VSSA Summer Symposium Abstracts

Summer 2024

Thursday August 1
2-3 pm
Langford Lobby

We want to thank everyone who participated in supporting the research summer experience for our interns: the principle investigators and mentors, lab personnel and staff, and program directors and our weekly speakers. It truly takes everyone to make the Vanderbilt Summer Science Academy happen.

Please join us in celebrating the accomplishments of the research interns, and visit the Poster Session to learn what they have done this summer.

Sincerely,
The VSSA Team

Stephanie Richards, Ph.D.,
Director

Angel Gaither,
Program Manager

Aaron Howard,
Program Coordinator

RC Stabile, Ed.D.,
Director of Trainee Well-being

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Presenter: Molly Crew, Iowa State University

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41. Development Of a Culturally tailored Motivational Interviewing-Based Health Coaching Intervention For Improving Hemodialysis Nonadherence in African Americans: "The MoVE Intervention"

Presenters: Kamsi Nwotite, Kent School, and Didi Umeukeje, Saint Cecilia Academy

ABSTRACTS

1. Knockdown of GLG1 and GLI2 reduces interactions within bone marrow and tumor microenvironments present in a bone metastatic breast cancer model

Presenter: Nneka Otuonye, Georgia State University

Program: MSTP Summer Research Program

Principle Investigator: Julie Rhoades, Ph.D., Department of Medicine

Project Mentor: Erik Beadle, Ph.D., Clinical Pharmacology

Project Authors: Nneka C. Otuonye, Erik P. Beadle, Ph.D., Rachel S. Mangano, Jade S. Miller, Emily A. Jaremba, Erykah D. Coe, and Julie A. Rhoades, Ph.D.

Abstract:

Breast cancer is the second leading cause of cancer-related deaths among women in the United States. While localized disease is treatable, the dissemination of tumor cells to distant organs introduces clinical complications and increased morbidity. Bone metastatic breast cancer currently has limited treatment options, and remains a significant clinical problem by promoting tumor-induced bone disease (TIBD). TIBD is a condition where tumor cells disrupt cell populations in the bone microenvironment and it results in increased osteoclast resorption. Previous research has highlighted two proteins, GLG1 and GLI2, as contributors to bone colonization and TIBD; GLI2 regulates transcription of PTHrP, an osteolytic factor secreted by tumor cells promoting osteoclast formation, as GLG1 promotes bone colonization through interactions with endothelial cells. Using the MDA-MB-231 breast cancer cell line, we generated gene expression knockdown models of GLI2 and GLG1 to determine if functional loss of these proteins could disrupt known mechanisms of TIBD. To test this question, we utilized western blots and qRT-PCR to measure protein and transcript expression, respectively, to evaluate the efficacy of our GLG1 siRNA and GLI2 CRISPR gRNA knockdowns. The knockdowns of GLG1 and GLI2 were successful, and we evaluated downstream gene expression. Loss of GLI2 resulted in subsequent loss of PTHrP, highlighting the vital role of GLI2 in TIBD. Future directions of this project aim to identify how GLG1 and GLI2 facilitate interactions between tumor cells, osteoblasts, and bone marrow endothelial cells to develop novel therapeutics towards treatment of TIBD.

2. Associations between prenatal stress and infant resting-state default mode and frontoparietal network functional connectivity

Presenter: Christian Rosig, Vanderbilt University

Program: START

Principle Investigator: Kathryn L. Humphreys, Ph.D., Ed.M.

Project Mentor: Sanjana Ravi Ph.D., Yanbin Niu Ph.D.**,** Department of Psychology and Human Development

Project Authors: Christian Rosig, Sanjana Ravi, Yanbin Niu, and Kathryn L. Humphreys

Abstract:

Background: The brain is highly sensitive to environmental influences in utero, with prenatal stress, being a key factor linked to altered development and later psychiatric symptoms. Cognitive networks such as the default mode and frontoparietal networks may be particularly impacted by stress and early differences in the functioning of these networks may offer the ability to identify risk for disorder before the onset of impairment. Further, it is less clear whether for prenatal stress the pregnant person's subjective experience of stress or objective exposure to stressful events is more influential.
Objective: This study examined associations between prenatal stress measured three ways (i.e., exposure to stressful life events, stress associated with daily hassles, major life events, and chronic stress, and perceived stress) and infant default mode and frontoparietal network functional connectivity.
Methods: As part of an ongoing longitudinal study, individuals completed sessions mid-gestation and 6 months postpartum involving questionnaires and clinical interviews. The Crisis in Family Systems–Revised questionnaire was used to assess stress associated with daily hassles, major life events, and chronic stress. The Perceived Stress Scale questionnaire was used to assess participants' perception of and ability to cope with stress. The Life Stressor Checklist–Revised interview was used to examine exposure to stressful life events during pregnancy. When their infants were approximately one month old, infants underwent resting-state functional magnetic resonance imaging during natural sleep. Robust linear regressions were conducted to examine associations between prenatal stress and infant functional connectivity, covarying infant age at scan, sex, and motion.
Results: Results indicated that the number of stressful life events experienced during pregnancy, assessed via the Life Stressor Checklist–Revised interview, was positively associated with default mode internetwork connectivity and this association was statistically significant (β=0.22 [0.02, 0.43], p=.039). Prenatal perceived stress and prenatal stress concerning daily hassles were not found to be statistically significantly associated with infant functional connectivity.
Conclusions: Result suggests that number of stressful events experienced during pregnancy may influence infant brain development. If replicated, these findings support calls to reduce stress exposure during pregnancy to benefit both pregnant individuals and their offspring.

3. IRTKS Controls Enterohemorrhagic Escherichia coli Attachment and the Localization of its Virulence Factors

Presenter: Carina Roman, University of Puerto Rico Arecibo

Program: Leadership Alliance

Principle Investigator: Matthew Tyska, Ph.D., Department of Cell and Developmental Biology

Project Mentor: Julissa Burgos, Department of Cell and Developmental Biology

Project Authors: Carina Roman, Matthew Tyska, Julissa Burgos

Abstract: Enterohemorrhagic Escherichia coli (EHEC) is a foodborne bacterial pathogen that causes outbreaks of bloody diarrhea and acute renal failure. During infection, EHEC attaches to the surface of nutrient-absorbing enterocytes and reorganizes the host cytoskeleton to form pedestal structures that facilitate bacterial motility for its colonization in the intestine. Pedestals form through the activity of two translocated virulence factors: translocated intimin receptor (Tir) and E. coli secreted protein F in prophage U (EspFU). Previous studies showed that binding of Tir and EspFU is mediated by host protein, Insulin Receptor Tyrosine Kinase Substrate (IRTKS). IRTKS uses its I-BAR (Inverse-Bin-amphiphysin-Rvs167) and SH3 domains to bind to Tir and EspFU, respectively. Even though prior investigations established that the Tir-IRTKS-EspFU complex drives actin polymerization for pedestal formation, whether this complex drives bacterial attachment remains unclear. To test this possibility, we infected HeLa cells overexpressing full length IRTKS with a bacterial strain that models EHEC infection (KC12+EspFU). We then stained infected samples for bacteria, Tir, and EspFU and imaged using confocal microscopy. Overexpression of IRTKS significantly increased the number of attached bacteria and also resulted in a striking mislocalization of Tir and EspFU. Although IRTKS is established to be important for pedestal formation, these results suggest that IRTKS is also responsible for EHEC bacterial attachment and controls the localization of its virulence factors during infection.

4. Effects of Repetitive Transcranial Magnetic Stimulation on Anxiety and Depression in Schizophrenia: A Randomized Crossover Study

Presenter: Gabriela Torres, University of Texas at El Paso

Program: MSTP Summer Research Program

Principle Investigator: Heather Ward, M.D., Department of Psychiatry and Behavioral Sciences

Project Authors: Gabriela C. Torres, Sophia Blyth and Heather Burrell Ward

Abstract:

The prevalence of comorbid depression and anxiety disorders in patients with schizophrenia (SZ) is relatively high. Effective treatment is needed to increase functional outcomes and reduce the heavy psychological burden in SZ. Repetitive Transcranial Magnetic Stimulation (rTMS) is used to treat various psychiatric disorders. Studies show that rTMS to the left dorsolateral pre-frontal cortex (L-DLPFC) reduces symptom severity in patients with depression. Another brain region associated with depression is the Default Mode Network (DMN), where SZ patients show abnormal connectivity. However, there are no current studies that focus on the effects of rTMS to the DMN for anxiety and depression. In this randomized crossover study, 15 SZ patients and 22 healthy controls (HC) received 5 daily sessions of continuous theta burst stimulation (cTBS) to the DMN followed by 5 daily session of intermittent theta burst stimulation (iTBS) to the L-DLPFC in a randomized, crossover design. Anxiety and depression scores were assessed with the Brief Psychiatric Rating Scale (BPRS-24). Effects in treatment target and group were explored using a two-way mixed ANOVA. Analyses revealed no significant changes in depression and anxiety scores after rTMS treatment to the DMN and DLPFC in the entire sample, nor between groups. Results indicate that rTMS was safe for participants and that 5 sessions of rTMS delivered to the DMN and L-DLPFC did not elicit significant changes in anxiety and depression in either HC or SZ groups.

5. The Burden of Maternal Syphilis: National Trends and Pregnancy Outcome Implications

Presenter: Hailey Mullins, Spelman College

Program: AHA SURE

Principle Investigator: Mulubrhan Mogos, Ph.D., Vanderbilt University School of Nursing

Project Authors: Hailey Mullins, Mulubrhan Mogos

Abstract:

Background: Maternal syphilis is on the rise in the United States, posing a substantial public health concern. Caused by Treponema pallidum subspecies pallidum, syphilis can be transmitted sexually or vertically during pregnancy. This study provides United States' national estimates on the prevalence, correlates, and outcomes of maternal syphilis-associated pregnancy hospitalizations.

Method: Using the Nationwide Inpatient Sample (NIS: 2016-2021), we analyzed maternal syphilis-associated pregnancy hospitalizations among women aged 13-49 in the United States. We examined demographic, behavioral, hospital, and clinical characteristics associated with maternal syphilis. Joinpoint regression was used to describe the Annual Average Percent Change (APC) of these hospitalizations. Survey logistic regression assessed the association between maternal syphilis-associated pregnancy hospitalizations and pregnancy outcomes across different racial groups.

Results: Out of 23,150,202 pregnancy-related hospitalizations during the study period, 22,700 involved maternal syphilis. Pregnant women who used alcohol, tobacco, cannabis, and opioids, as well as those with conditions such as bipolar disorder, HIV/AIDS, anxiety, depression, and obesity, were at increased risk of maternal syphilis. The prevalence of maternal syphilis was highest among Black women, followed by Hispanic women. However, White women had the highest APC (28.3%) from 2016 to 2021, compared to Black women (20.9%). Adjusting for demographic, behavioral, and clinical confounders, women with maternal syphilis had a higher risk of HIV/AIDS, preeclampsia, severe maternal morbidity, prolonged hospital stay, preterm birth, and intrauterine fetal demise.

