TEXAS A&M UNIVERSITY
School of Medicine

RESEARCH DAY

Summer Research Program
July 26, 2024

Medical Research & Education Building 2
Bryan, Texas

Schedule of Events

9:00 AM-12:00 PM	**Poster Viewing & Judging** MREB 2 Lower Level
12:00 PM-12:30 PM	**Lunch** MREB 2, Room 1403
12:30 PM-1:30 PM	**Keynote Speaker** Colonel Jim Lucas, MD, FACS, US Army (Ret.) Program Director, Military Medicine MREB 2, Room 1403 **"Reflections on Leadership (From a Somewhat Reluctant Leader)"**
1:30 PM-2:00 PM	**Presentation of Certifcates** Brett Mitchell, PhD, FAHA Director, Summer Research Program MREB 2, Room 1403
2:00 PM	**Group Photo & Adjourn**

Keynote Speaker

Colonel Jim Lucas, MD, FACS ’92, US Army (Ret.)
Clinical Professor
Director, Military Medicine Program
Title: "Reflections on Leadership (From a Somewhat Reluctant Leader)"

Colonel (Ret.) Jim Lucas, MD, FACS is Clinical Professor and Director of the Military Medicine Program at Texas A&M University School of Medicine. Dr. Lucas earned his baccalaureate degree in Biomedical Science from Texas A&M University and his MD from Texas A&M College of Medicine. Inducted into the Alpha Omega Honor Medical Society in 1996, Col. Lucas graduated with honors and was commissioned as a Captain in the United States Army on June 7, 1997. He completed residency training in Otolaryngology-Head and Neck Surgery at the San Antonio Uniformed Services Health Education Consortium (SAUSHEC), serving as Chief Resident in his final year. Following five years of ENT surgical practice at Fort Polk, Louisiana and Fort Carson, Colorado, Dr. Lucas completed his Facial Plastic and Reconstructive Surgery fellowship training at the University of Illinois Chicago Medical Center in 2010. He was then assigned to Carl R. Darnall Army Medical Center (CRDAMC), Fort Cavazos, Texas, as the Chief of Otolaryngology and the Director of Facial Plastic Surgery. As a Core Faculty member of the SAUSHEC Otolaryngology-Head and Neck Surgery residency program, he became widely recognized for his teaching excellence and clinical expertise in facial and complex nasal reconstruction. Over the course of 28+ years of service in the United States Army Medical Department, Col. Lucas served in numerous operational, clinical, educational, and leadership roles – culminating as a Deputy Commander and Chief Medical Officer at CRDAMC. In that capacity, he played a key role in establishing CRDAMC as a Clinical Training Site for Texas A&M School of Medicine. He was selected as the Associate Site Dean and served in that role until his Army retirement in 2021. His numerous achievements and exemplary leadership led to his election as a distinguished member of the Order of Military Medical Merit. Now serving as faculty at his beloved alma mater, Dr. Lucas brings a passion for mentoring and preparing the next generation of Aggie physicians to adapt, thrive, and lead with integrity through an increasingly dynamic healthcare landscape. Dr. Lucas is quick to acknowledge that none of his professional achievements even remotely approach his greatest accomplishment in life – marrying way out of his league and then somehow convincing his beautiful wife to keep him around for as long as she has. Together they have three adult children (plus a son-in-law and daughter-in-law) and one amazing granddaughter.

Abstracts

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Impact of Lymphatic Sphingosine-1-Phosphate Deletion on Autoantibody Levels following Kidney Injury

Gustave M. Allen, Heidi A. Creed, Thien Phan, Saranya Kannan, Andrea J. Reyna, Joseph M. Rutkowski
Dept. of Medical Physiology
Texas A&M School of Medicine
Bryan, TX

Acute kidney injury (AKI) results in damage to kidney cells followed by a feedback loop of fibrosis and inflammation that leads to reduced filtration and, ultimately, chronic kidney disease (CKD). In many renal pathologies, the immune system generates nephritogenic autoantibodies that bind damaged kidney structures. Because of lymphatic vessel roles in the adaptive immune response, we hypothesized that manipulating lymphatic endothelial cell (LEC) biology would impact this autoantibody response. To test this hypothesis, we utilized a mouse model in which LECs lack the sphingosine-1-phosphate (S1P) transporter, Spns2, which should limit effector lymphocyte response. AKI was induced in LEC Spns2 knockout mice using either cisplatin or sheep nephrotoxic serum. Mice were assessed at various days following injury and CKD progression. Using kidney proteins from uninjured mice, an enzyme-linked immunosorbent assay (ELISA) was developed to test whether injured mice demonstrated immunoglobulin (Ig) changes in their type and reactivity against kidney proteins. Using this new ELISA method, the relative concentrations of IgG, IgG1, IgG2, IgA, and IgM in each AKI model were measured. We identified that repeated cisplatin injury caused no Ig differences in LEC Spns2 KO mice, but a recall cisplatin reinjury model exhibited an impaired IgG response. In glomerulonephritis, IgG levels were significantly higher, driven primarily by IgG1, in Spns2 KO mice. Thus, LEC S1P plays a critical role in the antibody-mediated response to injury. Future work will utilize injured kidney proteins in the ELISA, measure IgE and IgD levels, and attempt to identify the specific autoreactive Ig antigens in CKD.

This work was supported by NIH DK119497 (to J.M.R.). G.M.R. was supported by a DRUMR Fellowship from NIH R25 DK126642.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

ALCOHOL AND CANNABIS USE IN LATINO COLLEGE STUDENTS: TRENDS IN FOREIGN-BORN STATUS IN THE AGGIES STUDY

Brandon Anderson, Ujwal Boinpally, Amy Adams, John Hettema, Shaunna Clark
Dept. of Psychiatry and Behavioral Sciences
Texas A&M School of Medicine
Bryan, TX

The A&M Going Genomic for Internalizing and Externalizing Syndromes (AGGIES) Study aims to increase Latino representation in genetic studies of mental health by leveraging the Latino student population at Texas A&M. Studies conducted in previous generations of Latinos established the Latino Paradox, a phenomenon where Latinos farther removed from immigration to the US are more likely to have worse health outcomes than Latinos that have migrated to the US more recently. However, this work is dated, and it is unknown if these trends are present in current Latino students, specifically regarding alcohol and cannabis use. We hypothesized that foreign-born Latinos would have better substance use outcomes than US-born Latinos. To evaluate this, AGGIES participants (N=618) completed an online survey, which included questions on their alcohol and cannabis use, including ever and current use, age of onset, and substance use disorder risk categories. Linear regression was used to determine if foreign-born status was related to alcohol and cannabis use. There were no significant associations between foreign-born status and alcohol use outcomes. Cannabis use showed similar results, except that US-born Latinos were more likely to have ever used cannabis than foreign-born Latinos. Analysis of foreign-born status and alcohol and cannabis use outcomes serves as a relevant method in generating substance use trends within the Latino college student community. Future research into the current presence of the Latino Paradox will require collecting data on generational status to provide a precise measure of time since immigration.

