of 2012

Sponsored by: Marie-Francoise Doursout, PhD, Department of Anesthesiology

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

Key Words: lactoferrin, lipopolysaccharide, cytokine

Lactoferrin (LF) is an iron-binding protein found in milk, epithelial secretions, and in the granules of neutrophils. Preliminary studies have shown that this glycoprotein controls the development of inflammatory responses and reactive oxygen-produced stressors in mice induced with an endotoxin. In a model of rats injected with lipopolysaccharide (LPS; an endotoxin that mimics the clinical features associated with inflammation and sepsis), lactoferrin effectively reduced the dysfunction of the mitochondria; mitigated the generation of pro-inflammatory cytokines; helped to retain the integrity and function of the small intestine; and defended against hypothermia resulting from the endotoxin. Based on this knowledge, it is hypothesized that lactoferrin protects against the progression of insult-induced inflammation by altering relative amounts of immune inflammatory mediators and oxidative stressors which in turn reduce cellular damage. It is speculated that lactoferrin's thermoregulatory activity is attributed to its ability to control blood pressure and other circulatory parameters *in vivo*.

24 Sprague Dawley rats were randomly assigned into four groups: a sham control saline group, an LPS-injected group, a lactoferrin-fed group, and an experimental lactoferrin-LPS group. 18 hours prior to LPS or saline injection, rats were fed lactoferrin orally. After 18 hours, the mean arterial pressure, blood pressure, and heart rate were recorded continuously for 6 hours while temperature readings and a blood sample were collected at 0, 1, 3, and 6 hours post-injection. The results of the MAP and heart rate were graphed and the level of cytokine production was measured using ELISA. The LF-LPS group showed a slightly higher MAP and lower heart rate than the LPS group, but the MAP was not completely stabilized in comparison to the rats in the sham control group. There were no significant detectable differences in the recorded temperatures of the rats among different groups. The level of cytokine production was also not drastically reduced in the LF-LPS group in comparison to the LPS-only group; production of IL-6, TNF- α , and TGF- β cytokines were only slightly lower in the LF-LPS group. The low level of responsiveness to the LF may have been a result of the low dosage of LF that was administered or the long gap of time between administration of LF and injection of LPS. Future studies c focus on finding an optimum dose and time of administration of LF in order to maximize hemodynamic stabilization after injection of the LPS.

ABSTRACT

Composite Bond Strengths to Enamel Using Various 5th and 6th Generation Dental Adhesives.

SAMIN HUQUE

University of Texas at Austin

Class of 2014

Sponsored by: Joe C. Ontiveros Jr., DDS, MS, The University of Texas Health Science Center at Houston - School of Dentistry

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

Key Words: Enamel, dental materials, adhesives, bond strength

Objective: To determine the shear bond strengths of different dental adhesives on enamel. **Methods:** Human molars and pre-molars were ground to 60 grit creating a flat surface on the enamel and polished to 320 grit. The five adhesives utilized were Moxie TE/5th generation and Moxie SE/6th generation (Discus Dental); OptiBond Solo Plus/5th generation and Optibond XTR /6th generation (KerrSybron); and Clearfil SE Protect Bond/6th generation (Kuraray). Composite resin (SDI Glacier) was bonded and cured to the enamel according to manufacturer's instructions. Specimens (n=10; cylinder mold, d=2.3) were stored in 100% humidity at 37°C for 24 hours. An Instron was utilized to load specimens and calculate the shear bond strength in megapascals (MPa). Analysis was performed using ANOVA and post hoc Tukey test at 0.05 level of significance. **Results:** The mean bond strengths, MPa, and standard deviations of the five adhesives were: Moxie TE 12.0 (5.0), Moxie SE 9.3 (4.1), OptiBond Solo Plus 11.2 (1.8), Optibond XTR 11.7 (3.6), and Clearfil SE Protect Bond 15.0 (4.9). No adhesives were significantly different from each other except between Clearfil SE Protect Bond and Moxie SE (p=0.02). **Conclusion:** Enamel bond strengths were similar among Moxie TE, Moxie SE, OptiBond Solo Plus and Optibond XTR, p>0.05, while Clearfil SE Protect Bond was significantly greater than Moxie SE. **Acknowledgements:** Materials were provided by manufacturers.

ABSTRACT

In-Hospital Morbidity and Mortality of Open Surgical Revascularization for Aortoiliac Occlusive Disease

RYAN KABIR

Indiana University

Class of 2014

Sponsored by: Kristofer Charlton-Ouw, MD, Department of Cardiothoracic & Vascular Surgery

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

Key Words: Aortoiliac occlusive disease, open surgical revascularization

Background: Aortoiliac occlusive disease (AIOD) is responsible for many of the presentations of debilitating intermittent claudication and symptomatic peripheral artery disease of the lower extremities. The Transatlantic Inter-Society Consensus (TASC II) classification system establishes the guidelines for treatment of AIOD based on the anatomical features and severity of the occlusive lesion. The purpose of the present study is to determine the major risk factors and morbidities of open repair. **Methods:** We retrospectively reviewed patients with open surgical revascularizations for AIOD. Patients were classified by their arterial lesions based on TASC II. Logistic regression was performed to determine risk factors for poor outcomes. **Results:** Between 1999 and 2011, 84 patients had aortoiliac revascularization including 69 (88%) aortobifemoral bypass, 6 (8%) femoral-femoral bypass, 2 (3%) aortounifemoral bypass, and 1 (1%) axillounifemoral bypass. 16 (21%) of these procedures were “redo” operations. The overall mortality rate was 5%. Redo patients experienced a morbidity rate of 69%. Comorbidities with the most significant risk associated with morbidity included dyslipidemia (69%; $p < 0.001$), CAD (63%; $p = 0.009$), hypertension (62%; $p = 0.005$), COPD (62%; $p = 0.006$), and smoking (58%; $p = 0.046$). Serious postoperative morbidities included GI complications (28%), respiratory failure (21%), renal failure (17%), and pneumonia (13%). **Conclusion:** Open aortoiliac revascularization has acceptable morbidity and mortality rates. Patients undergoing redo operations and with a history of dyslipidemia and CAD were at the greatest risk for surgical complications after open aortoiliac intervention. GI complications such as bleeding and ileus were associated with poor outcomes.

ABSTRACT

Identification of a thioaptamer against human serum albumin (HSA)

JENNIFER LASTIMOSA

Tulane University

Class of 2014

Sponsored by: David G. Gorenstein, PhD, Department of NanoMedicine and Biomedical Engineering, The Brown Institute of Molecular Medicine
David E. Volk, PhD, Department of NanoMedicine and Biomedical Engineering, The Brown Institute of Molecular Medicine

Supported by: David G. Gorenstein, PhD

Key Words: thioaptamer, human serum albumin (HSA)

Human serum albumin (HSA) is the most abundant protein in human blood plasma. Extensive studies have revealed that HSA has a high affinity to various materials. Although a negatively charged molecule overall, HSA is structurally favorable for binding to the negatively charged backbone of DNA due to its hydrophobic pockets lined with positively charged residues at the entrance. These pockets located at subdomains IIA and IIIA create the primary binding clefts for protein-DNA interactions. Despite the use of HSA as a drug carrier, a function often associated with aptamers, it is still advantageous to construct a high affinity oligonucleotide ligand in order to improve the efficacy of mass spectrometry readings among many other applications. Therefore, the objective of this experiment is to identify the DNA sequence that will provide the highest binding affinity to HSA.