Conclusion: The significant increase in maternal syphilis cases across all racial groups underscores the need for increased awareness, screening, and treatment efforts in these communities. This study highlights the urgency of addressing maternal syphilis as a public health priority and calls for measures to mitigate its impact on pregnancy outcomes.

6. Enhancing Surgical-Pathological Communication and Precision through 3D Scanning

Presenter: Helana Khalif, Lipscomb University

Program: UCRIP

Principle Investigator: Michael Topf, MD, MSCI, Department of Otolaryngology- Head and Neck Surgery

Project Authors: Helana M. Khalif, Whitney Jin, Sindhura Sridhar, Michael C. Topf, MD, MSCI

Abstract:

This research explores the use of three-dimensional (3D) scanning and mapping to enhance communication between surgeons and pathologists regarding oncologic specimen orientation and accurate margin assessment. Traditional methods often rely on two-dimensional imaging or manual descriptions, which can lead to difficulties with re-resecting close or positive margins due to the complex geometries involved in anatomical structures. By utilizing 3D-scanning, the precise orientation and spatial relationships of a specimen can be captured and shared among medical professionals to facilitate a more nuanced understanding of critical details. 3D models allow for visualization of tumor margins in relation to surrounding tissues from multiple angles, enabling pathologists to assess whether sufficient tissue has been removed to achieve clear margins. This collaborative approach not only improves diagnostic accuracy but also enhances preoperative planning and postoperative analysis by providing a common reference point that is visually rich in detail. In addition, 3D tumor models can be directly annotated with specific surgical landmarks or areas of concern, ensuring that essential information is clearly communicated without ambiguity. Overall, integrating 3D scanning technology into clinical workflows bridges the gap between surgical practice and pathological evaluation, leading to better patient outcomes through improved diagnostic precision and interdisciplinary collaboration.

7. Unveiling the Past to Inform the Future: Investigating the Role of Skeletal Trauma in Osteoporosis through Analysis of Femoral Samples from Historical and Modern Cohorts

Presenter: Evan Farach, Baylor University

Program: UCRIP

Principle Investigator: Katherine Van Schaik, M.D., Ph.D., M.A., Department of Radiology and Radiological Sciences

Project Authors: Evan S. Farach, Sasidhar Uppuganti, M.S., Seungweon Park, and Katherine D. Van Schaik, M.D., Ph.D., M.A.

Abstract:

Background: Osteoporosis (OP) is characterized by decreased bone mass and microarchitectural deterioration, leading to increased skeletal fragility and fracture risk. Over 50 million Americans are affected annually, with significant health implications. Notably, women have a risk of over 25% death within a year following an osteoporotic hip fracture.
Objectives: This study aimed to analyze femoral structural integrity in historical and modern postmortem cohorts to lay the groundwork for research linking skeletal imaging with DNA methylation levels in OP-related genes.
Methods: Thirty femora from 19th-century British Royal Navy sailors' remains at the Museum of London (MoL) were compared with 30 modern, age, and sex-matched postmortem samples from the Maxwell Museum of Anthropology (UNM). SCANCO Medical microCT software assessed the midshaft and distal femoral regions. An analysis script evaluated trabecular and cortical architecture.
Results: The MoL samples demonstrated more compromised bone structure than the UNM samples, with significantly lower bone volume fraction, fewer trabeculae, greater trabecular separation, and reduced cortical bone metrics. Notably, the MoL samples had significantly thicker trabeculae. Since all other metrics point toward reduced robusticity of the MoL samples likely because of postmortem decay, the thicker trabeculae of the MoL samples are noteworthy.
Conclusion: This analysis reveals differences in bone structure attributable to lifestyle, biomechanical loading, and postmortem decay. Historical evidence suggests active foragers built thicker trabeculae and stronger bones than sedentary agriculturalists. The MoL group demonstrated significantly thicker trabecular bone compared to controls (UNM), likely reflecting extensive physical activity during early adulthood, the time when trabecular bone structure is most vigorously established. Despite evidence of trauma and malnutrition, the MoL bones demonstrate remarkable robusticity in trabecular thickness after 200 years underground. Future research will investigate the relationships between bone morphology and skeletal epigenetics, focusing on DNA methylation and its role in bone metabolism and health in these cohorts.

8. Exploration of the Effects of Creatine on Myometrial Contractility

Presenter: Aerica Worrell, University of Georgia

Program: UCRIP

Principle Investigator: Jennifer Herington, Ph.D., Departments of Pediatrics and Pharmacology

Project Authors: Aerica Worrell, Alexus Brown, Stacey Ellery, Jennifer Herington

Abstract:

Creatine is an amino acid derivative that is synthesized by some tissues in the body and can be obtained from our diet. Creatine plays an essential role in muscle contractile force by providing spatial and temporal ATP buffering during periods of high energy demand or reduced oxygen supply. While dietary creatine supplements are commonly used to enhance muscle performance and recovery, the role of creatine in smooth muscle contraction is not fully understood. It has been reported the creatine's intracellular phosphorylated form (phosphocreatine) stores rise in the human myometrium during pregnancy. The myometrium stores all the enzymes required to use creatine for ATP production. It has also been found in mice models that maternal dietary supplementation during pregnancy increase uterine creatine concentrations at term. This study aims to investigate how creatine supplementation can be used in interventional medicine for pregnant mothers.

9. Quantification of Proliferating Transitional Epithelial Cells in the Developing Mouse Utricle

Presenter: Samuel Leonard, Sewanee: The University of the South

Program: V-SURE

Principle Investigator: Taha Jan, M.D., Department of Otolaryngology Head and Neck Surgery

Project Mentor: Sushobhan Biswas .Ph.D., Department of Otolaryngology Head and Neck Surgery

Project Authors: Samuel J. Leonard, Macey P. Soltis, Sushobhan Biswas, Taha A. Jan

Abstract:

Background:
The utricle is an inner ear vestibular sensory organ that depends on mechanosensitive hair cells (HCs) for detecting linear acceleration. In newly born mice, HCs are made from non-sensory supporting cells (SCs) and continue to be added for the first 7 postnatal days. HCs are interdigitated by SCs to form the sensory epithelium (SE) of the utricle. A rim of non-sensory cells surrounding the SE, called transitional epithelial cells (TECs), contribute to the expansion of the SE through a stepwise differentiation mechanism. We studied the proliferative response of the TECs here using in vitro and in vivo mouse models.
Methods:
Mouse utricles were dissected and stained with antibodies for proliferating cells, HCs, SCs, and DAPI. To observe the proliferative response of TECs to HC loss, transgenic Pou4f3DTR/+ damaged utricles were compared to undamaged wildtype (WT) utricles. To observe in vitro TEC proliferation, control (WT) utricles were cultured at different ages. Utricles were imaged using confocal microscopy and analyzed using FIJI.
Results:
In vivo analysis of WT utricles showed increased proliferation of TECs in comparison to damaged utricles in the early postnatal period (P2-P7). However, at P9, more proliferative TECs were observed in damaged utricles. The farthest proliferative TECs from the SE were determined to be at a distance of 150µM. In vitro analysis of cultured control utricles showed that there were more proliferative TECs at P3 than P7.
Conclusions:
HC damage leads to decreased TEC proliferation during the early postnatal period (P2-P7). The in vivo damage model showed that a 150µM distance from SE would be adequate for considering the TEC area. Quantification of proliferating TECs has paved the way for further gene expression analysis to understand utricular development.

10. The LncRNA Meg3 regulates epithelial cell fate decisions following lung injury

Presenter: Arlo Colvard, Lipscomb University

Program: UCRIP

Principle Investigator: Jason Gokey, Ph.D., Department of Medicine

Project Authors: Arlo C. Colvard, Gianluca DiGiovanni, Isabella Gaona, Sergey S. Gutor, Ujjal Singha, Taylor P. Sherrill, David S. Nichols, Yunli Zhou, Jonathan A. Kropski, and Jason J. Gokey

Abstract:

Idiopathic pulmonary fibrosis (IPF) is an interstitial lung disease (ILD) characterized by excessive fibrous extracellular matrix (ECM) deposition. While the cause of IPF is unknown, it is believed that recurrent injuries to the alveolar epithelium, resulting in an abnormal and prolonged tissue repair response, is associated with disease development and progression. The prognosis of IPF is poor, the average lifespan following diagnosis is 3-5 years, with the only curative option for the disease being lung transplantation. Prior studies have described increased expression of the lncRNA Meg3 in the lungs of IPF patients. An increased expression of Meg3 is associated with impaired lung repair processes through inhibition of the differentiation of lung basal progenitor cells. In this study, the lung alveolar epithelium was investigated in murine models of IPF and organoid culture. Lineage tracing and immunofluorescence confocal microscopy techniques were employed to identify the cell fate of type 2 alveolar epithelial cells (AT2), the stem cell of the alveolar epithelium, and restoration of type 1 alveolar epithelial cells (AT1) that conduct gas exchange essential for respiration. Previous work identified the abnormal differentiation of AT2 cells into airway-like epithelial cells associated with failed repair in IPF, and we therefore assessed airway cell markers in these lineage traced cells. Meg3 knockout lineage-traced AT2s showed decreases in expression of AT2, AT1, or transitional cell markers following injury with bleomycin. These data indicate a decrease in AT2 to AT1 transition following Meg3 knockout, resulting in a loss of normal alveolar repair. To determine the role of increased Meg3 in the IPF lung, Meg3 was expressed in human AT2 cell cultures. RealTime-qPCR data revealed that expressing Meg3 induced p53, a known Meg3 target, as well as Cebpa, a gene associated with maintenance of AT2 cells, while reducing Scgb3a2, a gene associated with airway secretory epithelial cells.

11. mAb Discovery & Measles

Presenter: Jacob Snipp, East Tennessee State University Quillen College of Medicine

Program: Vanderbilt Vaccine Center

Principle Investigator: James E. Crowe, Jr., M.D., Department of Pediatrics, Pathology, Microbiology and Immunology

Project Mentor: Laura Handal**,** Pathology Microbiology and Immunology

Project Authors: Jacob S. Snipp, Laura Handal, Nurgun Kose, Rob Carnahan, James Crowe

Abstract:

Measles is a highly contagious viral disease. One case can cause an average of 12 to 18 new instances. Despite the availability of a safe and effective vaccine, outbreaks persist globally, emphasizing the pressing need for new treatment options. We focused on identifying and characterizing antibodies against the measles virus using hybridoma technology. The antibodies we discovered target the viral glycoproteins on the surface, hemagglutinin (H), and the fusion protein (F). Using enzyme-linked immunosorbent assays (ELISA), we determined antibody glycoprotein specificity and quantified the strength of antibody binding. A real-time cell analysis neutralization assay was then used to evaluate viral neutralization for each antibody in the panel. Our results indicate that we have found several potent antibodies specific to the prefusion form of the F protein. Future directions include the structural characterization of these antibodies through X-ray crystallography and cryo-electron microscopy and in vivo viral protection studies in a cotton rat model of disease.