This work was supported by a Texas A&M HSC Seedling Grant (Award Number: 291007-23-12) to SC and JH. BA was supported by Texas A&M School of Medicine and the US Air Force Academy.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

THE EFFECT OF GUT METABOLITES ON HIPPOCAMPAL NEUROGENESIS AFTER SPINAL CORD INJURY

Amrit Bhakta, Erika Marks, Ashley Douthitt, Sydney Heimer, Cédric Geoffroy
Dept. of Neuroscience and Experimental Therapeutics
Texas A&M School of Medicine
Bryan, TX

It is estimated that more than 300,000 people in the United States live with a spinal cord injury (SCI), with approximately 18,000 new cases occurring each year. Following SCI, patients are more susceptible to developing health complications such as cognitive impairments. Cognitive decline is associated with a decrease in hippocampal neurogenesis as the hippocampus is the center for memory and learning. Therefore, adult neurogenesis is a compelling target to explain the cognitive decline associated with SCI. In this study, adult hippocampal neurogenesis is assessed in mice following a moderate T8 contusion compression SCI using the naturally occurring gut metabolites: indole and indole-3-propionic acid (IPA). The four comparison groups consisting of 10-week-old female mice are as follows: sham, SCI & vehicle, SCI & indole, and SCI & IPA. Immunohistochemistry was performed and mice hippocampi were stained for DAPI, a nuclear chromosomal marker, and doublecortin (DCX), an immature neuronal marker. Using Imaris, an artificial intelligence 3D image analysis software, machine learning models were created and trained to quantify DCX positive somas and neurites. It is hypothesized that the SCI & vehicle group will display a decrease in soma and neurite growth compared to sham mice, however, SCI & treatment groups will exhibit increased soma and neurite growth relative to the SCI & vehicle group. Future applications of Imaris include the quantification of astrocytes to assess the interplay between glial cells and hippocampal neurogenesis.

AB was supported by the Texas A&M School of Medicine

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

THE EFFECTS OF SPACE RADIATION AND MICROGRAVITY ON LIVER CELLS

Reginaldo Capati, Amy Barrett, Mary Falekulo, Jordan Faust, Mariam Khwaja, Abigail Rodriguez, Thien Phan, Dylan Pham, David Zawieja, Travis Hein, and Shannon Glaser
Dept. of Medical Physiology
Texas A&M School of Medicine
Bryan, TX

With the possibility of commercial space travel, it is increasingly important to understand the space environment's effects on organ systems. The liver is one of the human body's most vital organs, supporting metabolic and immune system functions. The aim of this study was to evaluate the effects of microgravity and space radiation on liver cells. First, immunohistochemistry (IHC) for CK-19 (biliary mass), F4/80 (inflammation) and Oil Red O (lipid deposition) was carried out in liver samples from mice subjected to microgravity and space radiation on the International Space Station. Second, qPCR gene profiles were evaluated in human biliary epithelial cells after a simulated microgravity protocol (Synthecon rotary cell culture system). Third, qPCR gene profiles were evaluated in pig liver samples after radiation exposure at Brookhaven. Immunohistochemistry showed an increase in ductular reaction, macrophage number, and fat deposition in spaceflight mice livers compared to the control groups. Human liver cells showed an increase in mRNA expression for genes associated with extracellular matrix remodeling and tissue renewal after simulated microgravity. Liver tissues in pigs exposed to radiation showed an upregulation of genes associated with inflammation and DNA damage repair mechanisms. These results support the conclusion that microgravity and space radiation play a role in altered liver metabolic and proliferative states. Future research includes investigation of the relationships between alterations in gene expression activated in microgravity and radiation, confirming gene expression at the protein level, and determining the cellular pathways affected by space to mitigate space environment damage.

This work was supported by DRUMR Fellowship by NIH R25 DK126642, Grant 80NSSC19K0392, and Non-DRUMR Fellowship by Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE SUMMER RESEARCH PROGRAM

EFFECT OF NEUROSTEROID THERAPY ON ABERRANT NEUROGENESIS IN THE SOMAN NEUROTOXICITY MODEL IN PEDIATRIC RATS

Darsh Darji, Xin Wu, and D. Samba Reddy*
Department of Neuroscience and Experimental Therapeutics
Texas A&M University School of Medicine
Bryan, TX

Children are highly vulnerable to nerve agents like soman (GD), with limited medical countermeasures available. Post-exposure neurosteroid therapy has been shown to be a more effective anticonvulsant and neuroprotectant than midazolam in adult animal models of organophosphate (OP) intoxication. This study investigated the neuroprotective effects of ganaxolone (GX), a synthetic neurosteroid, in a pediatric rat model of GD exposure. Postnatal day 21 (P21) rats were exposed to GD and treated with various doses of GX, alone or in combination with midazolam (MDZ). Neurogenesis was assessed 3 months post-exposure using doublecortin (DCX) staining in the hippocampal dentate gyrus (DG). Results showed that GD exposure significantly decreased neurogenesis (~40%) in the DG of P21 rats. All GX-treated groups exhibited significantly increased neurogenesis compared to GD alone, with GX combined with MDZ showing greater efficacy than GX alone. Similar trends were observed in neuronal density, brain slice thickness, and total volume. These findings indicate that GD-induced neurogenesis abnormalities can be mitigated by GX therapy in pediatric models. The neuroprotective effects of GX, especially when combined with MDZ, suggest its potential as a therapeutic agent for pediatric nerve agent exposure. Overall, this study confirms the efficacy of neurosteroid therapy in protecting the pediatric brain from neurotoxic insults.

This work was supported by NIH Grant #U01-NS117209 to Dr. Reddy.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

T-LYMPHOCYTE BETA-ADRENERGIC NEUROTRANSMISSION REGULATES TH17 INFLAMMATION DURING PSYCHOLOGICAL TRAUMA

Fatima G. Laureano, Tatlock H. Lauten, Safwan K. Elkhatib, Emily C. Reed, Tamara Natour, Kristen Giebel, Adam J. Case
Dept. of Medical Physiology
Texas A&M School of Medicine
Bryan, TX

Post-traumatic stress disorder (PTSD) leads to an elevated risk of inflammatory diseases. Using a preclinical mouse model of PTSD called repeated social defeat stress (RSDS) to model psychological trauma-induced inflammation, we demonstrated that sympathetic denervation of the spleen significantly attenuates this inflammatory response through T-lymphocytes that were incapable of producing the pro-inflammatory cytokine interleukin 17A (IL-17A) after RSDS. Therefore, we hypothesized that T-lymphocyte IL-17A production is dependent upon sympathetic neurotransmission. Using both male and female mice (N=48 males; N=35 females), we targeted T-lymphocyte adrenergic receptor blockade and concurrent Cyclic adenosine monophosphate (cAMP) production by pharmacological and genetic means to investigate the ability of T-lymphocytes to differentiate and produce IL-17A. Systemic infusion of the nonselective β-adrenergic receptor antagonist (i.e., propranolol) into wild-type mice diminished circulating levels of IL-17A. This was confirmed in mice globally lacking β1 and β2 adrenergic receptors after RSDS. Importantly, Rag2 knock-out mice adoptively transferred with β1/2 knock-out T-lymphocytes also showed attenuated circulating IL-17A levels compared to those receiving wild-type T-lymphocytes after RSDS. Outside of RSDS, T-lymphocytes lacking adrenergic receptors as well as wild-type T-lymphocytes treated with propranolol were poorly able to increase IL-17A mRNA levels or secrete IL-17A protein when cultured under TH17 polarizing conditions. Interestingly, T-lymphocytes lacking adrenergic receptors had diminished levels of cAMP and this cAMP depletion in T-Lymphocytes attenuated T-lymphocyte IL-17A mRNA levels. While adrenergic signaling has been known to regulate T-lymphocyte functions, this is the first observation for the necessity of β-adrenergic signaling and T-lymphocyte intracellular mechanisms regulating TH17.