In the aptamer selection process, a 70base long single-stranded DNA, with 30 random bases flanked by 20 nucleotide long primers (reverse primer is Biotinylated) was used in the experiment. To facilitate binding, adenosine bases were replaced with thioated dAs through PCR amplification. The single-stranded DNA template was then isolated using MPG Streptavidin beads, which bind to Biotin with high affinity. Subsequently, ssDNA FP-template was used for one round of selection. In each round of selection, a fixed ratio of DNA concentration is incubated with diminishing protein concentrations. Protein-DNA complexes are then captured onto a nitrocellulose filter while washing away weakly bound and unbound DNA. The protein-DNA complex is denatured in 8M urea, and the selected aptamer is with a molecular weight cutoff of 10kDa. The collected DNA is amplified and another round of selection begins. To improve the binding affinity of this lead ligand, each subsequent round has a decreased protein concentration ratio to ensure only tightly bound complexes will remain. After every fifth round, the templates are sent for sequencing and aligned to identify convergence and repeated motifs in the DNA sequences. Results of the tenth round sequencing show that two separate repeated motifs (proprietary results not shown) appear in the DNA sequences essentially dividing the possible high affinity binding sequence into two groups. Future studies will include synthesis of these two sequence motifs and their binding studies to quantify and to identify the best binding affinity.

ABSTRACT

Determinants for Net1 Localization During Mitosis

SEAV HUONG LY

Mount Holyoke College

Class of 2013

Sponsored by: Jeffrey A. Frost, PhD, Department of Integrative Biology and Pharmacology

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

Key Words: Net1, Chromatin, Localization, Mitosis

RhoA GTPase is a member of the Ras small GTPase super-family. It has an essential role in cytoskeleton organization, cell adhesion, cell migration, and cell proliferation. RhoA is overexpressed and hyperactivated in a number of cancers. The upstream regulators of RhoA, Guanine nucleotide Exchange Factors (GEFs), are also overexpressed in cancer, so it is possible that misregulation of Rho GEFs also leads to the hyperactivation of RhoA in cancer.

Net1 is a RhoA-specific GEF which is overexpressed in breast and gastric cancer, hepatocellular carcinoma, and glioma. However, during interphase Net1 is localized to the nucleus while RhoA is predominantly in the cytoplasm. It is, therefore, not clear what role Net1 may play in cancer initiation or progression. Our lab has discovered that Net may control mitosis. Inhibition of Net1 expression produces micronuclei and misshapen nuclei, which is indicative of mitotic error. Net1 co-localizes with chromatin during mitosis. This suggests that Net1 co-localization with chromatin may be important in regulating mitosis.

My project's objective was to characterize the determinants of Net1 co-localization with chromatin during mitosis. HeLa cells were transfected with HA-tagged Net1 wild type or particular N-terminus-deleted mutants. Co-localization with chromatin during mitosis was determined by immunofluorescence analysis. My results show that deletion of the first 20 and 40 amino acids of the N-terminus reduced co-localization, while deletion of the first 60 amino acids completely abolished co-localization with chromatin during mitosis. This suggests that the first 60 amino acids in N-terminus are important for Net1 co-localization with chromatin during mitosis. Future studies will determine how this region within Net1 controls its activity during mitosis.

ABSTRACT

Splicing regulation of nitric oxide receptor soluble guanylate cyclase in normal and diseased human aortas

KAVEETA MARWAHA

The University of Texas at Austin

Class of 2012

Sponsored by: Dr. Iraida Sharina, PhD, Department of Internal Medicine/Cardiology

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

Key Words: nitric oxide, soluble guanylyl cyclase (sGC), splicing, aorta

Soluble guanylyl cyclase (sGC) is an important enzyme in the Nitric Oxide (NO) signaling pathway. The disruption of sGC expression leads to endothelial dysfunction and vascular stiffness. Alternative splicing of sGC genes produces different sGC splice forms with altered enzymatic and regulatory properties.

We examined if major α_1 and β_1 sGC subunits undergo alternative splicing in human aortic tissue. De-identified aortic specimens were collected from patients undergoing surgical repair of the aorta, caused by aortic dissection, aortic aneurysm or advanced atherosclerosis, and compared with aortic samples from cardiovascular healthy donors. Total RNA was isolated from the samples and the expression of individual α_1 and β_1 sGC transcripts was assessed by semi-quantitative RT-PCR analysis. We observed statistically significant changes in the relative expression levels of α_1 and β_1 sGC splice variants. Tr5 of α_1 sGC, encoding an oxidative resistant splice variant was significantly decreased in diseased samples. On the other hand, Tr6 of α_1 , encoding a dominant negative isoform, was increased in diseased samples. These results suggest that changes in the expression of Tr5 and Tr6 splice variants will negatively affect sGC activity in diseased samples. We also observed an increase in β_1 - Ω 21 and β_1 - Δ 68 Ω 43 mRNAs, which encode alternative splice isoforms of β_1 sGC in diseased samples.

Based on our results, we conclude that α_1 and β_1 sGC genes undergo an alternative splicing in human aortas and the relative expression of individual splice variants is altered in diseased aortas. Therefore, regulation of sGC splicing may contribute to the development of vascular dysfunction.

ABSTRACT

The Effects of Dietary Supplement in the Post Injured Gut

ELENA MATHOPOULLOS

University of Texas at Austin

Class of 2012

Sponsored by: Anil D. Kulkarni, MSc, PhD, Department of Surgery

Supported by: Nestle'

Key Words: Nucleotides, gut, immune system, protein, ischemia-reperfusion

PURPOSE: Care directly following a trauma is critical in the health of a patient both during and after a surgical procedure. Dietary nucleotides (NT) are known to play an important role in the function of the immune system under chronic conditions; however, the action mechanism of nucleotides in acute recovery is not well known. We hypothesize that NTs trigger protein turnover through an increase in both structural and signaling protein synthesis, a decrease in proteolysis as well as an increase in overall cell energy status. A quick increase in protein turnover and cell energy could prove beneficial in clinical situations, especially in post-traumatic injury. The purpose of our study is to investigate the early metabolic events immediately following a trauma incident in order to analyze the effects of dietary exogenous nucleotides on the recovery of the gut following injury.

MATERIALS & METHODS: Twelve mice were divided into three different diet groups including chow (C), nucleotide-free (NF), and RNA supplemented nucleotide free (NFR). Groups were further divided into two surgical groups: a control sham group (laparotomy only) and a superior mesenteric artery occlusion (SMAO) group which underwent 45 minutes of ischemia and 30 minutes of reperfusion (I/R). Following the procedures, sections of both the ileum and the jejunum were removed for signaling protein analysis through western blot techniques and structural protein analysis through histological scoring.

RESULTS: No significant differences were observed between the different diet groups in terms of protein expression; such as AMPK, p-AMPK, p-70S6K, and ubiquitin. Histology analysis showed an increase in tissue damage in the SMAO group compared to the sham group with no significant difference in supplemented groups.