12. Bispecific antibody generation targeting different epitopes of Influenza B virus antigens

Presenter: Anushree Gade, University of South Alabama Frederick P. Whiddon College of Medicine

Program: Vanderbilt Vaccine Center

Principle Investigator: James E. Crowe, Jr., M.D., Department of Pediatrics, Pathology, Microbiology and Immunology

Project Mentor: Katherine Webb, Department of Biomedical Engineering

Project Authors: Anushree Gade, Katherine Webb, James Martinez, James E. Crowe, Jr.

Abstract:

Influenza viruses pose a significant public health threat due to their high transmissibility, causing billions of acute respiratory infections and at least 300-650,000 deaths annually. Monoclonal antibodies are a therapeutic option to address this threat due to their ability to bind to and neutralize a broad range of Influenza antigens. Hemagglutinin (HA) and neuraminidase (NA) are two surface glycoproteins that aid with viral infection and are the primary target of monoclonal antibodies (mAbs). However, Influenza viruses are prone to antigenic drift, allowing escape mutants to emerge, rendering some mAbs ineffective. Bispecific antibodies (bsAbs) simultaneously target two distinct epitopes on one virion. This feature allows for improved viral neutralization and broader protection against potential escape mutants. This project focuses on expressing and evaluating various bispecific antibody constructs for their potency in neutralizing Influenza B antigens. DNA for the bsAbs was derived via plasmid purification. Subsequently, EXPI293F cells were transfected with the isolated DNA to drive recombinant antibody protein expression. The expressed antibodies were harvested and purified using Protein A. An Enzyme-Linked Immunosorbent Assay (ELISA) was performed to evaluate bsAb binding compared to one another and their parent antibodies expressed as both IgGs and fragment antigen binding (FABs). The ELISA data indicated that the generated bsAb constructs exhibited binding comparable to or greater than their parent IgG and FAB antibodies. The results from this project demonstrate the successful expression and binding of bispecific antibodies to their corresponding antigens. This supports the functional design of these bsAbs and advances the efforts to generate bispecific antibodies for preventing and treating Influenza B infections. However, describing the effectiveness of the bsAbs in neutralizing Influenza B virus requires additional research efforts.

13. Circadian Regulation of STZ-induced beta cell dysfunction in Zebrafish

Presenter: Sarah Livingston, Sewanee: The University of the South

Program: V-SURE

Principle Investigator: Wenbiao Chen, Ph.D., Department of Molecular Physiology & Biophysics

Project Mentor: Brittney Covington, Department of Molecular Physiology & Biophysics

Project Authors: Sarah Livingston, Brittney Covington, Wenbiao Chen

Abstract:

Type 2 diabetes (T2D) has substantially increased in the United States. The major risk factor for T2D is obesity results from overnutrition. Obesity causes insulin resistance, which stresses the insulin-producing beta cells in the pancreatic islets, leading to beta cell dysfunction and loss and insulin insufficiency. Another risk factor for T2D is circadian (around 24 hours) rhythm (CR) disruption. Shift workers have increased risk for T2D. How overnutrition, insulin resistance, and CR disruption cause beta cell death is incompletely understood and is currently an active area of study. The Chen laboratory has developed a zebrafish model in which insulin resistance and overnutrition induces beta cell death. This summer project investigates the effects of circadian rhythm regulation on beta cell death using streptozotocin (STZ) injections in 6 days post-fertilization (dpf) zebrafish larvae. By injecting STZ and analyzing beta cell changes at different time points we aim to determine the vulnerability of beta cells throughout the day. We hypothesize that beta cell death will be greatest during the night when they are most vulnerable. This study will provide insight into the temporal dynamics of beta cell death and the potential influence of circadian rhythm on T2D pathogenesis.

14. Urine Luck: Urine Biomarker May Distinguish Childhood Asthma Phenotypes

Presenter: Lincoln Brown, Lipscomb University

Program: UCRIP

Principle Investigator: Tina Hartert, M.D., M.P.H., Department of Medicine, Division of Allergy, Pulmonary and Critical Care Medicine

Project Authors: Lincoln Brown, Kathleen Hiltz, Tebeb Gebretsadik, Sara Reiss, Kadijah Poleon, Justin Adler, Zhouwen Liu, Ferdinand Cacho, Christian Rosas-Salazar, Tina Hartert

Abstract:

Background: Club cell secretory protein (CC16) is secreted by club cells in the epithelium of the lower respiratory tract. This protein is thought to have anti-inflammatory, immunoregulatory and antioxidant roles in the lungs, which makes it a protein of interest actively being studied in certain respiratory diseases. Most studies focus on the association of CC16 with prevalent respiratory disease, including increased childhood asthma risk. However, options for predictive biomarkers and phenotypic biomarkers are limited. The objective of this study is to assess the association of urinary CC16 and asthma risk and phenotypes in children.

Methods: The study is a nested case control study of 150 children with and without asthma at 6 years old from the INSPIRE birth cohort. Using an ELISA assay, we determined the concentrations of CC16 in urine samples from children at age 6 years. CC16 levels were normalized to creatinine. We used multinomial logistic regression to assess the association of log standardized urinary CC16 concentrations with childhood asthma and allergic and non-allergic asthma phenotypes at 6 years old, adjusting for sex, race, secondhand smoke exposure, breastfeeding, maternal asthma, and presence of siblings.

Results: Among children with allergic asthma the adjusted median urinary CC16 levels were 76 ng (interquartile range [IQR] 30, 156); among children with non-allergic asthma, 83 ng (IQR 44, 242); and among children without asthma 101 ng (IQR 46, 230). Using a multinomial logistic regression (referent no asthma) for one unit log urinary CC16 difference, the adjusted odds ratio (aOR) for 6-year risk of allergic asthma was 0.71 (95% confidence interval [95% CI] 0.47, 1.07, p=0.101), and for risk of non-allergic asthma aOR 0.87 (95% CI 0.60, 1.28, p=0.490).

Conclusions: Urinary CC16 is lower in children with asthma, but this small study did not distinguish between asthma phenotypes. More data on this potential urinary biomarker may help to predict asthma risk.

15. The Relation of Early Adversity to Language Processing, Emotion Reactivity, and Working Memory

Presenter: Emily Drucker, CUNY Hunter College

Program: BP-ENDURE

Principle Investigator: James R. Booth, Ph.D., Psychology and Human Development

Project Mentor: Alisha B. Compton, Vanderbilt Brain Institute

Project Authors: Emily R. Drucker, Alisha B. Compton, Claire M. Tate, James R. Booth

Abstract:

Early adversity is known to affect emotion and cognition, but more research is needed on distinct effects of varying types of adversity. The dimensional model of adversity groups experiences postulated to have similar consequences and includes the dimensions of threat (harm or threat of harm) and deprivation (a lack of social and cognitive input). This project aims to examine deprivation as a unique factor underlying language skill, threat as a unique factor underlying emotion reactivity, and the relation of both to working memory, but perhaps more for deprivation.

48 children, 7-12 years (Mage=10.11), completed an experimental rhyming task that manipulates lexical processing (low- vs. high-frequency words), affective valence (negative vs. neutral images), and working memory (2- vs. 1-back load). Parents completed surveys on the child's threat (VEX-R) and deprivation (ECLS) experiences.

Using hierarchical regressions, we examined unique variance explained by threat and deprivation, above and beyond age and the other, in lexical processing, affective valence, and working memory performance (accuracy, reaction time, and reaction time variability (RTV)). Trends suggest a unique relation of deprivation to lexical processing accuracy ($\Delta R2=7.44\%$, $F(1,44)=3.91$, $p=0.054$), and deprivation to working memory RTV ($\Delta R2=6.74\%$, $F(1,44)=3.89$, $p=0.055$), in line with a dimensional model of adversity. We also see a significant unique relation of threat to lexical processing RTV ($\Delta R2=9.28\%$, $F(1,44)=6.08$, $p=0.018$) and a trend with reaction time ($\Delta R2=4.87\%$, $F(1,44)=2.96$, $p=0.09$).

Prior literature suggests threat, but not deprivation, relates to processing speed and response caution. Yet other studies have found an association between deprivation and response inhibition. Thus, a child who experienced adversity may exhibit increased RTV. More research should examine distinct or shared associations of the dimensional model with RTV, which children with anxiety and executive function difficulties exhibit. To further investigate these relations, we will analyze a larger sample and examine relevant neural correlates with fMRI.

16. Examining Bias Across Genetic Association Studies of Educational Attainment and Underlying European Population Structures

Presenter: Zinn Amos, Wake Forest University

Program: UCRIP

Principle Investigator: Nancy Cox, Ph.D., Department of Genetic Medicine

Project Mentor: Alexandra Scalici, MPH, Department of Genetic Medicine

Project Authors: Zinn Amos, Alexandra Scalici, Tyne Miller-Fleming, Nancy J. Cox

Abstract:

Educational Attainment (EA) is a trait that indicates the highest level of education that an individual has completed. This phenotype is influenced by a multitude of complex socioeconomic factors, including family income, parental EA, the environment in which the individual is raised, social status, and access to equitable education and enrichment opportunities. Genome-wide association studies (GWAS) have been conducted to identify genetic factors associated with EA. We hypothesize that the genetic associations to EA are largely driven by the underlying population structure within individuals of European ancestry, rather than representing true genetic underpinnings. To test this hypothesis, we conducted a GWAS to identify single nucleotide polymorphisms (SNPs) that were associated with specific regions in Europe in the 1000 Genomes data set. We used the summary statistics from this GWAS to construct a polygenic score (PGS) in HapMAP 3 individuals of European ancestry. We plan to compare this ancestry-based PGS with the EA PGS in the HapMAP3 individuals to test whether each score is predictive of the region-based case control definition. Our study aims to demonstrate that genetic factors are a weak contributor in determining EA. These findings could lead to the reconsideration of the genetic contributions to EA, shifting focus away from PRS-based policy for improving EA and eliminating dangerous assumptions of EA genetics. We anticipate that the results of our study will emphasize the importance of instituting policy that alleviates the socioeconomic factors causing disparities in EA and provide a cautionary tale for the interpretation of genetic association findings.