FGL was supported by a Fellowship from NIH R25 DK126642.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Blocking insulin-like growth factor 1 receptor in the gut reduces IGF-1 mediated long-term neuroprotection in middle-aged female rats

Hana Hasan, Hetvi Bhatt, Kaylin Pickle, Shameena Bake and Farida Sohrabji
Department of Neuroscience and Experimental Therapeutics
Texas A&M College of Medicine
Bryan, TX

Previous studies in a rat model of ischemic stroke identified that intraperitoneal administration of insulin-like growth factor (IGF)-1 treatment reduces stroke-induced gut permeability and peripheral inflammation in the acute phase and mitigates stroke-induced cognitive impairment in middle-aged females. These data suggest that the gut is an important target of IGF-1 for stroke recovery. To directly implicate the gut as a therapeutic target, the present study used a novel construct to block the IGF-1 receptor (IGF1R) in the intestinal crypt cells. Female Sprague Dawley rats (9-11 mo) were intragastrically gavaged with an rAAV construct containing IGFR-shRNA (IGFR-sh) downstream of the IESC promoter Lgfr5 in a tet-inducible system or rAAV-empty vector (Scr-sh) 4 weeks before experimental ischemia. Animals were subjected to sham surgery or middle cerebral artery (MCAo) via stereotaxic injections of endothelin-1 (ET-1). Doxycycline was administered 4h later and IGF-1 was given at 4 and 24 h post-stroke. Peripheral inflammation was assessed in serum samples during the acute phase (post-stroke 5d), long-term behavioral outcomes after 6 weeks, and animals were terminated at 60 days. Serum cytokine analysis reveals higher IL-17 levels in the animals with IGFR-Sh+IGF-1 compared to Scr_sh+IGF-1. Cognitive impairment assessed using Barnes maze test showed that the IGFR-sh group spent less time in the target quadrant compared to SCR-sh, suggesting poor spatial memory. H&E staining of the distal ileum showed no significant changes in villous morphology. Taken together, these findings indicate blocking IGFR in the gut reduces the IGF-1-mediated long-term improvement in post-stroke females.

This work was supported by NS119872 to FS and SB.
HH was supported by Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

BUILDING ROBUST 3D MATERIALS FOR IN-VIVO DRUG DELIVERY

Nasanna Henley, Paige Wilson, Britt Faulk, Francesca Agobe, Carolyn Cannon, Sarah Bondos
Dept. Of Medical Physiology
Texas A&M School of Medicine
Bryan, TX

Developing a successful drug takes an average of USD 1 billion and 10 to 15 years. Despite this staggering investment of time and money, 90% of drug candidates in clinical trials fail. Of these drug failures, 40-50% can be attributed to a lack of clinical efficacy, and another 30% can be attributed to uncontrollable toxicity. These challenges can be overcome with biotechnology-based drug delivery systems such as micelles, lipid nanoparticles, and protein-based materials. However, these systems tend to have issues with solubility, bioavailability, and targeted delivery to the site of infection. Ultrabithorax (Ubx), the Drosophila intrinsically disordered protein, has the unique ability to self-assemble into materials that can deliver other proteins, nucleic acids, nanoparticles, and small therapeutic molecules. Additionally, Ubx has the capacity to concentrate the amount of drug delivered 100-fold and be optimized for more targeted delivery. We have designed a model system in which Ubx will deliver C58, a biaryl compound capable of killing Methicillin-resistant Staphylococcus aureus (MRSA) as free bacteria and in biofilms. Though C58 is a potent antibiotic, exposure to plasma renders it ineffective. Ubx has demonstrated it can bind, concentrate, protect, and deliver C58 to successfully eradicate resistant bacteria on cell culture plates. The focus of this project is to develop more robust materials to treat infected wounds in mouse models with the ultimate goal of developing a form of Ubx-bound antibiotic for systemic use.

This work was supported by the NIH grant R01GM099827 to SB. NH was supported by a Fellowship from NIH R25 DK126642.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

TEMPORAL IMPACT OF DIABETES ON NEURAL RETINA DEGENERATION AND BLOOD FLOW VELOCITY IN THE OCULAR CIRCULATION OF INS2(AKITA) MICE

Zahi Hussain, Dylan Pham, Gabrielle Hightower, Shu-Huai Tsai, Lih Kuo, Travis Hein
Dept. of Medical Physiology
Texas A&M School of Medicine
Bryan, TX

Reduction of the ocular blood flow and degeneration of the neural retina are associated with diabetes before development of diabetic retinopathy. However, the temporal relationship of neural retina degeneration and vascular dysfunction and the potential underlying molecular mechanisms remain unclear. The Ins2(Akita) mouse spontaneously develops type 1 diabetes within 3 to 4 weeks of age. Herein, we examined the temporal impact of diabetes on neural retina degeneration and on retinal blood flow velocity in Ins2(Akita) mice and the mRNA expression of vascular function genes arginase (Arg) and Rho kinase (ROCK) in the retina. Diabetic Ins2(Akita) mice and control wild-type (WT) mice were studied from 6-8 weeks up to 24 weeks of age. Doppler ultrasound, optical coherence tomography (OCT), and qPCR were performed to measure central retinal artery velocity, total retinal thickness (TRT), and mRNA expression, respectively. Central retinal artery velocity was significantly lower in diabetic mice from 12 to 24 weeks. At 6-weeks old, OCT imaging showed that TRT was thinner in diabetic mice than in control mice, which was maintained through 24-weeks old. The mRNA expressions of Arg1, Arg2, ROCK1, and ROCK2 were comparable in the retina of control and diabetic mice at 8-weeks old. These findings indicate that neural retina degeneration precedes vascular dysfunction in diabetic Ins2(Akita) mice without changes in gene expression of retinal Arg and ROCK isoforms. Future studies will determine whether neurodegeneration causes retinal vascular dysfunction and whether therapeutic molecular targets can be identified to prevent these neural and vascular changes in early diabetes.

This work was supported by NIH grant #R01 EY034145-01 to TH. ZH was supported by the Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

EFFECTS OF IGF-1 TREATMENT ON HIPPOCAMPAL NEUROGENESIS FOLLOWING EXPERIMENTAL TRAUMATIC BRAIN INJURY

Angel M. Ifegbo, Reagan Dominy, Lavanya Venkatasamy, Jaclyn Iannucci, Lee A. Shapiro

Department of Neuroscience and Experimental Therapeutics, Texas A&M School of Medicine

Bryan, TX

Traumatic brain injury (TBI) occurs in 2-3 million Americans each year and is a leading cause of death and disability. Among the many physiological consequences of TBI, the hypothalamic-pituitary axis (HPA) is particularly vulnerable. Altered HPA signaling is associated with reduced growth hormone (GH) and insulin-like growth factor (IGF-1) after TBI. Phase II clinical trials and preclinical studies that supplemented IGF-1 after TBI have been mostly beneficial. However, the therapeutic mechanisms remain to be elucidated. IGF-1 stimulates cell growth in various cell types, including stem and progenitor cells. In the adult rodent brain, a population of neuronal progenitor cells persists in the hippocampal dentate gyrus. Adult hippocampal neurogenesis in rodents is associated with various aspects of affect and cognition. Importantly, in preclinical rodent models, TBI alters adult hippocampal neurogenesis and causes neurobehavioral impairment. Thus, we hypothesized that IGF-1 treatment would improve TBI-induced alterations to neurogenesis. To test this hypothesis, we used the fluid percussion injury (FPI) model of TBI. Male rats received FPI or Sham, followed by intraperitoneal (i.p.) IGF-1 at 3- and 24 hours post-injury. Brains were collected 3 days post-FPI, processed, and stained with anti-doublecortin (DCX) to visualize immature neurons in the hippocampus. Using unbiased stereology, DCX+ cells were quantified in the dentate gyrus granule cell layers and subgranular zone. Treatment-related changes in DCX+ cells were observed. Morphological changes to the dendrites of DCX+ cells were also observed. These preliminary findings suggest that exogenous IGF-1 may improve TBI-induced alterations to adult hippocampal neurogenesis.