CONCLUSION: Results indicate that no positive conclusions can be made in regard to the effects of dietary NTs on the acute phase recovery of the gut. It is possible that the experimental conditions of the ischemia-reperfusion model are too severe with respect to timing, the period of dietary conditioning and the dietary NT dose. The severity in this I/R model may override the dietary NT effects and therefore lead to no significant differences between the different dietary groups. Another limiting factor is the small number of animals per group. The project is being continued after this summer and will help delineate better experimental conditions by modifying the ischemia and reperfusion times. Further analysis with an increased number of animals as well as a cytokine profile of animals will corroborate the observed results.

ABSTRACT

Thromboelastography in patients with intracerebral hemorrhage

JESSICA E. MESSIER

University of Texas at Austin

Class of 2012

Sponsored by: James C. Grotta, MD, Department of Neurology

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

Key Words: Thromboelastography, intracerebral hemorrhage

Background: ICH is the least treatable form of stroke and is associated with high mortality. Hematoma expansion (HE) occurs in approximately one-third of patients and is related to worsened outcome. TEG measures the speed and strength of blood clotting. SP is the time until initial fibrin formation. R is the time until clot firmness reaches an amplitude of 2mm. Delta=R-SP reflects the thrombin “burst.” K and Alpha reflect the speed of clot strengthening. G measures clot firmness. This study examined whether TEG values in ICH patients differ from normal controls, the association between TEG values with demographic and clinical data, and if TEG values can predict hematoma expansion. Methods: Patients with a diagnosis of ICH presenting within 6 hrs of symptom onset to MMHED were included. Approximately 1 ½ teaspoons of blood were collected for TEG. The differences between TEG values in ICH patients versus normal controls were assessed using unpaired t-tests and Mann-Whitney Wilcoxon tests. The associations of TEG values with baseline demographics and clinical data were assessed using linear regression. Hematoma volume was calculated using the ABC/2 method on the admission and 24 hrs later images, and HE was defined as an increase of >33% with respect to baseline. The predictive value of TEG for HE was tested using the Mann-Whitney U test. Results: Included were 21 ICH patients and 49 controls. Of the 19 patients that had follow-up imaging, 4 (21.1%) had HE. TEG values were not significantly affected by demographic or clinical variables. Compared to local controls, ICH patients had a smaller R (4.48 ± 2.07 vs. 5.95 ± 1.67 , $P = 0.0026$), larger Alpha (65.98 ± 8.27 vs. 61.46 ± 6.20 , $P = 0.018$), smaller Delta-value (0.51 ± 0.27 vs. 0.86 ± 0.32 , $P = 0.0002$), and smaller SP (3.97 ± 1.88 vs. 5.08 ± 1.55 , $P = 0.012$), suggesting clots that started forming faster but with less development of fibrin strength. None of the TEG parameters predicted HE. Conclusions: Soon after ICH, patients frequently have abnormal TEG reflecting generalized hypercoagulability. In this small sample, TEG was unable to predict HE, and it does not support the idea that HE occurs in hypocoagulable patients. Further study of TEG in ICH patients is needed to understand any impact on HE.

ABSTRACT

Localization and Daily Rhythm of Expression of the Circadian Clock Protein Period 2 (PER2) in the Goldfish Retina

RICHARD M. M. MILLER

University of Texas at Austin

Class of 2014

Sponsored by: Dr. Christophe P. Ribelayga, PhD. Department of Ophthalmology and Visual Science

Supported by: The University of Texas Medical School at Houston - Summer Research Program and NIH - NEI-R01EY018640 to Christophe P. Ribelayga

Key Words: Circadian rhythms; circadian clocks; clock genes; Period 2; retina; goldfish

Autonomous circadian clocks are expressed in many tissues and organs throughout the body and orchestrate our physiology and behavior on a daily basis. The clock machinery is a self-sustained cell-based mechanism that is centered on the BMAL1/CLOCK dimer of transcription activators and its inhibitors, PER1 and PER2. Despite compelling evidence that the vertebrate retina contains circadian clocks, the exact cellular location(s) of the clocks has yet to be clearly identified. Here, we used an immunocytochemical approach to examine the cellular localization and rhythmic expression of PER2 in the goldfish retina. Goldfish were sacrificed every 4 h during a 12 h light/12 h dark cycle. The eyes were fixed in paraformaldehyde, sectioned, and then treated with a specific antibody against PER2. To identify particular retinal cells, antibodies against cone arrestin (cone photoreceptors), protein kinase C α (large mixed rod-cone Mb1 bipolar cells), tyrosine hydroxylase (dopaminergic amacrine cells) or Brn3a (ganglion cells), were added to sections. We found that PER2 expression was restricted to cone, and not rod, somata, as well as to many amacrine cells, including the dopaminergic amacrine cell, along with most ganglion cells. In all of these cells, PER2 expression was rhythmic with a peak around the middle of the day and a trough in the middle of the night. Our results are the first to demonstrate a rhythm of PER2 expression among identified neurons of the goldfish retina. They suggest that functional clocks are expressed in cones, as well as amacrine and ganglion cells, and that these clocks show synchronized activity. Since PER2 has also been found in cones, dopaminergic amacrine cells and most ganglion cells in the mouse retina, the cellular location of circadian clocks and consequently the circadian organization of the retina appear conserved among vertebrates.

ABSTRACT

A Phase III Randomized Double Blind Placebo Controlled Trial of LUMINENZ-AT™ (CM-AT) In Children with Autism

PUNYA NARAIN

Rice University

Class of 2012

Sponsored by: Deborah A. Pearson, PhD, Department of Psychiatry and Behavioral Sciences
Curemark

Supported by: Grant entitled "A Phase III Randomized Double Blind Placebo Controlled
Trial of LUMINENZ-AT™ (CM-AT) In Children with Autism"

Key Words: autism, clinical drug trials, digestion

Autism is a developmental disorder characterized by impaired social interaction, delays in communication and speech, and restrictive, stereotyped, or repetitive behaviors. Gastrointestinal symptoms and self-restricted diets have also been reported in children with autism, leading researchers to investigate the relationship between digestion and the core symptoms of autism. One possible concern associated with gastrointestinal symptoms in children with autism is a deficiency of digestive enzymes. Enzyme therapy may improve gastrointestinal function, which in turn may be linked with enhanced behavioral and cognitive function. The purpose of this study is to determine the safety and efficacy of CM-AT, a proprietary enzyme blend developed by Curemark, in treating symptoms linked to autism. Children between the ages of 3 and 8 with a diagnosis of autism were initially screened to determine if they were eligible to partake in the study. Qualifying children were then randomized and given either placebo or active study drug for the twelve-week duration of the trial. The investigational product was administered 3 times per day for 90 days. At each of the six study visits, changes in behavior and symptoms were measured through parent questionnaires and interviews, behavioral scales, stool tests, and a brief physical exam. Data collection in the study is nearing completion, and data analysis will begin this fall. If CM-AT is approved for pediatric use, it may help children with autism by improving their ability to digest dietary protein.