17. Dual Targeting of PGE2 Receptors, EP3 and EP4, Protects Against Type 1 Diabetes in the NOD Mouse

Presenter: Audrey Lucerne, Boston University

Program: Vanderbilt Diabetes Summer Research Program

Principle Investigator: Maureen Gannon**,** Ph.D., Department of Medicine

Project Mentor: Juliann B. Burkett, Molecular Physiology and Biophysics

Project Authors: Audrey Lucerne, Juliann B. Burkett, Jennifer Fuhr, Maureen Gannon

Abstract:

Type 1 Diabetes (T1D) is an autoimmune disease that occurs when immune T cells attack the insulin-producing pancreatic beta cells, causing chronic inflammation of the islet of Langerhans. Prostaglandin E2 (PGE2) is a significant mediator of inflammation and has been demonstrated to play a role in autoimmunity. In previous findings from the Gannon lab, two of the four PGE2 receptors, EP3 and EP4, have been shown to have opposing effects on beta-cell proliferation and survival in isolated islets. The Gannon lab has recently successfully delayed the onset of T1D using a dual target PGE2 receptor therapy by inhibiting EP3 receptors and activating EP4 receptors in non-obese diabetic (NOD) mice. The lab hypothesized that utilizing the opposing effects of these receptors is effective in delaying the onset of T1D by pushing the immune system to a pro-resolution state to restore the balance of regulatory T cells and effector T cells. We hypothesized this resolution shift is characterized by the preservation of functional beta cells and decreased islet inflammation. Insulitis, the inflammation of the islet, was studied using hematoxylin and eosin tissue staining. Islets within the tissue sections were quantitatively scored for level of inflammation, determined by the number of immune cells invading the islet. The mean insulitis score was significantly decreased in the treated NOD mice compared to vehicle, indicating lower inflammation and less immune cell islet infiltration. Additionally, there was a significant increase in beta-cell mass in treated mice; however, there was no change in beta cell proliferation. This project suggests that the dual target treatment delays the onset of T1D in NOD mice due to the drug's role in decreasing islet inflammation and maintaining functional insulin-producing beta cells. The lab will run flow cytometry to further explore the potential changes in immune cells in treated mice.

18. Identification of Epithelial Selenoprotein P Isoforms

Presenter: Danielle Walker, Texas Southern University

Program: MSTP Summer Research Program

Principle Investigator: Christopher Williams**,** M.D., Ph.D., Department of Medicine

Project Mentor: M. Diana Neely Ph.D., Nathaniel Berle, Department of Medicine

Project Authors: Danielle Walker, Nathaniel Berle, Lekha Yaramada, Jennifer Pilat Ph.D., Yash Choksi M.D, M. Diana Neely Ph.D., Christopher Williams M.D., Ph.D.

Abstract:

Background: Selenoproteins are a group of specialized proteins containing selenocysteine participating in multiple metabolic pathways. Selenoprotein P (SELENOP) falls under this group and contains ten selenocysteines. Nine are found in the C-terminus and one in the N-terminus. SELENOP is primarily produced in the liver where it is secreted, and one of its activities is thought to transport selenium to other tissues. We recently determined that the gut epithelium also makes SELENOP and that its altered levels of SELENOP have been linked to different cancer types. Objective: To determine the SELENOP isoform spectrum in the intestinal epithelium. Methods: The first step was to validate SELENOP antibodies for immunoprecipitation via Western blotting. Purified mouse and human SELENOP were used to evaluate the species specificity of the SELENOP antibodies. Then, we attempted to immunoprecipitate SELENOP from Caco2-BBE cells using the identified SELENOP antibodies. To increase SELENOP expression we serum-starved the cells for 48 hours and/or spiked the media with purified SELENOP for 24 hours. We performed a CellTiter-Blue assay (Promega) to find the cytotoxic threshold of sodium selenite. Results: We validated that two antibodies, BD1 and SantaCruz-#376858, can detect purified human SELENOP; however, could not detect SELENOP in Caco2-BBE cell lysates. This could be due to low levels of SELENOP expression, the immediate secretion of SELENOP, or proteolytic breakdown of SELENOP. Serum-starving and/or spiking the cells did not result in detectable levels of SELENOP. Lastly, we were unable to successfully precipitate SELENOP from the Caco2-BBE lysate. However, these results were difficult to interpret due to potential cross-reactivity between the primary mouse antibody and secondary antibody because SELENOP shares a similar molecular weight to heavy chain. Conclusions: We successfully detected purified human SELENOP with two different antibodies; however, these antibodies failed to detect SELENOP in Caco2-BBE cell lysates.

19. Investigating drug-rescue experiments of KCNH2 genetic variants for therapeutic intervention

Presenter: Molly Crew, Iowa State University

Program: UCRIP

Principle Investigator: Brett Kroncke, Ph.D., Department of Clinical Pharmacology

Project Authors: Molly Crew, Suah Woo, Matthew Ku, and Brett Kroncke

Abstract:

QT interval prolongation is a risk factor for sudden cardiac death and cardiovascular events, which are among the leading causes of death in the US. Mutations in the KCNH2 gene, an important potassium channel gene in the cardiac cycle, account for 30% of long QT syndrome (LQTS). Identifying genetic determinants of QT interval prolongation will allow for precise therapeutic intervention and risk stratification. This study aims to assess which KCNH2 variants can be rescued with varying treatments. These treatments include a DMSO control, E4031 drug rescue, Evacetrapib drug rescue, and 27℃ incubation rescue.

Our lab created a tile system to split the KCNH2 gene into five separate portions, allowing us to manipulate the gene easier and more efficiently. For this project, we used the HEK293 LP57 cell line due to its reproducibility, high robustness, and responsiveness to transfection. HEK cells were transfected with each tile, ensuring all theoretical single nucleotide mutations are expressed. The cells are then treated with E4031, Evacetrapib, or 27℃ incubation for 24 hours, and activation of the genes is preformed using a doxycycline-inducible system. Protein trafficking to the cell surface was measured using Alexa647, a self-labeling tag that is covalently coupled to a fluorophore. Flow cytometry was used to sort cells according to high, medium, low, and negative Alexa647 expression. High levels of Alexa647 expression correspond with high protein trafficking to the cell surface or wild type like. Following the sort, the cells are extracted, amplified via PCR, bead purified, and sent for next-generation sequencing for analysis.

The results of this study will provide us with specifics of drug efficacy, allowing for precise therapeutic intervention of KCNH2 gene variants. Further studies are needed to assess the protein trafficking on additional drug treatments, as well their effect on differing cell lines and types.

20. Investigating the Effects of TANK Deficiency on Monocyte and Macrophage Activity

Presenter: Taylor Holmes, Xavier University of Louisiana

Program: MSTP Summer Research Program

Principle Investigator: Janet Markle, Ph.D., Department of Pathology, Microbiology and Immunology

Project Mentor: Joseph Choi, Department of Pathology, Microbiology and Immunology

Project Authors: Taylor Holmes, Joseph Choi, Janet Markle

Abstract:

Inborn errors of immunity, genetic mutations that impair the immune system's development and function, can often be linked to rare diseases. Bronchiectasis, the abnormal and permanent widening of the bronchi, is a chronic condition often exacerbated by inflammation during repeated respiratory infection. Over time, bronchiectasis can contribute to increased lung damage and, in some cases, lead to death due to lung failure. Mutations in the TRAF family member-associated NF-κB activator (TANK) gene, leading to a deficiency of TANK protein, have been identified as a new inborn error of immunity. Interestingly, despite TANK-deficiency being identified as a monogenic cause of disease contributing to the development of bronchiectasis, little is known about the mechanisms of how TANK mutations lead to this disease. In mice, TANK has been shown to negatively regulate the activation of NF-kB, a transcription factor that controls the expression of pro-inflammatory cytokines in macrophages. However, TANK's role in regulating monocyte and macrophage cytokine production in humans is not well understood. My work focuses on understanding the mechanism of how mutations to the TANK gene impact the pathogenesis of bronchiectasis. To gain a better understanding of this mechanism, a knockout of TANK was performed in THP-1 cells, a human monocyte cell line, and the efficiency of the knockout was assessed using Western blot. Future studies utilizing this model system seek to advance understanding of TANK's role in macrophage function, its implications on disease progression, and may contribute to the discovery of new treatments and therapies.

21. Utilizing Digital Tools to Increase Communication Abilities for International Healthcare Workers

Presenter: Zebulon Trovinger, University of Colorado Boulder

Program: UCRIP

Principle Investigator: Ryan Buckley, M.D., Department of Medicine

Project Authors: Zebulon Trovinger, Ryan Buckley

Abstract:

As of 2024, basic healthcare services are out of reach for more than half of the world's population. Despite the United States investing upwards of $12 billion annually in international healthcare efforts, the World Health Organization (WHO) reports an alarming stagnation in the progress of providing people everywhere with accessible healthcare. In this report, issues in communication, supply management, and organization are identified as major barriers that impede cost-effective solutions and sustainable aid efforts. I hypothesize that incorporating a platform for shared resources amongst international healthcare workers will increase their ability to communicate and organize projects. In turn, global healthcare workers will be capable of streamlining the process of cross-country aid, making it more cost-effective and sustainable. To develop this hypothesis, I employed a human-centered design and Lean Six Sigma approach. Over the course of 8 weeks, I interviewed doctors, medical suppliers, and global health workers to determine themes amongst their needs. Their insights affirmed that there was a profound need for relationships between volunteers and the sites they were working with as well as a need for improving the accessibility and transportation of medical supplies. Based on these results, I concluded that a media-based app is needed to provide communication between sites, suppliers, doctors, and volunteers. Follow-up interviews emphasized that this product needs to be intuitive, visually appealing, and feedback-driven for global health teams to use it. If successfully supported, the proposed AppSheet platform will allow teams to have a universal resource for sustainable communication and organizational development. Post-deployment, an analysis of app usage and user feedback will guide further refinements and improvements. In this process, I hope to elucidate the problems that prevent international aid from progressing alongside a global network of users.

22. Mechanisms of Sarcopenic Obesity (Review)

Presenter: Baylee Baron, University of Tennessee

Program: UCRIP

Principle Investigator: Jason Samuels, M.D., Department of Surgery

Project Authors: Baylee D. Baron, Jason Samuels

Abstract:

Sarcopenia is characterized by the loss of muscle mass and strength, often accompanied by an increase in fat mass. Sarcopenia most commonly impacts a patient's quality of life by increasing frailty and muscle weakness. Diagnosis typically involves methods such as MRI imaging, grip strength analysis, and other performance-based assessments. Sarcopenia is frequently observed in obese patients following extensive weight loss. Commonly, a decrease in muscle mass is exhibited after bariatric surgery, including both Roux-en-Y Gastric Bypass (RYGB) and Sleeve Gastrectomy procedures. This muscle loss is routinely combated with high protein diets following surgery, but still extensive muscle loss can occur. These cases often present sarcopenic obesity. Sarcopenia contributing factors may include inflammation, insulin resistance, sedentary lifestyle, diet, hormonal changes, and aging. These factors are commonly present in obese individuals and may play a role in their development of sarcopenia. Sarcopenia remains a relatively recent focus in research, and its underlying mechanisms are not yet fully understood. Recent research has highlighted the interconnectedness of these contributing factors and their implications on metabolic health. The following information and data were sourced from PubMed articles using a series of defined search terms. This review focuses on exploring the potential mechanisms of obesity induced sarcopenia presented in the current literature.