This work was supported by funding from Texas A&M Neural-Gut Immune Axis group and the WoodNext Foundation.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Defining a role for ATP Citrate Lyase as an immune-metabolic sensor

Eunice Lara, Abigail Bauder, Xiaotong Li, Jason Karpac
Dept. of Cell Biology & Genetics
Texas A&M School of Medicine
Bryan, TX

Innate immunity and metabolism are integrated through enzymes and pathways to produce coordinated cellular responses to stressors, such as infectious microorganisms. Because extensive metabolic rewiring occurs upon pathogenic challenge, there is a need to untangle the distinct mechanisms shaping immune-metabolic integration. ATP citrate lyase (ACLY) is one such metabolic enzyme whose role during the immune response has yet to be uncovered. ACLY uses citrate as its substrate to synthesize acetyl-CoA for use in processes such as lipid synthesis and protein acetylation. Using Drosophila melanogaster as a model, ACLY was previously found to relocate within intestinal enterocytes from the nucleus to the cytosol upon infection with Pseudomonas entomophila (P.e.), a bacterial entomo-pathogen. Here, we explored the influences of mitochondrially-derived citrate and dietary citrate on ACLY's relocation. Mitochondrially-derived citrate was reduced in flies by knocking-down Citrate/isocitrate carrier (CIC), which is responsible for exporting citrate out of the mitochondria and into the cytosol. Additionally, to examine the role of dietary citrate, fly food was supplemented with citric acid. After P.e. infection, ACLY's subcellular location in enterocytes was determined and its correspondence to overall fly survival. Both dietary citrate supplementation and CIC knock-down hindered ACLY's ability to relocate into the cytosol. Importantly, this impaired relocation caused a significant decrease in survival. Together, these results demonstrate that ACLY is a key immune-metabolic sensor in enterocytes, where its citrate-driven relocation positively influences the infection response.

This work was supported by NIH R01 1DK133294 to JK, DRUMR Fellowship support by NIH R25 DK126642,

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

INTERFERON OMEGA IS AN EFFECTIVE ANTIVIRAL AGAINST HERPES SIMPLEX VIRUS IN GUINEA PIG CELLS

Alan Justin Lee, Alistair McGregor
Department of Microbial Pathogenesis and Immunology
Texas A&M School of Medicine
Bryan, TX

Interferons (IFNs) are an essential component of the innate immune system. In the case of viral infection, their antiviral activity is enhanced by the expression of Interferon Stimulated Genes (ISGs) via diverse modes of action. There are three of IFNs: I, II, and III, each with a specific receptor. IFN-I and IFN-II activity is ubiquitous across all cells, but IFN-III activity is only found in barrier and epithelial cells. Among the numerous IFN-Is encoded in humans, IFN-ω is among the most widely expressed by leukocytes; it is poorly studied but has potent potential as an antiviral strategy. Considering that IFN-ω is not found in mice, we aim to determine if IFN-ω would serve as an effective antiviral in a guinea pig model. The studies were carried out by transducing either short-term or long-term expression of IFN-ω in various guinea pig cell lines. Both strategies induced an antiviral state as determined by the detection of ISG protein expression, specifically the Mx protein. Additionally, IFN-ω induced cells demonstrated antiviral activity against Herpes Simplex Virus. A possible future direction is to study the standalone antiviral effects of specific ISG products, such as the Mx protein, in guinea pig cell lines via a similar methodology.

AJL was supported by the Texas A&M School of Medicine Office of Research.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Development of Novel assays to Detect Cytomegalovirus-specific Antibodies to Prefusion Glycoprotein B (gB) and gB Antigenic Domain 1(AD1) Antigens

Maria A. Lopez, K. Yeon Choi, and Alistair Mcregor
Texas A&M School of Medicine
Bryan, TX

Human cytomegalovirus (HCMV) is a leading cause of congenital disease resulting in cognitive impairment and deafness in newborns. The guinea pig is the only small animal model for congenital CMV (cCMV) but requires species-specific guinea pig CMV (GPCMV). This model is used to study virus pathogenicity and the development of CMV intervention strategies. In both HCMV and GPCMV, the viral glycoprotein gB is essential for infection on all cell types, including fibroblasts and non-fibroblast cells (epithelial, endothelial, and placental trophoblast). Consequently, gB is the primary antibody target for CMV vaccines. Novel enzyme-linked immunosorbent assays (ELISA) were developed to evaluate the specific immune response to the oligomerization domain of gB (AD1) and a gB prefusion antigen. Sera from animals infected by wild-type GPCMV strains (hyperimmune) or gB vaccines (trimeric and prefusion gB) were evaluated. Samples were tested for gB antibodies using an established anti-gB ELISA with titers ranging from 2560 – 20480. Antibodies to prefusion gB and gB AD1 antigens were also detected with titers ranging from 1280-10240 and 320-10240, respectively. Overall, hyperimmune sera to GPCMV and trimeric gB exhibited higher titers than animals vaccinated with the prefusion version of gB. We concluded that GPCMV prefusion gB and gB AD1 antigens are highly immunogenic, and antibodies to these targets can be detected by ELISA. Antibodies blocking multimerization would improve vaccine efficacy, as would targeting the prefusion version of gB to prevent viral cell entry.

MAL was supported by a Fellowship from NIH R25 DK126642.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

SEX-SPECIFIC MODULATION OF THE TUMOR MICROENVIRONMENT BY NIK: IMPLICATIONS FOR TREATMENT OF GLIOBLASTOMA

Hailey Maurer, Justin N. Keeney, Hasara Abeygunaratne, Kathryn M. Pflug, and Raquel Sitcheran
Department of Cell Biology and Genetics
Texas A&M School of Medicine
Bryan, TX

Glioblastoma multiforme (GBM), a WHO grade 4 brain tumor, is notoriously aggressive and treatment-resistant, partly due to its complex and immunosuppressive tumor microenvironment (TME). Within this milieu, microglia, together with tumor-associated macrophages, are among the most abundant immune cells. This study investigates the influence of NF-κB-Inducing Kinase (NIK) -- a critical upstream regulator of NF-κB signaling – on immune cell dynamics and GBM progression. Using orthotopic, syngeneic glioma mouse models, we demonstrate that male mice with microglia-specific NIK knockout (NIKcKO) exhibit reduced GBM growth and improved survival rates compared to their female counterparts. While immunohistochemistry analysis of GBM tumors showed that NIK microglial deficiency did not significantly impact overall immune cell numbers within the tumor, high parameter flow cytometry analysis revealed that NIK selectively suppresses proinflammatory, anti-tumor macrophage infiltration in a manner that is sex dependent. Taken together with our previous findings, these results highlight NIK's instrumental role in regulating immune cell polarization and recruitment, underscoring its contribution to GBM pathogenesis. Crucially, our data suggest that targeting NIK may lead to more personalized and effective GBM treatment strategies, particularly for male patients, who are less responsive to conventional therapies.

This work was supported by R01NS082554 to RS. HM was supported by a Fellowship from Texas A&M School of Medicine.