ABSTRACT

Transferring a deletion of the *fsrC*-EF_1841 region in *E. faecalis*

MENGWEI NI

Rice University

Class of 2014

Sponsored by: Barbara E. Murray, MD, Department of Internal Medicine, Division of Infectious Diseases

Supported by Molecular Basis of Infectious Disease NIH sponsored training grant **T32 AI055449-06**

Key Words: *E. faecalis*, *fsrC*-EF_1841 region, deletion

The Fsr system, encoded by the *fsrABDC* operon, in *Enterococcus faecalis* serves as the main regulator of the *gelE* gene. The absence of a functional Fsr system inactivates gelatinase production and attenuates virulence in animals, plants, and nematodes. The purpose of this study is to determine if the deletion of *fsrC*-EF_1841, corresponding to the 23.9 kb region, can be transferred between different strains of *E. faecalis* and if so, through what mechanism. The possibilities that aid in transferring the deletion include conjugative plasmids, insertional sequences, *efaB5* (ICE), or a more complex mechanism. The strains chosen were: JH2-2 tagged with a tetracycline marker in the 23.9 kb region, V583 with an intact 23.9 kb region, and OG1SSp with an insertion of 14.8 kb in the region. The experiment was conducted using three different methods. First, JH2-2 tagged deletion strain was mated with OG1SSp. No transconjugants resulted from the mating, which suggests that *efaB5* alone may not be sufficient to transfer the deletion. Secondly, pBEM10, a conjugative plasmid shown to assist in recombination, was placed into JH2-2 tagged deletion strain and then mated with OG1SSp. While pBEM10 was successfully placed into JH2-2, verified with β -lactamase test, no transconjugants resulted suggesting that a conjugative plasmid also may not be sufficient to transfer the deletion. Lastly, PCJK construct with Tet marker was used to create an allelic replacement of the V583 23.9 kb region. V583 was selected because it contains pTEF and IS256. CK111 competent cells were electroporated with the PCJK construct and then mated with V583. Single cross-over insertions were obtained and the plasmid excised using the *pheS** system. The V583 tagged strain will need to be verified and mated with OG1SSp. Under the conditions tested, the deletion was not able to be transferred. Future research involves determining the factors, alternative strains, or plasmids that may permit the transfer of the deletion and benefits of having this deletion.

ABSTRACT

Effects of Analog Microgravity on Immune Response: Evidence for Impaired Control of Mycobacterial Infection

CASSIE PAN

Yale University

Class of 2014

Sponsored by: Jeffrey K. Actor, PhD, Department of Pathology and Laboratory Medicine

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

Key Words: Microgravity, immune modulation, mycobacteria, BCG

Introduction: Space represents the next major frontier for advancement in science and technology. However, spaceflight itself may hold inherent challenges towards achieving goals due to unpredicted spacecraft related environments (1,2). Specifically, the diminished gravitational forces may influence crewmember immune status (3), allowing alterations in normal immune homeostasis and function. In particular, regulation of intracellular pathogens may be compromised (4). Lack of either innate or adaptive immune control towards intracellular agents could yield devastating consequences on personnel living in close quarters.

General methods: To investigate whether microgravity conditions can influence immune function towards control of intracellular mycobacteria, splenocytes or purified monocytic U937 cultures maintained in a High Aspect Rotating Vessel (HARV) were challenged with virulent *Mycobacterium tuberculosis* (Erdman) or with *M. bovis* Bacillus Calmette Guerin (BCG). Responses were compared to flask grown controls. Global induction parameters were assessed by stimulation with mitogens ConA and LPS. Growth of organisms and induced cytokines were analyzed.

Results: Both innate and adaptive immune function was diminished under microgravity conditions. Overall control of organism growth was impaired, and production of proinflammatory mediators from both infected and stimulated cells were diminished. Of interest, the major deficiencies also included global T cell responses to Con A, but not to LPS, which indicates that control of active infection would be compromised during conditions of microgravity. Splenocytes infected with BCG showed mixed responses to microgravity conditions.

ABSTRACT

The development of a RNA interference based *Drosophila* Model for functional study of Parkinson's disease gene *parkin*

ANINDYA SAMANTA

Rice University

Class of 2012

Sponsored by: Sheng Zhang, Ph.D., Institute of Molecular Medicine for the Prevention of Human Diseases

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

Key Words: *Drosophila*, RNAi, *parkin*

Parkinson's disease (PD) is a chronic and progressive disease that leads to both motor and non-motor dysfunctions. Mutations in the *parkin* gene cause an early onset form of PD, which is identified as autosomal recessive juvenile parkinsonism (AR-JP). Previously, a specific *Drosophila* fly model has been developed that bears null alleles of *parkin* and is marked by reduced longevity, abnormal wings, flight and climbing deficits. However this particular animal model is also sterile and thus cannot be used easily in large-scale genetic screens. The purpose of our project was to create several different *parkin* loss of function lines in *Drosophila* through an alternative method, which would reduce levels of *parkin* expression without affecting the animal's fertility. The models use RNA interference (RNAi) combined with Gal4/UAS system to achieve targeted partial knock down of *parkin* gene expression. The Gal4/UAS binary system consists of the GAL4 transcriptional activator and its specific binding target Upstream Activation Sequence (UAS). By specifying GAL4 expression in particular subset of tissues, one can control where a particular protein or dsRNA encoded downstream of UAS promoter will be expressed. In our case, a selected GAL4 driver line (neuronal *elav-*, muscular-specific 24B and MHC-, and ubiquitous *arm-*, *da-* or *tubulin-*) was crossed with another line containing the UAS-(*parkin* dsRNA) transgene, thus inducing RNAi-mediated targeted *parkin* inactivation. We are attempting to create the respective recombination lines that would contain both GAL4 and UAS transgenes on the same third chromosome, which were identified through PCR. Initial results indicate that a recombinant line with ubiquitous *parkin* RNAi expression has been established.

ABSTRACT

Tissue Engineering Approach to Fibrocartilage Repair

ERIC SIELOFF

University of Tulsa

Class of 2013

Sponsored by: Philip C. Noble, PhD, Department of Orthopedic Research

Supported by: Institute of Orthopedic Research & Education, Methodist Hospital

Key Words: soft-tissue scaffold, chitosan, hydroxyapatite, silk

Many tissues in the body have a regenerative capacity; however there is a limit in defect size that can be self-repaired. Tissue engineering, a branch of biomaterials research, attempts to address the 'defect size limit' problem by introducing scaffolds that bridge the defect gap and promote tissue regeneration.

A scaffold should provide the mechanical stability, support, and architecture required by the specific tissue type that the scaffold is replacing. Additionally, the biocompatibility, porosity and rate of degradation of possible materials are important factors influencing tissue regeneration and ingrowth into the scaffold.

As a preliminary study, we investigated scaffolds potentially suited to fibrocartilage repair. The materials that we examined included; chitosan, silk and hydroxyapatite for bone attachment to the scaffold. These materials were made into microspheres that formed a porous scaffold after assembly.

The beads used were approximately 1mm in diameter. Porosity for scaffolds of each material depended on the amount of water that could be reabsorbed. Chitosan, chitosan/hydroxyapatite and chitosan/silk scaffolds were 11.2, 7.75 and 8.49 percent porous, consecutively.

We examined the compressive properties of scaffolds fabricated from chitosan, hydroxyapatite (HA) and *Bombyx mori* silk. Beads were made from mixtures of: chitosan, chitosan/hydroxyapatite and chitosan/silk (2:1 mass ratio,) and were fused into cylinders with a 2:1 height-to-width ratio in preparation for testing. The compressive modulus of chitosan, chitosan/HA and chitosan/silk scaffolds were 2, 3 and 1.9 MPa respectively. The stiffness and compliance was 6.4 N/mm and 0.16 mm/N for chitosan/HA, 4.8 N/mm and 0.23 mm/N for pure chitosan and 5.97 N/mm and 0.19 mm/N for chitosan/silk.