23. Understanding the Role of Alveolar Type 1 Cells in Alveologenesis Using an In Vivo AT1-Ablation Model of Lung Injury

Presenter: Shriya Garg, University of Georgia

Program: Independent Research Intern

Principle Investigator: Jennifer Sucre, M.D., Department of Neonatology

Project Authors: Shriya Garg, Nicholas Negretti, Alex Sharkey, Devan Wilkins, Shawyon Shirazi, Chris Jetter, Arline Pierre-Louis, Jonathan Kropski, Jennifer Sucre

Abstract:

Introduction: Bronchopulmonary dysplasia (BPD) is a leading preterm birth complication. Defined by impaired alveologenesis and angiogenesis, BPD patients have lifelong respiratory insufficiency. The alveolar type 1 cell (AT1) lines the distal lung surface and forms the gas exchange unit with alveolar capillaries (aCaps). While our preliminary data suggest that saccular stage injury alters the AT1 expression of cell-signaling and cell-matrix genes, the precise role that AT1s themselves play in alveologenesis is not known.

Materials and Methods: We used transgenic mice with selective killing of AT1s through cytotoxic diphtheria toxin (DTA) expression driven by Ager-CreERT2. AT1-expression of DTA was tamoxifen-induced at P3 and P4, and lungs were collected at P7 and P10. Immunofluorescence (IF) and RNA in situ hybridization (ISH) were performed for quantification of AT2s, AT1s, and aCaps by expression of cell-specific hallmark genes. We quantified histologic changes using mean linear intercept (MLI) and air space volume density (ASVD).

Results: Lung morphometry showed a significant increase in MLI and ASVD between P10 control and Ager-DTA mice, with no significant difference at P7. We found a significant increase in the proportion of AT1 cells (marked by Hopx expression), a significant decrease in AT2 cells, with a trend toward fewer aCaps in Ager-DTA mice.

Conclusion: Selective elimination of AT1s results in larger, fewer alveoli (histopathology similar to neonatal lung injury) suggesting that AT1s themselves play a critical role in alveologenesis and decreased AT1 expression of critical cell-signaling post-injury could contribute to impaired lung development and BPD. The increased Hopx gene expression in Ager-DTA mice could be compensatory for initial AT1 loss. Further characterization of this phenotype is an important future direction. Taken together, these data provide the foundation for future work exploring AT1s' role in alveologenesis and the discovery of new targeted therapies to promote lung development post-injury.

24. microRNA-21 Inhibits Staphylococcus aureus Phagocytosis

Presenter: Mary Courtney Finn, Sewanee: The University of the South

Program: V-SURE

Principle Investigator: C. Henrique Serezani, Ph.D., Department of Medicine, Division of Infectious Disease

Project Mentor: Ana Salina Ph.D., Department of Medicine, Division of Infectious Disease

Project Authors: Mary Courtney Finn, Ana Salina, and C. Henrique Serezani

Abstract:

Staphylococcus aureus (S. aureus) is a significant cause of skin infections in community and nosocomial settings. Skin infections caused by S. aureus are orchestrated by the actions of tissue-resident cells and recruited immune cells. Furthermore, proper infection control is dictated by balancing the inflammatory response and bacterial clearance while also avoiding tissue damage. Phagocytes, such as macrophages, serve as microbe killers and induce inflammatory mediators in these skin infections. MicroRNAs (miRs), 20-24 nucleotide non-coding RNAs, inhibit transcriptional and post-transcriptional gene expression and can also inhibit the expression of both pro- and anti-inflammatory genes that modulate this immune response. Previously, our lab has shown that miR-21 is important for producing inflammatory mediators in macrophages challenged with LPS, but whether or not miR-21 regulates microbial ingestion remains to be determined. Our recent data shows that S. aureus infection increases the expression of miR-21 in macrophages. Additionally, preliminary data indicate that miR-21 deficiency protects mice from S. aureus skin infections; however, the mechanisms underlying this event are still unknown. We hypothesize that miR-21 inhibition increases S. aureus phagocytosis and improves bacterial control. Our data shows that transfection of macrophages with miR-21 antagomir increases phagocytosis of pHrodo-labelled S. aureus compared to cells transfected with a scrambled antagomir. With this knowledge, we are currently investigating whether miR-21 could specifically target phagocytic receptors. Our study demonstrates the importance of miR-21 in bacterial phagocytosis and lays the foundation for future research into infection clearance.

25. Investigating how VU809 an inhibitor of Myc and WDR5 interactions impacts macrophage differentiation and phenotype

Presenter: Monique Armelle Dacanay, North Carolina Central University

Program: MSTP Summer Research Program

Principle Investigator: Justin Balko, Pharm.D., Ph.D., Department of Medicine, Division of Hematology and Oncology

Project Mentor: Ann Hanna, Ph.D., Department of Medicine

Project Authors: Monique Armelle Z. Dacanay, Ann Hanna, Taekyu Lee, Gregory C. Howard, Stephen W. Fesik, William P. Tansey, and Justin M. Balko

Abstract:

Breast cancer is the most diagnosed and second leading cause of cancer deaths in women. When treated early, patient 5-year survival rate is 99%, emphasizing the importance of advancing treatment and implementing early detection practices. In the breast tumor microenvironment (TME), tumor associated macrophages (TAMS) play a role in cancer progression by suppressing $CD8^+$ T cell functions, leading to immunotherapy resistance. Macrophages, important innate immune cells, are highly plastic, existing in a spectrum of phenotypes spanning M1 (immune activating), and M2 (tumor promoting). In several cancers, the Myc oncogene is hyper activated and regulates the expression of genes that promote cell proliferation, differentiation, and immune surveillance. Myc also induces polarization of M2-like macrophages, contributing to immune evasion. Recruitment of Myc to chromatin is important for their role in increasing oncogenic gene expression, and is dependent on interactions with cofactors such as chromatin regulator WDR5, allowing for tumorigenesis. Our project investigates the impact of blocking Myc function using the small molecule inhibitor VU809 (aka C10), which inhibits Myc and WDR5 interactions, on macrophage differentiation and polarization. To evaluate VU809's effect on macrophages, we are assessing markers associated with M1 (*iNOS, IFNy, IL-12*) and M2 (*Mrc1, Arg1*) macrophages by RT-qPCR and flow cytometry. Our preliminary data suggests that VU809 increases the expression of some M1 markers and decreases expression of some M2 markers, thus promoting an anti-tumor macrophage phenotype. Elucidating VU809's role in macrophage differentiation and polarization may provide rationale to target macrophages to improve responses to immunotherapy in breast cancer.

26. Investigating the Effect of Competitive Cadherin Engagement on Renal Fibroblast Activation

Presenter: Charlene Pobee, Washington University in St. Louis

Program: MSTP Summer Research Program

Principle Investigator: David Merryman, Ph.D., Department of Biomedical Engineering

Project Mentor: Camryn Johnson, Ph.D. Caleb Snider, Ph.D., Department of Biomedical Engineering

Project Authors: Charlene Pobee, Camryn Johson, Caleb Snider and David Merryman

Abstract:

Severe or prolonged injury to the kidney can lead to a fibrosis-mediated disease known as Chronic Kidney disease (CKD). With many CKD patients relying on dialysis and kidney transplants, investigation of pharmacological treatment options is of high interest. Cadherin-11 (CDH11), a transmembrane protein involved in cell-cell and cell-substrate adhesion, has been implicated in several fibrotic diseases, such as calcific aortic valve disease, rheumatoid arthritis and myocardial infarction; therefore, we hypothesize it as a key mediator in renal fibrosis. CDH11 has been shown to mediate mechanical signaling by encouraging matrix deposition and remodeling by fibroblasts. To assess the effect of Cadherin-11 in renal fibroblasts, wild-type and Cdh11-/- renal fibroblasts were plated on surfaces coated with CDH11, N-cadherin, E-cadherin as well as an uncoated condition as a control. Previous studies have shown an inverse relationship between CDH11 and N-CDH. E-CDH was chosen as a negative control as it is mainly present in epithelial cells. qPCR, Western Blotting and immunostaining were utilized to assess potential outcomes of CDH11 interacting with other Cadherins and the lack thereof. CDH11 coated wells treated with transforming growth factor-**β** (TGF**β**) demonstrated decreased fibrotic markers shown through the limited presence of collagen I, α-smooth muscle actin, fibronectin, and TGF**β**. Altered behavior may be due to CDH11 engagement with substrates rather than cells. Further investigation is warranted to determine the downstream effects of CDH on renal fibrosis.

27. Evaluation of Ultrasonographic Metrics for Predicting Pleural Effusion Volume

Presenter: Altea Thompson, Tufts University

Program: UCRIP

Principle Investigator: Samira Shojaee, MD, MPH, Department of Medicine, Division of Allergy, Pulmonary and Critical Care Medicine

Project Authors: Altea Thompson, Samira Shojaee MD, MPH

Abstract:

In clinical settings, pleural effusions are frequent concomitant symptoms of multisystem disorders, linked to high rates of morbidity and mortality. Traditionally, the fluid volume in pleural effusions is measured using computerized tomography (CT) scans, which subject patients to high costs, ionizing radiation, and logistical challenges. Recent studies, however, suggest that ultrasonography can serve as a safer and more efficient alternative. Specifically, the Gonke 2 formula– which predicts effusion volume based on ultrasound measurements of the lateral height of the effusion and distance between the lung and the diaphragm– has shown potential. This study aims to evaluate the accuracy of predicting pleural effusion volume using ultrasonographic images of the posterior, midaxillary, and anterior regions of the pleural space. The primary goal is to assess the effectiveness of both the Gonke 2 formula and the number of rib spaces as predictive metrics for pleural effusion volume. Conducted across six academic centers in the United States, this research utilizes a comprehensive dataset of patient demographics, procedural details, and imaging data. Ultrasound images were analyzed to measure the pleural effusion volume using the Gonke 2 formula and the number of rib spaces occupied by the effusion in the three aforementioned regions. While the study is still in progress, preliminary data collection has been completed. Comparisons will be made between the predicted volumes and the actual fluid volumes drained, with results pending. This research has the capacity to provide a comprehensive evaluation of ultrasound metrics in predicting pleural effusion volume, thereby establishing a more accurate, non-invasive method for clinical use. Indeed; the study's findings could improve patient care by offering a safer and more efficient alternative to CT scans for pleural effusion assessment.