Texas A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Protective Effect of Ganaxolone on Astrocyte Neuroinflammation in a Rat Model of Gulf War Illness

Grant McNatt, Xin Wu, D. Samba Reddy
Dept. of Neuroscience and Experimental Therapeutics
Texas A&M School of Medicine
Bryan, TX

Gulf War Illness (GWI) is a chronic neuropsychiatric disorder characterized by cognitive and emotional impairments in veterans. Astrocytes, key regulators of brain homeostasis, become reactive in GWI, releasing pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-6, contributing to persistent neuroinflammation. This study investigated the therapeutic efficacy of the synthetic neurosteroid ganaxolone (GX) on astrocytic inflammation in a rat model of GWI. Male rats were exposed to GWI-related chemicals (pyridostigmine bromide orally, DEET and permethrin transdermally) and stress for 28 days. After a 15-month waiting period, GX (10 mg/kg, sc) was administered for one month. Astrogliosis was assessed using glial fibrillary acidic protein (GFAP) immunohistochemistry in hippocampal and extra hippocampal regions. GFAP(+) expression was quantified using densitometry and pathological scoring. Results showed significant astrocyte activation in hippocampal subfields (CA1, CA3, dentate gyrus and extra hippocampal regions (thalamus, amygdala, somatosensory cortex) 15 months post-GWI induction, indicating sustained neuroinflammation. GX treatment significantly reduced GFAP(+) expression in both hippocampal and extrahippocampal areas, attenuating astrocyte reactivity and pathological scores compared to untreated GWI rats. These findings demonstrate GX's neuroprotective potential in reducing chronic astrogliosis and inflammatory responses in GWI. Neurosteroid treatment may effectively mitigate long-term neuroinflammation associated with GWI, potentially improving neurological outcomes for affected veterans. Future studies should investigate GX's impact on specific inflammatory cytokines and cognitive function in GWI treatment.

This work was supported by DOD #W81XWH-19-1-0702 to DSR. GM was supported by Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Conditional Expression of Intein-containing Orco-QF2 in Drosophila melanogaster

Pranav Nalam, Ji-Eun Ahn, Hubert Amrein
Department of Cellular Biology and Genetics
Texas A&M School of Medicine
Bryan, TX

Mosquito-transmitted viruses such as dengue, Zika, and chikungunya affect millions of people globally. As such there is an urgent need to reduce the spread of these viruses. Using D. melanogaster, we aim to design novel, controllable protein expression tools that can be implemented in mosquito Ae. aegypti with the goal of disrupting effective disease propagation of insect species. We used the bimodal Q-S system to modulate key olfactory circuits by incorporating temperature-sensitive intein modules, which are self-splicing endopeptidases, into the transcription factor QF2 with the goal of controlling olfactory receptor gene expression. QF2 is expressed under the Orco promoter, which is expressed in all olfactory neurons, providing us with a tool to manipulate gene expression in these neurons, and consequently their function. Orco is essential for odor perception and odorant receptor trafficking in Drosophila olfactory sensory neurons and is conserved in mosquitos. The goal of the study is to determine the temporal dynamics of intein-containing QF2 proteins in the antenna and the maxillary palps of the Drosophila. To do so, we performed experiments in which (i) QF2 was inactivated by shifting flies from a permissive to restrictive temperature range and (ii) QF2 was activated by shifting flies from a restrictive to permissive temperature range. QF2 inactivation is slow, taking several days, while activation of QF2 expression is rapid and can be seen within 6 hours. This intein-based approach holds promise for temporal gene expression control and warrants the development of additional temperature-sensitive tools including the QS, the QF2 inhibitor.

PN was supported by a Fellowship from the Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

THE ROLE OF 17--ESTRADIOL IN SEX-SPECIFIC CYTISINE-MEDIATED NEUROPROTECTION AGAINST PARKINSON'S DISEASE

Tan Nguyen, Roger C. Garcia, Gauri Pandey, Sara M. Zarate, Rahul Srinivasan
Dept. of Neuroscience and Experimental Therapeutics
Texas A&M School of Medicine
Bryan, TX

Parkinson's disease (PD) is the second-most common neurodegenerative disorder in the United States. Motor symptoms in PD are caused by the loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNc). However, treatments to reduce SNc DA neuron loss do not exist. In this regard, drugs that reduce hyperactive endoplasmic reticulum (ER) stress, which is known to cause SNc DA neuron loss, can provide an effective treatment for PD. Interestingly, the smoking cessation drug cytisine reduces ER stress, and this is associated with an increase in ER exit sites (ERES) in DA neurons. Therefore, ERES upregulation could play a key role in the ability of cytisine to reduce ER stress and exert neuroprotection. Additionally, cytisine upregulates ERES only in female parkinsonian mice, however, the mechanisms behind this sex-specific ERES upregulation of cytisine are not understood. We hypothesize that the sex hormone 17-β-estradiol is required for cytisine-mediated ERES upregulation in SNc DA neurons. To test our hypothesis, we performed two methods of 17-β-estradiol depletion in female parkinsonian mice exposed to either saline or cytisine: ovariectomy and administration of the aromatase inhibitor, letrozole. Midbrain sections were immunostained for expression of SEC24D, which is a marker for ERES and tyrosine hydroxylase (TH), which labels SNc DA neurons. All sections were then imaged using confocal microscopy. Our preliminary results show that 17-β-estradiol depletion in female parkinsonian mice prevents cytisine-mediated upregulation of ERES. These data suggest that the combination of 17-β-estradiol and cytisine may be necessary for ERES upregulation in SNc DA neurons.

This work was supported by NIH R01 NS115809 to RS. TN was supported by the Texas A&M School of Medicine

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

INVESTIGATING THE NON-ADDICTIVE POTENTIAL OF NOVEL CB1 RECEPTOR POSITIVE ALLOSTERIC MODULATORS FOR NEUROPATHIC PAIN MANAGEMENT

Thanh N. T. Nguyen1, Yuhong Guo, Dheeraj Govu, Rithika Venna, Belen Cocke, Dana E. Selley, Tao Feng, Dai Lu, & Laura N. Smith1,
Department of Neuroscience & Experimental Therapeutics, Texas A&M University; Department of Pharmacology and Toxicology, Virginia Commonwealth University; Department of Biomedical Sciences, Texas A&M University; Department of Pharmaceutical Sciences, Texas A&M University; Institute for Neuroscience, Texas A&M University.

The U.S.'s severe opioid epidemic, worsened by the COVID-19 pandemic, highlights the urgent need for substitute analgesics. Preclinical evidence indicates that cannabinoids' opioid-sparing effect could reduce the dose of opioids necessary to alleviate pain, but their addictive psychoactive effects remain a challenge. Our team aims to modulate the endocannabinoid system by targeting positive allosteric modulators (PAMs) of the Cannabinoid 1 receptor (CB1 receptor) as an alternative approach to alleviate neuropathic pain. We optimized a CB1 PAM, PTDP-15 (P-15), and successfully tested its pharmacokinetics and metabolic stability by examining how it interacts with the target receptors in the brain in a previous study. We then assessed the addictive properties of the CB1 PAM by designing a 35-day operant conditioning learning program with different phases on mice using an Intravenous Drug Self-Administration (IVSA) chamber. The computer recorded all data, particularly the time of nose-poking behavior at an active port, which would trigger a light to illuminate above the port and inject the drug via the catheter. Preliminary results suggest differences among mice from three groups: Cocaine (positive control), Vehicle (negative control), and P-15. The findings propose a potential low addictive liability for the test compound. With these results, we hope to increase the sample size or use the program to examine the addictive properties of other experimental compounds that also bind to the CB1 receptor.