ABSTRACT

Lowry-Wood Syndrome and SULT1C2

KRISTEN E. SIMMONS

Harvard University

Class of 2014

Sponsored by: Jacqueline T. Hecht, PhD, Department of Pediatrics

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

Key Words: Lowry-Wood Syndrome, SULT1C2, short stature, microcephaly, multiple epiphyseal dysplasia, autosomal recessive inheritance

Lowry-Wood Syndrome (LWS) is a rare autosomal recessive microcephaly-dwarfing condition first described in 1975. To date, only 9 cases have been reported and all 9 patients had multiple epiphyseal dysplasia (MED) (causing short limb dwarfism) and microcephaly. Variable other features of the syndrome include mental retardation, congenital nystagmus, retinitis pigmentosa, restricted elbow extension, hip dislocation, knock-knees, coxa vara, and leukonychia totalis. While LWS is known to have a genetic cause, the underlying molecular etiology has not been identified.

Two siblings, a boy and a girl, with LWS were identified and characterized. Both siblings had MED and microcephaly. DNA samples were collected from both siblings and analyzed using chromosome microarray analysis. Thirty-three areas of shared homozygosity between the two affected siblings were found and contained approximately 500 genes. Of these genes, only one, SULT1C2, is highly expressed in cartilage. SULT1C2 is a member of the human cytosolic sulfotransferase (SULT) super family. It has 8 exons and is located on chromosome 2q11.2. The function of SULT1C2 is not currently known. Based on the above findings, we hypothesized that a mutation in the SULT1C2 gene in the two affected siblings is responsible for their LWS.

To identify mutations in the coding sequences of SULT1C2, primers were designed to PCR amplify the 8 exons encoding the gene. The amplified exons were sequenced and the results were compared to reference sequence. Only one variant was identified, rs76908083, also called rs1047312, in the 3' UTR of exon 8 in both siblings. Because this SNP is located in the 3' UTR, it is unlikely that it has any effect on protein expression and thus, is most likely not the causative LWS mutation. For future studies, DNA samples from both parents will be collected and analyzed for the presence of this SNP in SULT1C2. The presence of this variant in either parent would further exclude it as the causal mutation.

ABSTRACT

Defining the molecular mechanism of phosphatidic acid regulation of myosin-1b

WILLIAM K. TA

University of Texas at Austin

Class of 2013

Sponsored by: Guangwei Du, PhD, Department of Integrative Biology and Pharmacology

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

Key Words: myosin-1b, phosphatidic acid, TH-1 domain

Phospholipase D (PLD) is an enzyme found in humans that results in the formation of phosphatidic acid (PA) and choline. Recent findings reveal that PLD regulates cell migration and membrane trafficking. The PA created by PLD binds to several motor proteins including myosin-1b, suggesting that PA binding of myosin-1b may be a critical component for cell migration. We hypothesize that the TH-1 domain of myosin-1b is responsible for the interaction of PA and myosin-1b. To test this hypothesis, we will examine the direct binding between PA and the TH-1 domain of myosin-1b purified from *E. coli* using a liposome pulldown assay. We have generated several bacterial expression constructs for TH-1, which contain a His or a GST tag at different positions of the recombinant protein. Our results reveal that the protein containing an N-terminal His tag works best for protein purification. We have also changed several candidate PA-interacting residues to alanine by PCR site-directed mutagenesis to examine which region of the TH-1 domain is responsible for PA binding. This project uses several molecular biology techniques: restriction enzyme digestion, gel electrophoresis, PCR, DNA ligation, transformation, recombinant protein purification, Western blotting, etc. Understanding which region of the TH-1 domain is responsible for PA-binding may assist us in defining a mechanism for the binding of motor proteins to membranes.

ABSTRACT

Comparison of Storz C-MAC and D-MAC Orotracheal Intubation System in Morbidly Obese Patients

PAUL A. TRAN

University of Houston

Class of 2013

Sponsored by: Carin A. Hagberg, MD, Department of Anesthesiology
Davide Cattano, MD, PhD, Department of Anesthesiology

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

Key Words: Video laryngoscope, C-MAC, D-MAC, intubation

Traditional laryngoscopy in morbidly obese patients may be difficult. The C-MAC is a battery-powered video laryngoscope equipped with standard shaped interchangeable Macintosh blades which has been successfully used in morbidly obese patients. The D-MAC laryngoscope is a new blade that consists of a Doerges D-Blade, which has an elliptical tapering shape and is intended to be used in cases where direct or indirect laryngoscopy, including the use of the C-MAC, has failed to obtain an adequate view. This study compared the safety and efficacy of the D-MAC blade with the C-MAC blade in morbidly obese ($BMI \geq 40 \text{ kg/m}^2$) patients. For each patient consented and enrolled, the anesthesia resident (CA 2 or 3) first performed laryngoscopy with either the C-MAC or D-MAC, depending on the randomization order. Upon the second look, the resident performed laryngoscopy with the alternate video laryngoscope and proceeded to intubate the patient. Factors recorded and analyzed included time and ease of both laryngoscopy and intubation. Laryngoscopic view was also recorded. All patients were successfully intubated on the first attempt. Time to intubation was 14.76 ± 13.09 sec in the first group (C-MAC 1st) and 8.28 ± 4.53 sec in the second group (D-MAC 1st). Intubation was reported to be extremely easy to easy throughout the 13/50 patients. Preliminary results demonstrated that laryngoscopic views with the C-MAC and D-MAC blade are not statistically different in morbidly obese patients. Based on these results, both the C-MAC and D-MAC video laryngoscopes allow excellent visualization and allow successful intubation without any complications thus far in this preliminary study.

ABSTRACT

Identification of potential regulators of fimbrial synthesis in *Actinomyces oris* by Tn5 transposon mutagenesis

DUY C. TRINH

University of Nevada, Las Vegas

Class of 2013

Sponsored by: Hung Ton-That, PhD, Department of Microbiology and Molecular Genetics

Supported by: Molecular Basis of Infectious Disease NIH sponsored training grant T32
AI055449-06

Key Words: Transposon mutagenesis, type 2 fimbrial synthesis, *Actinomyces naeslundii*, transcriptional regulators

Gram-positive bacteria use covalently-linked protein polymers called fimbriae/pili to attach to specific host surfaces. *Actinomyces oris*, one of the early colonizers of oral biofilms or dental plaque, employs two types of fimbriae: type 1 fimbriae are necessary for adherence of the bacterium to the tooth surface, while type 2 fimbriae are required for its attachment to other bacterial species in the community. The purpose of this study is to identify possible regulators of the type 2 fimbria, which is encoded by the *fimB-fimA-srtC2* locus. Tn5 transposon mutagenesis was employed to introduce mutations in a genetically modified strain of *A. oris*, which has a fluorescence gene (mCherry) under the control of the *fimB* promoter. Eleven non-fluorescent colonies, indicative of diminished type 2 fimbria production, were selected from approximately 20,000 transposon mutant colonies. Further characterization of these candidates by PCR analysis eliminated 10 false-positive candidates, due to mutations found in either the promoter region or the mCherry gene itself. Chromosomal DNA of the remaining candidate was isolated for TAIL-PCR and DNA sequence to identify the mutated gene. The transposon was found to be in *sucA*, a gene coding for oxoglutarate dehydrogenase E1, a component of the Krebs cycle. Fluorescence intensity and growth analyses revealed a 37% reduction in fluorescence signal and reduced growth of this candidate, respectively. Thus, it is conceivable that inactivation of *sucA* may lead to reduction in energy output that induces the expression of stress-related regulator proteins, which in turn reduce protein synthesis, including fimbrial synthesis, in order to conserve energy. Further investigation of this proposed model is needed.