28. Characterization of outer capsid-exchanged reoviruses

Presenter: Ryan Xavier, Sewanee: The University of the South

Program: V-SURE

Principle Investigator: Kristen Ogden, Ph.D., Department of Pathology, Microbiology and Immunology

Project Mentor: Alejandra Flores, Ph.D. Candidate, Department of Pathology, Microbiology and Immunology

Project Authors: Ryan D. Xavier, Alejandra Flores, Kylie Sartalamacchia, Julia R. Diller, Sydni Caet Smith, and Kristen M. Ogden

Abstract:

Nonenveloped virus cell exit is often poorly understood. Reoviruses, nonenveloped viruses with a double capsid and segmented double-stranded RNA (dsRNA) genome, are useful for studying cell egress due to their genetic tractability. Two highly studied strains, T3D and T1L, differ in membrane disruption and virus egress properties. T3D efficiently lyses host cell membranes, whereas T1L is nonlytic. The outer capsid (OC) proteins primarily determine the ability of reovirus to lyse the cell. Previous work indicates that both lytic T3D and nonlytic T1L escape host cells as free particles and in association with extracellular vesicles, but the properties of the vesicles differ for the two reovirus strains. To identify proteins that drive a specific phenotype, we engineered recombinant reoviruses in which select segments (L2, M2, S1, and S4) are exchanged between T1L and T3D to exchange their OC proteins. Characterizing the properties of these recombinant viruses is necessary before attempting further assays. Firstly, genotypes of the parental and OC-exchanged viruses were verified through electropherotyping, where dsRNA segments are separated by size. We found that T1L-T3D OC contained the correct collection of segments, while T3D-T1L OC did not. Further assays were discontinued with the incorrect virus. We then quantified virus titers at different time points by plaque assay to measure the ability of the viruses to replicate. To ascertain the membrane disruption phenotypes of parent and the OC-exchanged virus, we performed trypan blue exclusion assays. We found that the OC-exchanged virus replicates efficiently and has an intermediate cell lysis phenotype. We have begun a reverse genetics experiment to engineer T3D-T1L OC and will perform the same assays to characterize the virus. Our findings so far suggest T1L-T3D OC will be a useful tool to study OC protein involvement with extracellular vesicles and improve our understanding of nonenveloped virus egress.

29. The Effects of Glucose Concentrations on Mitochondrial Morphology in Aging Yeast

Presenter: Kyrie Frazier, Vanderbilt University

Program: MARC

Principle Investigator: Jason MacGurn, Ph.D., Cellular and Developmental Biology

Project Mentor: Adam Ebert, Cellular and Developmental Biology

Project Authors: Kyrie Frazier , Adam Ebert, Nathaniel Hepowit , Jason MacGurn

Abstract:

It has been shown in various studies that mitochondrial dysfunction is connected with various diseases such as cancer, Parkinson's disease and Alzheimer's disease. A plethora of model organisms have shown that, with age, mitochondrial organization and function decline. Our lab is using yeast as a model organism to dissect mechanisms of mitochondrial swelling. In Saccharomyces cerevisiae, budding yeast, aging is associated with mitochondrial swelling. However, mechanisms contributing to mitochondrial swelling are not yet understood. It is not known whether mitochondrial swelling is a consequence of the yeast aging, or if mitochondrial swelling is resulting in age-related dysfunction. The MacGurn Lab is using yeast as a model organism to dissect mechanisms of mitochondrial swelling. Other model organisms have also shown a conserved metabolic longevity promoting pathway called dietary restriction that also has implications in human health and disease. Dietary restriction has been linked with cellular longevity, but how this plays a specific mechanism of mitochondrial swelling isn't known. To investigate this hypothesis, we will observe mitochondrial morphology in yeast over a 72 hour time span in the presence of different glucose concentrations to simulate dietary restriction. We attached fluorescent tags Tom70-mcherry and Mdh1 to mitochondrial proteins to be able to observe and see the effects of the various glucose concentrations on the mitochondrial swelling. Results led to the finding that when glucose levels are increased the mitochondrial swelling also increases as the cell ages , and when the glucose levels decrease the mitochondrial swelling is also decreased.

30. Defining Endocrine Cell Composition of Human Islets in Diabetes

Presenter: Haley Aichlmayr, University of California, Irvine

Program: Vanderbilt Diabetes Summer Research Program

Principle Investigator: Marcela Brissova, Ph.D., Department of Medicine

Project Authors: Haley Aichlmayr, Shaojun Mei, Heather Durai, Anastasia Coldren, Corey Davis, Conrad V. Reihsmann, Diane C. Saunders, Alvin C. Powers, Marcela Brissova

Abstract:

AIM OF STUDY: Pancreatic islets are multicellular mini-organs representing approximately 1-2% of pancreatic mass. They play a critical role in the regulation of blood glucose homeostasis that is in part influenced by islet endocrine cell composition and cell-cell communication. Our goal was to determine if endocrine cell composition changes in diabetes. To address this question, we analyzed islets from a cohort generated by the Human Pancreas Analysis Program including adult organ donors positive for autoantibodies associated with development of type 1 diabetes (AAB, N=8), those with type 2 diabetes (T2D, N=18) and controls without diabetes (ND, N=26).

MATERIALS AND METHODS: Isolated pancreatic islets were immobilized in type 1 collagen and processed for cryo-sectioning. Islet histological sections were labeled for three primary endocrine cell types, β, α and δ cells using their respective hormone markers and indirect immunofluorescence. Whole-slide imaging and HALO v3.6.4 tissue classifier module were used for cell quantification. Statistical analysis was done with GraphPad Prism v9.3.1.

RESULTS: By tissue classifier algorithm, we found that proportion of β cells was statistically higher (p=0.0339) in AAB individuals (71.0±3.2%) compared to those with T2D (57.4±3.3%), while there was no difference (p=0.1848) compared to controls without diabetes (62.0±2.4%). α cell composition was significantly lower (p=0.0069) in AAB (71.0±3.2%) compared to T2D individuals (57.4±3.3) but was not significantly different (p=0.0874) compared to ND controls (62.0±2.4%). δ cell composition was unchanged across ND (62.0±2.4%), AAB (71.0±3.2%), and T2D (57.4±3.3%) islets.

CONCLUSION: While higher β cell proportion in AAB compared to T2D islets is interesting, a larger AAB cohort will be needed to confirm these outcomes. By the analysis of islets from T2D individuals, we confirmed our prior findings that endocrine cell composition is unchanged in pancreas of organ donors with early-stage T2D, and islet isolation process does not influence the islet endocrine cell composition.

31. Comparative Analysis of Large Language Models in First-Aid Scenario Recognition and Management: An In-silico Evaluation of GPT-4o and Claude 3.5 Sonnet

Presenter: Norvin West, Jr., Yale College

Program: UCRIP

Principle Investigator: Jeffrey Upperman, M.D., Department of Pediatric Surgery

Project Authors: Norvin West Jr. and Jeffrey Upperman

Abstract:

The integration of artificial intelligence (AI) into healthcare has opened unexplored territories in medical information accessibility, with particular relevance to time-critical first-aid scenarios. Large Language Models (LLMs), which are advanced AI systems trained on vast amounts of text data and can generate human-like text, have demonstrated proficiency in medical knowledge, yet their utility, safety, and efficacy in successfully guiding emergency interventions remains contentious and largely unexamined. This controversy is amplified in regions with limited access to professional medical services, where AI-driven guidance could potentially address critical deficiencies in human resources. This research seeks to address this unexamined frontier by evaluating the performance of two advanced and widely accessible LLMs, GPT-4o and Claude 3.5 Sonnet, when prompted with 5 diverse first-aid case vignettes. We interrogated both models on each case three times, and evaluated the quality of the responses across diagnostics, first-aid advice, and triaging, as well as safety, comprehensiveness, and consistency across interrogations. Claude 3.5 Sonnet outperformed GPT-4o on first-aid accuracy, comprehensiveness, and consistency and performed equally on diagnostics, triaging, and safety. Both models persistently correctly identified the primary condition or emergency within each of the vignettes and always made the appropriate recommendation for seeking professional medical help. And both models were very accurate in giving first-aid recommendations in line with American Red Cross' most recent guidelines, with a few key first-aid step omissions in some interrogations. These results provide initial evidence of the potential utility of advanced LLMs in guiding first-aid interventions, with Claude 3.5 Sonnet demonstrating superior performance in key areas. While these findings suggest LLMs could serve as valuable supplementary tools in emergency situations, further research is needed to validate these results and address potential limitations before considering widespread implementation.

32. Major histocompatibility complex class II regulation in alveolar epithelial cells during endoplasmic reticulum stress

Presenter: Salma Elhandaoui, Vanderbilt University

Program: START

Principle Investigator: Ana Serezani, Ph.D., Department of Allergy, Pulmonary and Critical Care Medicine

Project Authors: Salma Elhandaoui, Isabella Gaona, Jason Gokey, Ph.D., Bruno Pascoalino, Ph.D, Ana Serezani, Ph.D.

Abstract:

Idiopathic pulmonary fibrosis (IPF) is the most common form of pulmonary fibrosis (PF), distinguished by fibrotic progression that often leads to respiratory failure and death. In experimental studies, administering bleomycin to the lungs of mice induces inflammation, apoptosis of alveolar epithelial cells (AECs), and interstitial fibrosis resembling IPF. AECs in fibrotic lung areas express increased levels of major histocompatibility complex class II (MHCII) compared to less fibrotic sites. MHCII is crucial for antigen presentation and regulates the activation of inflammatory lymphocytes, but its regulation during fibrosis remains unclear. We therefore hypothesized that cellular injury (bleomycin) regulates MHCII expression in some AECs during PF. To test this, we studied the impact of bleomycin on endoplasmic reticulum (ER) stress and MHCII expression in AECs. Immortalized Mouse Lung Epithelial Cells (MLE-12) were cultured at a density of 2x105 cells per well and stimulated with 0, 0.01, and 0.1 U/mL of bleomycin for 24 hours. We then isolated mRNA and synthesized cDNA, performing reverse transcription quantitative PCR to examine the expression of ER stress markers (*Ddit3* or *Chop*, *Xbp1U/S*), MHC class I (*Iqaia*), and MHCII (*H2-Ab1*) in controls and bleomycin-simulated MLE-12 cells. We found that bleomycin resulted in increased levels of *Xbp1U/S* and *Ddit3* (ER stress), and also raised MHCI (*Iqaia*) and MHCII (*H2-Ab1*) expression. Our results suggest that bleomycin induces ER stress, potentially upregulating MHCII expression in AECs, which could enhance antigen presentation and lymphocyte activation, contributing to fibrotic progression in IPF. The induction of ER stress markers like *Ddit3* and *Xbp1S/U* indicates that the unfolded protein response (UPR) pathway may be significant in this process, suggesting a link between ER stress and immune modulation in the fibrotic lung environment. Our next goal is to test the transcription factor associated with MHCII expression (CITTA).