This work was supported by NIH 1UG3 NS128439-01. TN was supported by the Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Development of NanoBRET as a Screening Tool in Mycobacteria

Keya Patel, Chuan Liang, Kent Koster, Aaron Benjamin, and Jeffery Cirillo
Department of Microbial Pathogenesis and Immunology
Texas A&M School of Medicine
Bryan, TX

Tuberculosis (TB) is a serious bacterial infection that targets the lungs and is one of the top causes of death globally, causing 10.6 million infections and 1.3 million deaths according to the World Health Organization (2021). Despite the extensive research done on TB, there is still little understood about the genetic makeup and how the bacteria evades the immune system. To elucidate many of these functions, we constructed a promoter-less NanoLuc/NanoBRET reporter assay, which uses light to measure gene expression and a transposase as the mechanism of integration. Recently, a novel putative autoinducer molecule was identified in the genus Mycobacterium, but the mechanisms of gene expression and regulation remain relatively unknown. Using techniques such as electroporation, qPCR, and fluorescent imaging, we were able to validate the reporter in mycobacteria. All transformed mycobacterial colonies expressed similar levels of bioluminescence with an increase in radiance at a greater CFU, suggesting genes that are controlled by this molecule are expressed at a higher density. Furthermore, the presence of the reporter construct was observed in all colonies, confirmed by PCR of the inserted kanamycin resistance gene in the construct we built. This confirms the NanoLuc/NanoBRET system is a viable tool that will be used to investigate which genes are regulated by the autoinducer molecule. This enables us to create a transformant library in the future to screen for differential expression.

KP was supported by Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

DEVELOPMENT OF PRIMERS FOR THE ANALYSIS OF PRENATAL ALCOHOL EXPOSURE ON X-INACTIVE SPECIFIC TRANSCRIPT

Arianna Perez, Rosaline Kumar, and Rajesh C Miranda
Dept. of Neuroscience and Experimental Therapeutics
Texas A&M School of Medicine
Bryan, TX

Prenatal alcohol exposure (PAE) impairs the development of fetuses during gestation and can result in cognitive and neurobehavioral deficits that are collectively termed 'Fetal Alcohol Spectrum Disorders' (FASD). We have previously reported that PAE can result in diminished X-chromosome inactivation (XCI) in the fetal female mouse neocortex. XCI is an epigenetic dosage compensation mechanism that occurs in females and results in randomized silencing of one of the pair of female X-chromosomes. In mammalian females, one X-chromosome is randomly silenced by the transcript of X-inactive specific transcript (XIST), a long non-coding RNA (lncRNA) that's encoded with three other lncRNAs (TSIX, JPX, FTX) in the x-inactivation center. Previous research has shown that XIST decreased in neural progenitor cells following PAE. Our overarching hypothesis is that PAE will decrease expression levels of XIST in a non-sex-segregated neurosphere culture. An immediate goal was to design and validate a primer set for the evaluation of baseline XIST expression in female control mouse tissues as well as non-sex-segregated (mixed male and female) neurospheres derived from gestational day 12.5 fetal telencephalon. Primers were verified by qPCR amplification, by gel electrophoresis to verify amplicon size and by amplicon sequencing to confirm target transcript identity. Baseline expression of XIST was assessed using qRT-PCR with validated primer sets for XIST. We found that XIST expression was suppressed following PAE in a non-sex-segregated neurosphere culture, suggesting that PAE can affect X-chromosome inactivation. Future directions include using a sex-segregated female neurosphere culture to examine the effects of prenatal alcohol exposure on XIST and TSIX.

This work was supported by NIH RO1 AA028406 to RCM. AP was supported by NIH R25 DK126642.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

PROTECTIVE EFFECTS OF CANNABIDIOL ON MICROGLIAL NEUROINFLAMMATION IN AN EXPERIMENTAL MODEL OF GULF WAR ILLNESS

Shreya Ravichandar, Xin Wu, D. Samba Reddy*
Department of Neuroscience and Experimental Therapeutics
Texas A&M University School of Medicine
Bryan, TX

Gulf War Illness (GWI) is a chronic multisymptomatic illness affecting many veterans exposed to certain chemicals during the Gulf war, such as pyridostigmine bromide and insect repellent. These exposures lead to adverse effects and potentially cause inflammation or neuronal death. We hypothesize that the phytocannabinoid cannabidiol (CBD) has neuroprotective effects in GWI. In this study, we investigated the therapeutic efficacy of the CBD in a rat model of GWI using neuro-histological techniques. We analyzed the distribution pattern and basal density of IBA1(+) microglia in the hippocampal and extrahippocampal regions using denistometry. Ten months after GWI induction, significant microglial activation was observed in the hippocampal CA1, CA3, and dentate gyrus subfields, as well as in extrahippocampal regions such as the thalamus, hypothalamus, amygdala, piriform cortex, somatosensory cortex, and the entorhinal cortex regions. In the CBD-treated group, there was a significant reduction in IBA1(+) expression in both the hippocampal subfields and extrahippocampal regions, indicating its neuroprotective activity. Additionally, this treatment demonstrated a significantly lower neuroinflammation compared to the GWI group and a higher percentage of microgliosis protection. These results confirm that chronic GWI is associated with persistent microgliosis, and that CBD therapy has promising protective effects in reducing such chronic inflammation in GWI, which reinforce CBD as a potential treatment for GWI.

This work was supported by DOD grant #W81XWH2110314 (to D.S.R.).

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Activation of the 5-HTR7 Signaling Axis Increases Cholangiocyte Angiogenin Expression Triggering Ductular Reaction and Liver Fibrosis

Abigail Rodriguez, Regi Capati, Mariam Khwaja, Thein Phan, Joseph Rutkowski, Amy Barrett, Jordan Faust, Shannon Glaser
Medical Physiology
Texas A&M School of Medicine
Bryan, TX

Cholangiocytes are epithelial cells that line the bile ducts and are the target of cholestatic liver diseases such as primary sclerosing cholangitis (PSC). The cause of PSC, a disease characterized by fibrosis and reduced bile flow, is unknown. PSC is also characterized by ductular reaction (DR), which is an active phenotype of cholangiocytes. We tested the hypothesis that the 5-HTR7 signaling axis stimulates a reactive cholangiocyte phenotype (DR) by inducing angiogenin (ANG)-mediated stress response mechanisms, which promotes inflammation and fibrosis during cholestasis. Mdr2 knockout mice which have a PSC phenotype were crossed with mice lacking the 5-HTR7. Liver sections were stained with CK-19 (cholangiocyte maker), Sirius red and F4/80 to observe relative amounts of DR, fibrosis, and inflammation. In mice lacking 5-HTR7 or treated with a 5-HTR7 antagonist, a lower amount of DR, fibrosis and inflammation was observed. ANG levels were elevated in cholangiocytes isolated from the Mdr2 KO mice and reduced in mice lacking 5-HTR7. Treatment of cholangiocytes with AS19 (5-HTR7 agonist) triggers the gene expression of ANG. To evaluate the stress response on the cells as a damage signaling mechanism, a reactive oxygen species (ROS) assay was conducted in H69 cells (cholangiocytes) treated with angiogenin and AS19. The relative amount of ROS increased significantly. A proteomic assay was performed and increased ERK1/2, PDGF RB, PYK2, YES, and RSK1/2/3 of both ANG and AS19 treatments. These results indicate a connection between the 5-HTR7/ANG/ROS signaling axis in the elevated levels of DR, fibrosis and inflammation during cholestasis.