ABSTRACT

Flexible Optical Intubation via the Ambu Aura-I Versus Blind Intubation via the Disposable Fastrach™ – A Prospective Randomized Clinical Trial

D'ARCY WAINWRIGHT

Northwestern University

Class of 2012

Sponsored by: Carin A. Hagberg, MD
Davide Cattano, MD

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

Key Words: Fiberoptic scope, Ambu Aura-I, Ambu aScope, Intubating LMA,

Fiberoptic scopes are often utilized during difficult airway intubations and provide a view along the entire airway which assists in placement of the ETT. This study was designed to determine whether the Ambu® Aura-I™ combined with the use of the Ambu aScope provides a view which makes intubation faster, safer and easier than a blind intubation using the disposable Fastrach™. Prior to the study, the residents were trained to intubate using both the Ambu® Aura-I™ and the disposable Fastrach™. Patients were randomized to either group. For patients in the Ambu® Aura-I™ group, residents inserted a LMA into the glottis and intubated using the Ambu® aScope™. When the resident achieved a clear view of the carina, the ETT was advanced over the aScope, and when in proper position the aScope was removed. For patients in the disposable Fastrach™ group, residents intubated with an ETT using standard Intubating LMA procedures. The quality of the airways were evaluated using the Mallampati and Wilson scoring system, thyromental scoring system of Patil, interincisor gap distance, neck mobility and sternomental distance. The time and number of attempts were recorded for each patient, as well as ease of intubation and any other influential factors. The case is ongoing and there is not enough data as of yet to come to a conclusion as to the success of the Ambu® aScope™ in comparison to the disposable Fastrach™, but it is expected to be a more successful means of intubation.

ABSTRACT

Effectiveness of Stimulants in Promoting Treatment for Substance Use Disorder in Adolescence

LYNDIA A. WALKER

University of Rochester

Class of 2012

Sponsored by: Oscar G. Bukstein, MD, Department of Psychiatry

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

Key Words: adolescence, stimulants, substance use disorders (SUD), treatment, attention-deficit hyperactive disorder (ADHD)

In this nation, more than 12% of 12- to 17-year-old children have used illicit drugs; this ranges from experimentation to severe abuse and dependence. Maladaptive pattern of overuse of drugs (substance abuse) combined with persistent use of drugs despite the necessity (drug dependence) is called substance use disorder (SUD). There exist various interventions for SUD, which includes pharmacological, psychosocial, detoxification, and substitution. Problem arises, however, in a step before receiving these interventions. Often times, adolescents with SUD fail to recognize the importance of managing their maladaptive behavior. Thus they are unable to provide sufficient amount of attention and effort to seek any treatment.

This lack of focus is major trait noted in children with attention-deficit hyperactive disorder (ADHD). ADHD children are often treated with stimulants to increase their focus to various tasks they are usually inattentive to. Administration of stimulants to adolescents with SUD is hypothesized to raise their attention toward interventions and therefore lead to more successful treatment for SUD.

ABSTRACT

Thalidomide prevents sunitinib-induced cardiotoxicity

KATHARINE YANG

Rice University

Class of 2013

Sponsored by: Heinrich Taegtmeyer, MD, DPhil, Department of Internal Medicine, Cardiology

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

Key Words: Sunitinib, angiogenesis, cancer, cardiac dysfunction

BACKGROUND: Sunitinib malate (SM) is a drug used to treat metastatic renal cell carcinoma (RCC). However, more than 20% of Sunitinib-treated patients develop heart failure within three weeks. SM is a receptor tyrosine kinase inhibitor that hinders cardiomyocyte PDGFR- β , a receptor tyrosine kinase, which regulates angiogenesis. In this pilot study, we assessed whether another drug, thalidomide, is capable of reversing the cardiotoxic effects of SM-treatment without interfering with its anti-tumor effects.

METHODOLOGY: 8 week old male nude mice were all injected with RCC tumor xenograft. Mice were divided into 4 groups – Vehicle Control (Ctrl), SM treatment, Thalidomide treatment, and SM+Thalidomide treatment. Mice were administered with SM at 40 mg/kg/d and with thalidomide at 75mg/kg/d for 28 days. Coronary flow reserve (CFR) and left ventricular ejection fraction (LVEF) were measured by cardiac MRI and Doppler ultrasound, respectively. Pericyte coverage were assessed by immunofluorescent co-staining of CD31 (for vessels) and NG2 (for pericytes). Expression of PDGFR- β was measured using Western blotting.

RESULTS: Thalidomide does reverse sunitinib-induced cardiotoxicity without interfering with SM's anti-cancer effects. When co-administered with SM in mice cardiomyocytes, thalidomide was found to preserve pericyte coverage, an indication of microvasculature presence. There was no significant difference between Day 28 tumor sizes of SM-treated and SM+Thalidomide-treated mice, indicating that thalidomide did not interfere with the anti-tumor effect of SM. Expression of PDGFR- β in SM+Thal-treated mice remained the same as that in controls, while SM-treated mice expressed significantly lower levels of PDGFR- β , indicating that the additional thalidomide provided a protective effect against cardiac and coronary dysfunction. Administration of both SM and thalidomide also prevented SM-induced reduction in LVEF (SM-LVEF: 41%; SM+thalidomide: 49%, $p < 0.01$) and preserved CFR (SM-CFR: 2.14; SM+thalidomide: 2.95).

CONCLUSION AND FUTURE DIRECTIONS: Knowing the correlation between co-administration of thalidomide with SM and its cardiac rescuing effects, we can further investigate the mechanism behind thalidomide-induced pericyte preservation and protection of the heart.

ABSTRACT

E1-E2 Specificity Determination in Ubiquitin Conjugation Pathways

ZHIXING YAO

Cornell University

Class of 2014

Sponsored by: Jianping Jin, PhD, Department of Biochemistry and Molecular Biology

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

Key Words: ubiquitin, E2 activation

Ubiquitin, a key signaling molecule in protein turnover, cell cycle regulation, and many other pathways, tags target proteins through a cascade of enzymatic reactions catalyzed by an E1 activating enzyme, an E2 conjugating enzyme, and an E3 ubiquitin ligase. The human genome encodes two known E1s, Uba1 and Uba6, which activate distinct sets of E2s. We investigate the specificity of Uba1 and Uba6 in activating specific E2s, such as Cdc34 and Use1 using *in vitro* assays with purified wild type and mutant enzymes. Our goal is to identify sequence features of both E1s and E2s that grant specificity to E2 activation. We found that wild type Uba1 charges Cdc34 and Uba6 does Use1 with no cross reaction. However, a mutant Cdc34 constructed with an α -helix in its UBC domain switched with a Use1 α -helix can be charged with ubiquitin by Uba6, indicating that the helix region is important for specificity determination. We also found that the negative-charged residues on the crossover loop of Uba6 and the acidic loop of Cdc34 play critical roles to prevent non-specific activation of Cdc34 by Uba6.