33. The Effect of ATF4 Expression Levels on Mitochondrial Morphology, Metabolism, and Association with Endoplasmic Reticulum

Presenter: Benjamin Rodriguez, University of Iowa

Program: MSTP Summer Research Program

Principle Investigator: Antentor Hinton, Ph.D., Department of Molecular Physiology and Biophysics

Project Mentor: Zer Vue Ph.D., Department of Molecular Physiology and Biophysics

Project Authors: Benjamin I. Rodriguez, Amber Crabtree, Andrea Marshall, Zer Vue, Larry Vang, Antentor Hinton

Abstract:

The mitochondria is a membrane-bound organelle that is responsible for cellular metabolism under aerobic conditions. Mitochondria are dynamic structures that undergo fusion, fission, and interactions with other organelles. Of interest is contact between mitochondria and endoplasmic reticulum (ER), which are referred to as MERCs. MERCs are sites of lipid and calcium transfer between mitochondria ER, as well as regulating mitochondrial morphology. Knockdown of the mitochondria fusion protein OPA1 has been found to increase the amount of MERCs. Further investigation has demonstrated that OPA1 knockdown increases expression of transcription factor ATF4. We investigated the effects that changes of ATF4 expression have on mitochondrial morphology, metabolism, and MERCs. Western Blot analysis and 3D Reconstruction of Drosophila skeletal muscle found that ATF4 knockdown decreased the expression of MERC-associated proteins and decreased the number of MERCs, while over-expression of ATF4 had increased both factors. 3D Reconstruction of Drosophila skeletal muscle further demonstrated that ATF4 knockdown decreased average mitochondrial size, whereas over-expression increased size. Metabolomic data of mouse myotubes show changes in mitochondrial metabolism, with ATF4 knockout increasing pyruvate metabolism and decreasing glucose metabolism. ATF4 over-expression had decreased both glutamate and glucose metabolism. These data demonstrate that ATF4 is involved in the regulation of mitochondrial structure and function, but further investigation into whether these effects are modulated through MERC formation needs to be conducted.

34. Disruption of MICOS Complex and Myofibrillar Architecture in Mitochondrial Dysfunction, Lipid Accumulation, and Heart Failure

Presenter: Andy Barillas, Cerritos College

Program: AHA SURE

Principle Investigator: Antentor O. Hinton, Ph.D., Molecular Physiology and Biophysics

Project Mentor: Zer Vue, Ph.D., Molecular Physiology and Biophysics

Project Authors: Andy Barillas[1,2], Larry Vang[1], Zer Vue[1], Andrea Marshall[1], Edgar Garza Lopez[3], and Antentor Hinton, Jr. [2]

[1] Cerritos College, Norwalk, California, USA, [2] Vanderbilt University, Nashville, TN, USA ,[3] University of Iowa, Iowa City, IA, USA

Abstract:

Patients with diabetes mellitus face over twice the risk of developing heart failure (HF) compared to non-diabetic individuals, experiencing worse cardiovascular outcomes despite advancements in antihyperglycemic therapies. This persistent risk suggests factors beyond glycemia are involved.

Mitochondrial dysfunction and chronic inflammation are critical in HF progression. While acute inflammation helps repair cardiomyocyte injury, chronic inflammation can damage the heart, impairing function and reducing cardiac output. Mitochondria, making up a third of cardiomyocyte volume, are dynamic and involved in processes like fusion and fission. They are a potential therapeutic target for HF. In aged patients with HF, there is a shift in the primary energetic substrate from fatty acids to glucose, leading to lipid accumulation and cytotoxicity. We hypothesize that aging disrupts myofibrillar architecture and lipid formation in cardiomyocytes due to loss of the mitochondrial contact site and cristae organizing system (MICOS) complex, specifically Mic25/CHCHD6, leading to mitochondrial dysfunction. Using serial block face-scanning electron microscopy (SBF-SEM), we reconstructed the myofibrillar apparatus, crucial for ATP production in the heart. Myofibrils in HF showed increased cross-sectional area and reduced circularity, with more branching sarcomeres compared to controls. In HF, myofibrils were misaligned at angles myofibrils were observed to be oriented at angles of 0°, 7°, and 45°compared to the well-aligned apparatus in controls, indicating pathological remodeling.

Focusing on Mic25/CHCHD6 within the MICOS complex, we knocked out Mic25/CHCHD6 in induced pluripotent stem cell-derived cardiomyocytes. Transmission electron microscopy showed reduced mitochondrial area, number, and perimeter. Lipidomic analysis revealed changes in lipid classes, such as increased acylcarnitines in HF. Mic25/CHCHD6 knockdown led to reduced mitochondrial calcium uptake and retention, and increased intracellular ROS production. These findings suggest that MICOS complex loss impairs mitochondrial ROS homeostasis and calcium regulation, contributing to HF. Our data highlight the MICOS complex, particularly Mic25/CHCHD6, as a potential therapeutic target.

35. Insulin Signaling in p75$^{NTR-/-}$ Rat Schwann Cells

Presenter: Abigail French, Sewanee: The University of the South

Program: V-SURE

Principle Investigator: Bruce Carter, Ph.D., Department of Biochemistry

Project Mentor: Vishwanath Prablu, Ph.D., Department of Biochemistry

Project Authors: Abigail J. French, Vishwanath Prablu, and Bruce D. Carter

Abstract:

Peripheral nerve hypomyelination, a decrease of myelin sheaths, can cause muscle weakness in many peripheral neuropathies by impairing nerve conduction. Under normal conditions, myelin sheaths serve as an insulating structure surrounding the axon of a neuron to accelerate propagation and decrease dissipation of action potentials. In the peripheral nervous system, myelin sheaths are composed of Schwann cells which express the protein p75, a neurotrophin receptor that regulates lipid metabolism and neuron survival. Previously, the Carter lab observed hypomyelination and lipid accumulation in the absence of p75^{NTR}. Lipid accumulation often results in insulin resistance, blocking insulin receptor pathways that also induce myelination in Schwann cells. This study aims to investigate insulin resistance in the model of p75^{NTR} knockout (KO) rat Schwann cells (RSC). We observed the activation of the insulin receptor pathway proteins ERK and AKT in insulin-treated p75^{NTR} KO RSC via western blot analysis. Contrary to our hypothesis, data revealed no significant statistical differences in the activation of either ERK and AKT in p75$^{NTR-/-}$ RSC compared to wild-type RSC, suggesting proper insulin signaling and, thus, no insulin resistance. Replication of the study with more variations of insulin concentration would be helpful to validate the observed results.

36. Mimicking Pro-Inflammatory Conditions in HMC3 Cell Line Microglia to Study the B7-1/p75^{NTR} Interaction

Presenter: Emmanuel Makinde, New York University

Program: BP-ENDURE

Principle Investigator: Bruce Carter, Ph.D., Department of Biochemistry

Project Mentor: Hrshita Das, Ph.D., Department of Biochemistry

Project Authors: Emmanuel Makinde, Hrshita Das, Bruce Carter

Abstract:

The neuroimmune response is crucial to understanding neurodegenerative disease. Microglia are motile brain resident macrophages that perform three core functions to maintain homeostasis: surveillance of the brain parenchyma, phagocytosis, and release of signaling molecules to regulate the tissue microenvironment. As part of the neuroimmune response, microglia activity increases following the recognition of damage-associated molecular patterns (DAMPs), engulfment of pathogens or dying cells, and response to/production of pro- and anti-inflammatory cytokines to modulate inflammation. T-cells are also major players during the immune response. Cytotoxic T-cells release perforins to destroy pathogens while helper T-cells release molecules to support cytotoxic T-cells and other players in the immune response. For T-cell activation, T-cells must detect two proteins on the microglia membrane: an antigen and a costimulatory factor called B7-1. Recent research has found a primate-specific interaction between the p75 neurotrophin receptor (p75NTR) and the B7-1 protein that contributes to the degradation of synapses in hippocampal neurons. Due to the primate-specificity of this interaction, we chose the Human Microglial Clone 3 cell line (HMC3) to model microglia for this study. The mechanism of the B7-1/p75NTR interaction is unknown. It is also unknown whether the HMC3 cell line is suitable for studying this protein/protein interaction and any downstream effects. In this study, we performed western blots and immunocytochemistry to study B7-1, and markers of inflammation and microglia. We observed increased B7-1 and Iba1 expression in HMC3 cells following lipopolysaccharide treatment, indicating that these cells appropriately respond to inflammatory stimuli. Interestingly, we also found that NLRP3 expression increases with lower doses of LPS. Validating this cell line will enable subsequent studies to investigate microglia-neuron cocultures under inflammatory conditions to clarify the mechanisms of this B7-1/p75NTR interaction, why it leads to synapse degradation, and how that contributes to neurodegenerative diseases.

37. Exploring the Validity and Reliability of the Emergency Preparedness and AI Survey in Professional Contexts

Presenter: Ajani Edwards, Tennessee State University

Program: UCRIP

Principle Investigator: Jeffery Upperman, M.D., Department of Pediatric Surgery

Project Authors: Ajani Edwards, Norvin West, Harrison Lucas, Jeffery Upperman

Abstract:

Background:
Emergency preparedness is essential for mitigating the impacts of disasters. Integrating artificial intelligence (AI) can significantly enhance decision-making, communication, and resource allocation. Additionally, understanding mental health strategies within this context is crucial for comprehensive disaster management. The Emergency Preparedness and AI Survey aims to gather insights from professionals on their knowledge and attitudes towards AI in disaster management, their roles in emergency response, and strategies for addressing mental health needs during and after large-scale emergencies. Validating and ensuring the reliability of survey instruments in quantitative research is vital for producing accurate and actionable data, supporting the development of evidence-based policies and training programs.
Objective:
To assess the validity and reliability of the Emergency Preparedness and AI Survey in professional contexts, including government, non-profit, and private sector organizations. Methods:
A cross-sectional study design was employed to collect data at a single point in time, allowing for the assessment of current knowledge, attitudes, and practices. The target population included professionals involved in emergency preparedness and disaster management across various sectors. Data were collected through an online survey platform, ensuring accessibility and convenience for participants. The survey included sections on demographics, knowledge about AI in disaster preparedness, attitudes towards AI, mental health preparedness, and incident command systems. Factor analysis was conducted to identify the underlying structure of the survey items, and criterion-related validity was assessed by comparing survey results with other established measures. Internal consistency was evaluated using Cronbach's alpha, and test-retest reliability was assessed by administering the survey to a subset of participants at two different points in time.
Results:
Databases including PubMed yielded 200 articles related to AI tools in mental health. Using keywords such as "artificial intelligence," "machine learning," "mental health," "psychiatry," "psychology," and "digital health tools," we screened these articles for relevance. After a thorough review, 50 articles were included in the final analysis. The resulting survey instrument consists of 50 items across three main sections: 1) Demographic information and professional background (10 items), 2) Knowledge and attitudes towards AI in emergency preparedness (25 items), and 3) Mental health preparedness strategies (15 items). Of these items, approximately 60% were adapted from previously validated surveys published in peer-reviewed studies, ensuring a robust and reliable measurement tool.
Conclusion:
The Emergency Preparedness and AI Survey is a valid and reliable instrument for assessing professionals' knowledge and attitudes towards AI in disaster management and their strategies for addressing mental health needs during emergencies. The findings suggest that this survey can contribute to more resilient disaster management frameworks by informing future policies and training programs. Future studies should explore the longitudinal application of the survey to assess changes in knowledge and attitudes over time and extend validation efforts to other professional contexts and regions.