Funding support for the project, DRUMR Fellowship support by NIH R25 DK126642,

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

EVALUATING VARIATION IN PRECLINICAL COLORECTAL CANCER STUDIES USING MOUSE MODELS TO IMPROVE TRANSLATIONAL MEDICINE

Rohit Satish, Dr. David Threadgill
Cell Biology and Genetics
Texas A&M School of Medicine
College Station, TX

Mouse models are widely used in preclinical colorectal cancer research to evaluate the efficacy and consequences of existing and novel drug and genome therapies. However, current mouse models often struggle to translate consistently to human medicine and suffer from low reproducibility due to numerous confounding variables in trials which makes scientific consensus on cancer medicine increasingly difficult. By systematically analyzing and synthesizing information about the diverse genetic and environmental factors that contribute to variability in mouse model trial outcomes, we are able to elucidate the underlying causes of inconsistencies and aim to enhance the reliability of preclinical colorectal cancer research, ultimately aiding in improving the translation of animal-model findings to human medicine. Utilizing qualitative analysis and detailed examination of current experimental design models, protocols, control measures, and sample sizes provides an approach that considers numerous variables. Through investigation of these aspects, we then aim to understand and present how confounding variables frequently appearing in current mouse models can cause downstream phenotypic manifestations in mice, leading to skewed study data. We determined that the mouse model type and susceptibilities to specific colorectal cancer subtypes, genetic background, as well as inconsistencies in environmental conditions were all major contributing factors to study variation in their own way. Thus, an increase in robustness testing standardization of experimental protocols to enhance the reproducibility and reliability of preclinical research would elevate the translational value of mouse studies in numerous research areas, especially colorectal cancer study.

This work was supported by the Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

A T11 SPINAL CORD INJURY DECREASES SYMPATHETIC SIGNALING TO BONE

Kayari Suganuma, Jessica Bryan, Michelle Hook
Department of Neuroscience and Experimental Therapeutics
Texas A&M School of Medicine
Bryan, TX

Spinal Cord Injury (SCI) affects millions globally, causing severe complications such as paralysis, loss of bowel and bladder function, increased stroke risk, and depression. One often overlooked complication of SCI is bone loss, with individuals losing up to 50% of bone mass below the injury within two years. Our previous research showed that despite weight-bearing recovery on hindlimbs, rats with lower thoracic (T11) SCI also lose 50% of bone mass in the hindlimbs post-injury. This suggests that SCI-induced bone loss is not solely due to disuse. Other studies propose that neural dysregulation, especially sympathetic dysregulation, may significantly contribute to bone loss. We tested whether blocking sympathetic signaling could prevent bone loss in the T11 SCI rat model but found no effect of noradrenergic antagonists. Considering that sympathetic preganglionic neurons innervating the femur and tibia originate from the T13-L1 spinal cord region, we hypothesized they might be damaged by the T11 injury. Loss of sympathetic innervation, rather than gain, may drive bone loss after a T11 SCI. To investigate this, rats were given a contusion injury at the T11 level of the spinal cord, euthanized 28 days post-surgery, and their spinal cords were collected for immunohistochemical (IHC) analysis. Sympathetic neurons were identified using choline acetyltransferase (ChAT) staining. IHC analysis revealed a reduction in ChAT-positive neurons after SCI, relative to shams. These findings support the premise that a decrease in ChAT-positive neurons, and sympathetic signaling to bone, may underlie bone loss in the T11 SCI model.

This work was supported by grant to MH from the Craig H Neilson, Mission Connect, and TAMHSC seedling grant. KS was supported by Texas A&M School of Medicine.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

ENHANCING THE ANTIBIOTIC DELIVERY POTENTIAL FOR UBX MATERIALS

Paige Wilson, Nasanna Henley, Britt Faulk, Francesca Agobe, Carolyn Canon, Sarah Bondos
Dept. of Medical Physiology
Texas A&M School of Medicine
Bryan, TX

Antibiotic resistant bacteria killed 1.27 million people and contributed to 4.95 million other deaths in 2023. Of these resistant bacteria, MRSA, or Methicillin-resistant Staphylococcus aureus, causes almost half of all deaths. Staphylococcus aureus is a gram-positive opportunistic pathogen that is the predominant cause of nosocomial and community infections. Only a few antibiotics target gram-positive bacteria, and those effective against S. aureus have been used to the point of resistance. An antibiotic in which MRSA is targeted and still sensitive is needed to combat the growing resistance problem. The novel biaryl antibiotic C58 outperforms vancomycin (current gold standard) in bactericidal activity. C58 was found to not be hemolytic at therapeutic concentration. However, when used in vivo C58 binds to the plasma serum of the blood causing it to be inactive upon administration. We believe that Ultrabithorax (Ubx) can be used for targeted delivery of C58. Dityrosine bonds form during Ubx assembly, and the biaryl structure of C58 mimics that of dityrosine allowing them to bind to one another. Upon binding Ubx materials, C58 concentrates 100-fold. Ubx has the potential to enable C58 to be delivered in medically significant quantities. Ubx has traditionally been used as long fibers with microscale diameters or incorporated into very thin electrospun sheets. Neither form is suitable for drug delivery. We expressed and purified Ubx and developed new forms of Ubx materials that could be deployed in a wound to deliver sufficient quantities of Ubx, and thus C58, to treat an infection.

This work was supported by NIH grant NIH R01GM099827 to SEB. PW was supported by a Fellowship from NIH R25 DK126642.

TEXAS A&M HEALTH
SCHOOL OF MEDICINE
2024 SUMMER UNDERGRADUATE RESEARCH PROGRAM

Salt or Angiotensin II Induce Pro-Inflammatory and Pro-Lymphangiogenic CD38+ Innate Immune Cells

Emily Zamora, Hannah L. Smith, Bethany Goodlett, Brett M. Mitchell
Department of Medical Physiology
Texas A&M School of Medicine
Bryan, TX

Hypertension (HTN) affects millions worldwide, contributing significantly to cardiovascular disease, stroke, and kidney dysfunction. Salt-sensitive HTN (SSHTN) and angiotensin II (A2)-induced HTN (A2HTN) both include broad activation of the immune system and are hallmarked by infiltration of innate immune cells such as macrophages and dendritic cells (DCs) into the kidneys. Analysis of mouse kidneys from mice with SSHTN and A2HTN by flow cytometry confirmed macrophages and DCs were elevated in both models, as well as identified subpopulations of activated innate immune cells that express CD38. Renal CD38+ M1 macrophages and CD38+ type 2 conventional DCs (cDC2s) were increased in both HTN models. These populations were replicated in vitro when bone marrow derived monocytes (BMDMs) were treated with either salt or A2. In the context of HTN, the role of CD38+ M1 macrophages and CD38+ cDC2s is unknown. To explore this, BMDMs were treated with either salt or A2 and CD38+ M1 macrophages and CD38+ cDC2s were sorted. After cell sorting, RNA was isolated from each cell type and converted into cDNA for real-time PCR. PCR analysis revealed that salt and A2 treated CD38+ M1 macrophages and CD38+ cDC2s had increased expression of the pro-inflammatory cytokines IL-1β, IL-6, and TNF-α and the pro-lymphangiogenic genes NRP2, VEGF-A, and VEGF-D. Overall, these data suggest that the increase in CD38+ M1 macrophages and CD38+ cDC2s is associated with SSHTN and A2HTN. Further investigation of these cells could further characterize this association and provide new therapeutic targets for both SSHTN and A2HTN.

This work was supported by NIH grant DK120493 to BM. EZ was supported by a Fellowship from NIH R25 DK126642.

Acknowledgements

The Texas A&M School of Medicine's Summer Research Program (SRP) continues to attract the top students from the best colleges and universities across the country. This year we had 24 participants who completed the ten-week program and two Air Force Academy Cadets who participated for five weeks. These students were selected from a large pool of applicants based on their research experience, desire to attend graduate/medical school, grades, and recommendations. I would like to thank the selection committee who dedicated their time.

I would also like to thank the faculty that gave their time as mentors. You have provided each of these students with a valuable experience that will undoubtedly help them achieve their career goals.