ABSTRACT

Connexin 34.7 Is Co-localized with Connexin 35 in Zebrafish Retina

YI ZHOU

Colorado State University

Class of 2012

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

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

Key Words: Gap junction, photoreceptors, heterotypic coupling

Gap junction proteins form the substrate for electrical coupling between neurons. Coupling reduces voltage noise in photoreceptors and rod-cone coupling provides a means for rod signals to enter the cone pathway, extending the dynamic range of rod-mediated vision. Previously it was shown that fish retina contained two closely-related genes, connexin (Cx) 34.7 and 35, that were both expressed in photoreceptors. In bass retina, both Cx35 and Cx34.7 were present in cones in separate gap junctions. In zebrafish retina, Cx35 has been located at cone-cone and rod-cone gap junctions, but the connexin contributed by rods has not been identified. Cx34.7 has not been localized in zebrafish retina. Therefore, we tested the hypothesis that Cx34.7 was present at rod-rod or rod-cone gap junctions. Wild-type adult zebrafish were used in the study, of which the isolated retina was fixed in 2% carbodiimide, cryostat sectioned and immunostained. Cx34.7 immunostaining was observed primarily beneath cone pedicles, some within the basal invagination of cone pedicles. Cx35 was not restricted to cone pedicles. Most Cx34.7 plaques were colocalized with Cx35 while not all Cx35 plaques contained Cx34.7. In some cases, Cx34.7 and Cx35 were present at telodendria of cone terminals, indicating that Cx34.7 and Cx35 both participated in gap junctions between cone photoreceptors. No definitive evidence was found for the presence of Cx34.7 in rods. Further study is needed to understand whether Cx34.7 and Cx35 form heterotypic, heteromeric or mixed gap junctions in cones.



International Medical Students

ABSTRACT

A phase I-II clinical trial of 5-Fluorouracil, Liposomal Doxorubicin and interferon-alpha combined with Fever-range whole-body thermal therapy

HIROKO HAYASHI

The University of Tokushima

Class of 2014

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

Key Words: 5-Fluorouracil, liposomal doxorubicin, interferon-alpha, fever-range whole-body thermal therapy

The purpose of this Phase I-II Clinical Trial was to assess toxicity, tumor response and response duration of an innovative combined modality therapy of 5-Fluorouracil (5-FU), liposomal doxorubicin (Doxil) and interferon-alpha combined with fever-range whole-body thermal therapy (FR-WB-TT) (40 °C for 6 h). The regimen was developed in the preclinical thermal laboratory. Eligible patients were those with chemotherapy-resistant endometrial, ovary and breast cancer. A treatment cycle consisted of 5-day continuous intravenous infusion (i.v.) 5-FU, FR-WB-TT on day 6; then i.v. administration of Doxil 2 hours later; and daily subcutaneous injection interferon-alpha. Twenty-three patients entered the trial. At 30-55mg/m² Doxil dose, leucopenia, neutropenia, and thrombocytopenia as hematological toxicities were tolerable, but grade 1-3 anemia was induced. No grade 4 hematological toxicity was observed. Grade 2-3 hand-foot syndrome, grade 3 mucositis, grade 2 nausea, and pressure burn were observed at 40-45 mg/m² Doxil. Grade 3 hand-foot syndrome, mucositis, and pressure burn were observed at 30 mg/m² Doxil, and One patient experienced grade 3 diarrhea and grade 1 burn at 30mg/m² Doxil. At 50-55mg/m² Doxil, one patient experienced grade 1 cardiotoxicity. No other non-hematological toxicity was seen at 50-55mg/m² Doxil. Complete and partial responses were 13%. One patient experienced CR. The overall median duration of response was 4 months. The protocol therapy was well tolerated and exhibited very modest antitumor activity in patients with advanced, chemotherapy-resistant endometrial, ovary and breast cancer.

ABSTRACT

Risks of Re-infection in Infrarenal Aortic Graft Replacement

GUANMENJQIAN HUANG

Shanghai Jiao Tong University

Class of 2014

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

Key Words: 5-Fluorouracil, liposomal doxorubicin, interferon-alpha, fever-range whole-body thermal therapy

Background: Graft infection is an uncommon but devastating complication of aortic reconstruction. Treatment of infrarenal aortic graft infection includes excision of the infected graft with either extra-anatomic or *in situ* revascularization of the lower extremities. Autogenous vein reconstructions have been advocated by some groups since they are thought to be resistant to infection. We reviewed our cases of infrarenal aortic graft infection to determine morbidity and risk of reinfection.

Methods: All cases of open abdominal infrarenal aortic reconstruction from 1999-2011 were retrospectively reviewed. Cases of graft infection were preferentially managed with graft excision. *In situ* reconstruction was with autogenous femoropopliteal vein, homograft, polyester (Dacron), and polytetrafluoroethylene (PTFE). Extra-anatomic reconstruction was with axillobifemoral PTFE. Patient co-morbidities, surgical outcomes and re-infection rates were calculated.

Results: During the study period, 359 infrarenal abdominal aortic reconstructions were performed for both aneurysmal and occlusive disease. 25 of 359 cases were referred to us for treatment of graft infection consisting of 11 *in situ* with autogenous femoropopliteal veins, 2 homograft, 3 Dacron, and 1 PTFE; 5 were with axillobifemoral bypass with PTFE. 4 cases were managed nonoperatively. In-hospital mortality was 2/25 (8%). Re-infection occurred in 9/25 (36%) over the follow-up period (range: 1 month to 11 years). 3 of 9 re-infection cases were with *in situ* aortobifemoral bypass using autogenous femoropopliteal veins; 2 of 9 cases were with axillobifemoral PTFE.

Conclusion: Surgical excision of infected infrarenal aortic grafts with revascularization can be done with acceptable in-hospital morbidity and mortality rates. Aortic reconstructions using autogenous femoropopliteal veins were still susceptible to re-infection.

ABSTRACT

Title Phenotypic characteristics of granzyme B producing memory T cells

HIROYUKI KUREBE

The University of Tokushima

Class of 2014

Sponsored by: Dr. Dorothy E. Lewis, PhD, Department of Infectious Disease

Key Words: HIV, Granzyme B, Integrin β 7, CD45RO, CCR5

HIV preferentially infects CCR5⁺ (chemokine receptor for HIV) , integrin beta7⁺ (mucosal integrin) memory CD4⁺ T cells in the gut mucosa. Granzyme B (GrB) , a serine protease typically associated with CD8 and NK cell activity is released from activated or HIV infected memory CD4 T cells , which may play a key role in HIV pathogenesis. However the phenotypic characteristics of these GrB producing cells are unknown. This study characterized GrB⁺ memory T cells phenotype from blood in both healthy (n=15) and HIV (n=2) infected humans. Cells were stained with antibodies to GrB , CCR5 , integrin beta7 , CD45RO (memory) , CD25 (IL-2 receptor) , CXCR4 (chemokine receptor for HIV) , CD4 , and TLR2 (GrB inductive molecule) and analyzed by flow cytometry. Some GrB⁺ cells expressed integrin beta7 and CCR5 , but none expressed TLR2 , CXCR4 , nor CD25. These results indicate that the cells preferentially infected by HIV in the gut also make GrB. This may be important for initiation of the gut breach in HIV pathogenesis.