38. Altered SERCA2a Expression in Mitral Valve Leaflets in Chronic Ischemic Mitral Regurgitation

Presenter: David Mankarios, Vanderbilt University

Program: AHA SURE

Principle Investigator: Yan Ru Su**,** M.D., Department of Medicine, Division of Cardiology

Project Authors: David B. Mankarios, Tarek S. Absi, Michael Glennon, Kelsey Tomasek, Yan Ru Su

Abstract:

Every year, roughly 800,000 people in the USA experience a heart attack, 6-12% of whom will go on to develop ischemic mitral regurgitation (IMR). Post myocardial infarction (MI), the left ventricle (LV) undergoes cardiac remodeling where the papillary muscles are displaced and cause the posterior or apical tethering of mitral valve leaflets. This abnormal tethering in cardiac remodeling is believed to be a contributing factor to IMR. Although the mechanical and physical properties of cardiac remodeling can contribute to IMR, the underlying molecular and cellular mechanisms are still under investigation, particularly in the mitral valve leaflets. Previous studies have shown that sarco(endo)plasmic reticulum Ca2+ -ATPase (SERCA2a), a calcium transporter protein, and its inhibitor phospholamban (PLN) are significantly downregulated in the myocardium of the LV. To explicate the molecular and cellular mechanisms in the mitral valve leaflets, both healthy control and diseased mitral valves were procured from unmatched donors and patients who underwent mitral valve repair surgery. RNA were extracted from the leaflets and subjected to cDNA microarray which allowed for differential gene expression analysis. Through this, we observed that SERCA2a along with its inhibitors, PLN and Sarcolipin (SLN), were downregulated in diseased mitral valves. Our finding may shed light on a potential novel molecular mechanism of calcium dysregulation in the mitral leaflets of IMR.

In the valvular interstitial cells (VICs) of the mitral valve, the downregulation of SERCA2a may be indicative of a decrease of Ca2+ transport from the cytosol of the cell to the sarcoplasmic reticulum, causing a buildup of calcium in the cytosol of the cell. This can cause the VICs to become calcified which may possibly lead to mitral annular calcification (MAC). When severe, MAC can lead to the stiffening of the valve, and the development of IMR.

39. Regulation of Fasting Blood Glucose Levels

Presenter: Emil Dominguez, University of California, Los Angeles

Program: MSTP Summer Research Program

Principle Investigator: Richard O'Brien, Ph.D., Molecular Physiology and Biophysics

Project Authors: Emil Dominguez, Tenzin Wangmo, Ken Oeser, Benjamin Brown, Richard O'Brien

Abstract:

Two glucose-6-phosphatase catalytic subunits, that hydrolyze glucose-6-phosphate (G6P) to glucose and inorganic phosphate, designated G6PC1 and G6PC2, are important for the regulation of fasting blood glucose (FBG). Elevated FBG has been associated with multiple adverse clinical outcomes, including increased risk for type 2 diabetes (T2D) and various cancers. T2D affects 34.2 million Americans, disproportionately affecting communities of color. Early detection and preventative measures are crucial to combat this growing health burden. Therefore, G6PC1 and G6PC2 inhibitors that lower FBG may be of prophylactic value for the prevention of T2D, as well as various cancers. My summer research in the O'Brien lab focused on two separate projects. In my first project, performed in collaboration with Dr. Ben Brown, a structure for human G6PC1 was generated using the AlphaFold2 algorithm and then various AI-based programs were used to predict small molecules that might bind G6PC1. These molecules were purchased and tested for their ability to block the hydrolysis of G6P by G6PC1. Several inhibitors were identified, and detailed kinetic analyses will now be performed. In my second project, I used fusion genes to demonstrate that a conserved, intronic genomic region within the Nostrin gene is likely a transcriptional enhancer, designated enhancer J, that regulates G6PC2 gene expression. Future studies will examine the impact of multiple single nucleotide polymorphisms (SNPs) within enhancer J on its transcriptional activity and then link their impact to changes in human health using Vanderbilt BioVU biobank, in which genotyping information is linked to de-identified patient records.

40. The Role of MICOS Complex in Mitochondrial Dysfunction and Heart Failure: Implications for Therapeutic Targeting

Presenter: Kevin Lebron, University of Puerto Rico Cayey Campus

Program: AHA SURE

Principle Investigator: Antentor O. Hinton Jr, Ph.D., Department of Molecular Physiology and Biophysics

Project Mentor: Zer Vue Ph.D. & Andrea Marshall Ph.D., Department of Molecular Physiology and Biophysics

Project Authors: Kevin Lebrón Acosta, Larry Vang, Zer Vue, Andrea Marshall, Edgar Garza Lopez, and Antentor Hinton, Jr.

Abstract:

Heart failure remains a leading cause of morbidity and mortality globally despite advancements in clinical and scientific research. Mitochondrial dysfunction and inflammation play critical roles in heart failure's development and progression. While inflammation is essential for reparative healing after acute cardiomyocyte injury, chronic inflammation can damage the heart, impair function, and reduce cardiac output. Mitochondria, comprising one-third of cardiomyocyte volume, are dynamic structures undergoing fusion, fission, and interactions with other organelles, making them a potential therapeutic target.

We hypothesized that aging causes structural remodeling of mitochondrial architecture in cardiomyocytes due to the loss of the mitochondrial contact site and cristae organizing system (MICOS) complex, leading to mitochondrial dysfunction. We utilized serial block face-scanning electron microscopy (SBF-SEM) for 3D reconstruction of mitochondria in the left ventricle of human samples with and without heart failure. Mitochondria in heart failure showed increased volume, surface area, and perimeter with significant inter-sample variability. Focusing on MICOS, we used siRNAs to knock out Mic25/CHCHD6 in induced pluripotent stem cell-derived cardiomyocytes. Transmission electron microscopy revealed decreased mitochondrial area.

Given Mic25's robust effect on mitochondria structure, we investigated mitochondrial calcium (mCa2+) regulation by examining mCa2+ uptake and retention in C2C12 myotubes. Knockdown of Mic60/Mitofilin, the core subunit of MICOS, resulted in reduced mCa2+ uptake and early permeability transition pore opening, significantly lowering mCa2+ retention capacity compared to controls. Fluorescent dye assessments showed increased intracellular ROS and mitochondrial superoxide production in Mic60/Mitofilin silenced cells. Similarly, MIC60 knockdown increased intracellular ROS and mitochondrial H2O2 production. These findings imply MICOS's role in mitochondrial ROS homeostasis, with disruptions leading to mCa2+ flux dysregulation and Ca2+-induced cell death.

Overall, our data suggest that in heart failure, the loss of the MICOS complex contributes to mitochondrial dysfunction, including ROS and calcium dysregulation, and structural changes, highlighting its potential as a therapeutic target.

41. Development of a Culturally tailored Motivational Interviewing-Based Health Coaching Intervention For Improving Hemodialysis Nonadherence in African Americans: "The MoVE Intervention"

Presenters: Kamsi Nwotite, Kent School, Kent Connecticut and Didi Umeukeje, Saint Cecilia Academy

Program: Independent Research Intern

Principle Investigator: Ebele Umeukeje, MD, MPH, Department of Medicine (Nephrology)

Project Mentor: Ruth Wolever, PhD, Vanderbilt Health Coaching Program, Osher Center for Integrative Health, Dept of PMR, VUMC

Project Authors: Kamsi Nwotite*; Didi Umeukeje* (*co-1st authors); Rebecca Weinand; Ruth Q. Wolever

Abstract:

Background:
African Americans (AAs) comprise 33% of end-stage kidney disease (ESKD) patients but only 13% of the US population. Compared to Whites, AAs have higher hemodialysis non-adherence. Motivational interviewing (MI) improves adherence, and cultural tailoring optimizes outcomes for racial minorities. Earlier work on Steps 1-3 of the 8-step ADAPT-ITT framework for adapting interventions qualitatively derived themes with AA ESKD patients and others; selected MI as the intervention to adapt; applied the PEN-3 cultural adaptation model, and identified 6 key drivers of dialysis adherence in AAs. We hypothesized that it would be feasible to develop a culturally tailored MI-based intervention, addressing these drivers.

Methods:
An existing MI-based health coaching intervention for behavior change was refined to support hemodialysis adherence in AAs by using "My Dialysis Treatment Wheel" with 6 adherence drivers for self-assessment (Step 4). Expert input on cultural adaptation, MI, coaching, and dialysis, was integrated, situating these 6 drivers and the MI-based coaching intervention within the context of racial identity (Step 5). Iterative intervention drafts were created and refined (Step 6). MI-based health coaches were instructed with refresher MI training; intervention fidelity assessment feedback; and relevant intervention tools (Step 7).

Results:
The intervention included 4 weekly (consolidation) and 2 bi-weekly sessions (maintenance) (Table 1). Each session integrated MI processes (engagement, focusing, evoking, and planning) with visioning and goal setting around an adherence driver. Health coaches used MI skills and strategies to elicit and leverage patients' values and strengths to address the patient-selected driver, using the Culturally Tailored Vanderbilt Health Coaching funnel (Figure 1).

Conclusions:
The ADAPT-ITT model provided a framework for developing a culturally tailored MI-based health coaching intervention for improving dialysis adherence in AAs. Next steps will involve a pilot randomized controlled trial to test the feasibility of using this intervention to improve dialysis adherence in AAs (Step 8).