The SRP was made possible by the following who provided funding and programmatic support:

- **Amy Waer, M.D. – Dean**
- **Allison Rice-Ficht, Ph.D. – Interim Senior Associate Dean of Research**
- **National Institute of Diabetes and Digestive and Kidney Diseases (R25DK126642)**
- **Fernando Vasquez, M.A. – Assistant Dean of Admissions**
- **Samba Reddy, Ph.D. – Director, Institute of Pharmacology and Neurotherapeutics**
- **Air Force Academy Cadet Summer Research Program**

The following faculty selected eligible students to represent their school in the NIDDK sponsored **Developing and Readying Underrepresented Minority Researchers (DRUMR)** SRP:

- **Laura Weiser-Erlandson, Ph.D. – Texas A&M University – Central Texas**
- **Venu Cheriyath, Ph.D. – Texas A&M University – Commerce**
- **Riccardo Mozzachiodi, Ph.D. – Texas A&M University – Corpus Christi**
- **Richard Laughlin, Ph.D. – Texas A&M University – Kingsville**
- **Dennis Daniels, M.P.H, Dr. PH – Prairie View A&M University**
- **Chris Mares, Ph.D. - Texas A&M University- San Antonio**
- **Michael Kidd, Ph.D. – Texas A&M University – International**
- **Max Sanderford, PhD. & Phil Sudman, Ph.D. – Tarleton State University**
- **Nurul Alam, Ph.D. & David Allard, Ph.D. – Texas A&M University – Texarkana**
- **Neil Terry, Ph.D. – West Texas A&M University**

Each week, we had Roundtable Discussions and professional development sessions in which participants got to engage with faculty, guest speakers, and alumni. Participants also learned more about Texas A&M University's various graduate and medical programs in the School of Medicine.

Finally, I would like to thank the Associate Director, **Stacy De Leon**, Senior Administrative Coordinator, **Shelly Daughters,** and student assistants, **Kennedy Barrett** and **Meray Lewis,** who did a lot of work arranging the arrival, housing, registration, processing, and the weekly meetings. Thank you to our poster judges who had an extremely difficult task of picking the best out of the best. Thank you, students, for your hard work and for a memorable summer – Gig 'em!

Brett Mitchell, Ph.D., F.A.H.A.
Director, Texas A&M School of Medicine Summer Research Program

2024 Texas A&M School of Medicine
Summer Research Program Participants

Gustave Allen	Tarleton State University	Dr. Joseph Rutkowski
Brandon Anderson	Air Force Academy	Dr. Shaunna Clark
Amrit Bhakta	Texas A&M University	Dr. Cedric Geoffroy
Reginaldo Capati	Air Force Academy	Dr. Shannon Glaser
Darsh Darji	Texas A&M University	Dr. Samba Reddy
Fatima Gonzalez Laureano	Texas A&M University-Commerce	Dr. Adam Case
Hana Hasan	University of Toronto	Dr. Farida Sohrabji
Nasanna Henley	Texas A&M University-Corpus Christi	Dr. Sarah Bondos
Zahi Hussain	Texas A&M University	Dr. Travis Hein
Angel Ifegbo	Texas A&M University-Kingsville	Dr. Lee Shapiro
Eunice Lara	Texas A&M University-Kingsville	Dr. Jason Karpac
Alan Lee	Case Western University	Dr. Alistair McGregor
Maria Lopez	Texas A&M International	Dr. Alistair McGregor
Hailey Mauer	Rowan University	Dr. Raquel Sitcheran
Grant McNatt	Texas A&M University	Dr. Samba Reddy
Pranav Nalam	Grand Valley State University	Dr. Hubert Amrein
Tan Nguyen	Cal Poly Pomona	Dr. Rahul Srinivasan
Thanh Nguyen	DePauw University	Dr. Laura Smith
Keya Patel	University of Illinois	Dr. Jeff Cirillo
Arianna Perez	Texas A&M-San Antonio	Dr. Rajesh Miranda
Shreya Ravichandar	Texas A&M University	Dr. Samba Reddy
Abigail Rodriguez	West Texas A&M University	Dr. Shannon Glaser
Rohit Satish	Johns Hopkins University	Dr. David Threadgill
Kayari Suganuma	Hillsdale College	Dr. Michelle Hook
Paige Wilson	Prairie View A&M	Dr. Sarah Bondos
Emily Zamora	Tarleton State University	Dr. Brett Mitchell

Texas A&M School of Medicine
Summer Research Program Weekly Schedule for 2024

DATE	TIME	TOPIC	PRESENTER
5/20	9:00 AM	Orientation and Laboratory Safety Training	
5/23	9:00 AM	Professional Development #1 - Icebreaker	Dr. Brett Mitchell
5/24	9:00 AM	RCR – Data Management	Dr. Brett Mitchell
5/28	12:00 PM	TAMU School of Medicine MD Program	Mr. Fernando Vasquez
5/30	9:00 AM	Professional Development #2 – Career Q&A	Dr. Brett Mitchell
5/31	9:00 AM	RCR – Transparency & Reproducibility	Dr. Brett Mitchell
6/4	12:00 PM	CST*R Grand Rounds	MD/PhD Students
6/6	9:00 AM	Professional Development #3 – Alumni Q&A	Madison Wang & Abby Bauder
6/7	9:00 AM	RCR – Animal Subjects	Dr. Farida Sohrabji
6/11	12:00 PM	TAMU School of Medicine MS and PhD Programs	Dr. Van Wilson
6/13	9:00 AM	Professional Development #4 – MD School Interviews	Dr. Brett Mitchell
6/14	9:00 AM	Roundtable – Writing an Abstract	Dr. Brett Mitchell
6/18	12:00 PM	TAMU School of Medicine MD/PhD Program	Dr. Carolyn Cannon
6/20	9:00 AM	Professional Development #5 – Professional Writing	Dr. Barbara Gastel
6/21	9:00 AM	Roundtable – Marketing and Interviewing	Dr. Brett Mitchell
6/25	12:00 PM	A&M Rural and Community Health Institute	Dr. Nancy Dickey
6/27	9:00 AM	Professional Development #6 – Physician Assistant Q&A	Lorin Catalena, PA-C
6/28	9:00 AM	Roundtable – Organizing Your Poster	Dr. Brett Mitchell
7/2		RCR – Scientific Misconduct Air Force Academy Poster Session	Dr. Brett Mitchell Cadets
7/4		Holiday	
7/5		Holiday	
7/9	12:00 PM	Roundtable – Giving a 10 Minute Talk	Dr. Brett Mitchell
7/11	9:00 AM	Professional Development #7 – Graduate School Interviews	Dr. Brett Mitchell
7/12	9:00 AM	Roundtable – Presenting at Conferences	Dr. Brett Mitchell
7/16	12:00 PM	Southwest Rural Health Research Center	Dr. Jane Bolin
7/18	9:00 AM	Professional Development #8 – Presentation Preparation	
7/19	9:00 AM	Roundtable – Applying to School	Dr. Brett Mitchell
7/22	9:00 AM	Student Presentations	
7/23	9:00 AM	Student Presentations	
7/24	9:00 AM	Student Presentations	
7/25	9:00 AM	Texas A&M University Walking Tour	
7/26	9:00 AM	RESEARCH DAY Poster Presentation, Reception, Keynote Speaker, Awards Ceremony and Pictures	

Program Director

Brett Mitchell, PhD, FAHA
Professor, Department of Medical Physiology
Director, Summer Research Program
School of Medicine, Texas A&M Health
MREB 2, room 2412
Bryan, TX 77807
Email: brettmitchell@tamu.edu
Ph. 979.436.0751

Please keep us updated with your contact information & career or school decisions after graduation.

Thank you for your hard work this summer!