ABSTRACT

Glutamine regulates expression of syndecan-1 in intestinal epithelial cells in vitro

JUNJIE WANG

Shanghai Jiaotong University School of Medicine

Class of 2013

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

Supported by: Zhanglong Peng, MD, PhD, Department of Surgery
Wei Lin, PhD, Department of Surgery

Key Words: glutamine, syndecan-1, hypoxia and reoxygenation injury

Background: Gut injury induced by hypoxia and reoxygenation (HR) can result in an increase in cell permeability, and even cell death. Glutamine plays vital roles in maintaining gut epithelial cell function. We have shown that glutamine protects the post ischemic gut. Syndecan-1 is the predominant heparin sulfate cell proteoglycan found on the cell surface of gut epithelia cells and regulates cell proliferation, adhesion, and permeability. **Aim:** We hypothesized that glutamine protects against gut intestinal epithelia cell permeability induced by HR by up-regulating the synthesis of syndecan-1. **Methods:** IEC-6 cells were cultured in Dulbecco's modified eagle media. After receiving treatment of 0, 1.25, 2.5, 5, 10 and 20mM glutamine, cells were exposed to 24 h hypoxia(1%O₂) followed by 4 h of reoxygenation or normoxia as a control. Cell permeability was assayed with an vitro vascular permeability kit. Expression of syndecan-1 mRNA and protein were measured with real-time PCR and western blot. **Results:** HR significantly increased epithelial cell permeability, which was reduced by treatment with glutamine. Glutamine also increased syndecan-1 mRNA expression in a concentration-dependent manner both under normoxic and hypoxic (HR) conditions. Lastly, under normoxic conditions, glutamine increased both glycosylated and unglycosylated syndecan-1 protein in a concentration-dependent manner. After HR, glycosylated syndecan-1 protein decreased and unglycosylated syndecan-1 increased, a finding that was partially reversed by glutamine. **Conclusion:** Glutamine may prevent HR- induced intestinal epithelial cell permeability by up-regulating syndecan-1 expression and glycosylation.

ABSTRACT

The influence of joint proximity to scar formation following burn injury

NIMING WU

Shanghai Jiaotong University School of Medicine *Class of 2013*

Sponsored by: David J. Wainwright, MD, Division of Plastic and Reconstructive Surgery

Supported by: Division of Plastic and Reconstructive Surgery

Key Words: Hypertrophic Scars, joints, non-joints, burn patients

Introduction: Hypertrophic Scarring is defined as a scar raised above the skin level that stays within the confines of the original lesion. Hypertrophic Scars (HTS) are often distressing to patients and their families even after successful operations on them due to functional and aesthetic problems. It is important to determine factors (e.g., healing time, wound location, constant strain, etc) causing HTS as this can facilitate prevention and management. We postulate that increased scar is particularly prominent around joints, where tension is greater. There are no scientific reports addressing the question of whether the site of post-burn injuries, especially those around joints and non-joints can affect HTS development.

Materials & Methods: Acute burn injuries were evaluated for inclusion to the John S. Dunn Burn Center at Memorial Hermann Hospital - TMC or UTPB Burn Clinic. Inclusion criteria were patients with burns across joints. The anatomic sites studied were the dorsal wrist, antecubital fossa, popliteal fossa and dorsal ankle. All patients must have uniform second or third degree burn over joint and the non-joint contiguous skin. Patients with electrical burn, chemical burn, friction burn, contact burn or radiation burn were excluded. Qualified patients were photographed on a scheduled basis and their demographic information, general injury data, general treatment data and any other ongoing data were documented. For the assessment of HTS we used the Modified Vancouver Scar Scale. Patients were assessed weekly for the first month and then biweekly for the next month and eventually monthly until scar maturation. We used SPSS to analyze all data collected.

Results & Discussion: Patients are now being screened for inclusion. The study is still ongoing.

ABSTRACT

Comparing the specificity of antibodies against Epstein-Barr virus in blood serum and cerebrospinal fluid

WANG YUEH-HSIN

China Medical University

Class of 2016

Sponsored by: J. William Lindsey, M.D., Department of Neurology

Key Words: Multiple Sclerosis, Epstein-Barr virus

Multiple sclerosis (MS) is an immune-mediated demyelinating disease of the central nervous system of unknown etiology. It has been associated with the Epstein-Barr virus (EBV) infection, but the relationship between the virus and the disease is not yet defined. Our hypothesis is that the antibody response to EBV is different in the cerebrospinal fluid (CSF) than in serum and also, in MS than in controls.

Serum and CSF were collected from 9 MS patients and 18 controls, and frozen at -80°C until use. The controls were non-MS patients with a variety of diagnoses including inflammatory and non-inflammatory conditions.

EBV protein was run on 4-12% gradient gels, blotted onto nitrocellulose, blocked with 2.5% dry milk, and then cut into single lane strips. Strips were incubated with different pairs of 100 µl CSF or a volume of serum with the equivalent amount of IgG, followed by anti-human (H+L)-alkaline phosphatase and NBT/BCIP. Blots were scanned and analyzed using the Kodak 1D software to measure band densities.

There were 14 distinct antigens of different molecular weights present in EBV. The antibody response to the different antigens varied considerably between individuals. Overall, the antibody response against EBV in the serum and CSF was similar in each person, both in the MS patients and controls. When we compared the antibody response between the MS and control groups, we found no significant difference between them.

ABSTRACT

Cellular and Subcellular Locations of the Gap Junction Protein Connexin36 among Photoreceptors in Rabbit Retina

SHAN YUHUA

Shanghai Jiao Tong University School of Medicine

Class of 2016

Sponsored by: Dr. Christophe P. Ribelayga, Ph.D., Department of Ophthalmology and Visual Science

Supported by: The University of Texas Medical School at Houston - Summer Research Program and NIH - NEI-R01EY018640 to C.P.R.

Key Words: electrical synapse; gap junction; connexin36; retina; photoreceptor; cone; rod; rabbit

Electrical synapses, or gap junctions, are fundamental components of neural networks. These specialized intercellular channels are composed of two connexons (or hemichannels) made of connexins. In the vertebrate retina, gap junctions are widely distributed and several connexins expressed. Electrophysiological experiments indicate that photoreceptors, namely cones and rods, are electrically coupled through gap junctions. In addition, connexin36 (Cx36) is expressed in the outer plexiform layer (OPL) where photoreceptors terminals synapse onto second order neurons. In lower vertebrates, Cx36 expression in the OPL has been clearly associated to both cones and rods. However, in mammals, the exact location of Cx36 in the OPL remains unknown. Here we sought to determine the exact cellular and subcellular locations of Cx36 in the OPL of the rabbit retina. Paraformaldehyde-fixed rabbit retinal sections were reacted with a monoclonal antibody against Cx36 and a polyclonal antibody against cone arrestin to visualize cones. Cx36-linked immunofluorescence revealed abundant gap junctions in cones in the rabbit OPL, more specifically on the top of cone pedicles and along the axon up to cone somata, as well as in telodendria, terminal arborizations that connect adjacent cones together. In the OPL we were not able to detect Cx36 outside of the cones. Our data indicate that in the rabbit OPL Cx36 is clearly expressed in cones and thus is likely involved in cone-cone electrical coupling. In addition, Cx36 plaques on the top of cone pedicles appear ideally positioned to form gap junctions between cones and rods. However, whether rods express Cx36, but Cx36 plaques in rods are too small to be detected by immunofluorescence, or whether rods express another connexin remains an open question in the mammalian retina.