Minimizing Health Disparities (MHD)

Coordinator: Holly Lopez **Sponsors:** University of Arizona, University of Arizona Graduate College, Western Alliance to Expand Student Opportunities (WAESO), Building Undergraduate Infra-structure Leading to Diversity: Southwest Consortium of Health-Oriented Education Leaders and Research Scholars (BUILDing SCHOLARS)-University of Texas, El Paso

Basmah Abdallah Maiga

Ohio State University, Biochemistry

Mentor: Dr. Michael Johnson - Immunobiology

Determining Copper resistance in *Streptococcus pneumoniae*.

ASTRACT: *Streptococcus pneumoniae* is a Gram-positive bacterium that causes pneumonia, bronchitis, otitis media, septicemia, and meningitis. Globally, *S. pneumoniae* accounts for about one million deaths a year, most of which are children. The innate immune system is the first line of defense against invading organisms, and one method utilized is the sequestering of copper through nutritional immunity. Since the introduction of antibiotics against *S. pneumoniae*, the prevalence of new resistant serotypes emerged and are increasing globally. Despite copper being an essential nutrient for *S. pneumoniae*, it is toxic at high concentrations. With this in mind, our intent was to first examine whether or not *S. pneumoniae* would adapt to copper. Recently, compound 240W, a metal chelator, was discovered and found to increase the toxicity of copper. 240W was also used to test if we would get a similar resistance pattern with Cu2+ alone. After finding the minimum inhibitory concentration of copper, we tested *S. pneumoniae* exposed to copper and copper + 240W. After 10 passages, we were able to identify that even though *S. pneumoniae* is very susceptible to copper, the bacteria developed an increased resistance to copper. The genomic DNA was extracted and sent for sequencing in hopes of revealing the mutations and mechanism associated with *S. pneumoniae* resistance to copper. Further understanding of the mechanism and mutations in play can lead to the future discovery of a copper-based drug treatment to combat this resistance.

Cynthia Bautista

University of Texas, El Paso, Biochemistry

Mentor: Dr. Heidi Mansour and Dr. David Encinas-Basurto – Pharmacology and Toxicology

Synthesis and Physicochemical Analysis of PLGA-based Nanoparticles for Drug Delivery

ASTRACT: The advantage of nanoparticle-mediated drug delivery has proven useful in the administration of different agents to treat numerous diseases within the human body. Poly Lactic-co-Glycolic Acid (PLGA), a biodegradable and biocompatible polymer, is commonly used for the syntheses of these nanoparticles. PLGA-based nanoparticles (NPs) facilitate drug encapsulation, can lessen the risk of toxicity within the human body by sustained drug release, and can enhance the drug's physical and chemical stability. Polyethylene glycol (PEG) is a hydrophilic polymer that is commonly surface-conjugated to PLGA NPs to avoid clearance from bloodstream, often leading to an improvement in the efficacy of drug delivery. The purpose of the research herein was to encapsulate albuterol sulfate, an FDA-approved short-acting beta2-agonist, in PLGA NPs and PEGylated PLGA NPs by a double-emulsion (W1/O/W2) technique. These nanoparticles were then analyzed by high-performance liquid chromatography for % encapsulation efficiency and drug release; Malvern Zetasizer for zeta (ζ) potential, polydispersity index, and hydrodynamic diameter; and scanning electron microscopy (SEM) for particle morphology, surface morphology, and size of the NPs. When compared, PLGA-PEG nanoparticles exhibited a pronounced surface charge in comparison to PLGA-only nanoparticles. Although both PLGA and PEGylated PLGA nanoparticles expressed similar values for polydispersity index, PEGylated PLGA NPs were larger in hydrodynamic size than PLGA-only counterparts. The analysis of these physicochemical differences contributes to an understanding of nanoparticle behavior and the implications of using PLGA and PEGylated PLGA in nanoparticle synthesis for the encapsulation of albuterol sulfate.

Kiana Burnett

University of Texas, El Paso, Cellular & Molecular Biochemistry

Mentor: Dr. Karen Herbst - Medicine

Women with Stage 3 Lipedema have Venoarterial Reflex Impairment and Neuropathy

ASTRACT: The venoarterial reflex (VAR) is a signal that exists in all tissue which serves as a form of communication between arteries and veins, indicating when to contract or expand depending on changes in posture. This prevents fluid from entering the extravascular system. Lipedema is a fat disorder which is characterized as fluid stagnating in the connective tissue of the body. Women with lipedema experience painful fat tissue and fluid on the lower extremities; the arms are less affected. Last year we investigated VAR among women with lipedema, and found that VAR impairment increases with stage. The progressiveness of the impairment suggests structural damage to the blood vessels or weakening of the peripheral nervous system. Many women with stage 3 lipedema complain of numbness in addition to pain; an attribute of neuropathy. The aim of this study is to establish further the trend of VAR impairment and to investigate the existence of neuropathy of women with late stage 2 and stage 3 Lipedema, which may indicate a relationship between the impairment of VAR and neuropathy.

Jasmine Cano

Florida Atlantic University, Biological Sciences

Mentor: Dr. Donna Zhang and Dr. Matthew Dodson – Pharmacology and Toxicology

The Effects of Arsenic on Diabetic Phenotypes: The Role of the NRF2 Signaling Pathway

ASTRACT: Arsenic is a carcinogenic metalloid that is a major contaminant in soil and water located near certain industrial sources, such as mining and agriculture, in a number of countries. Due to their proximity to these industrial sources, populations in these countries are chronically exposed to arsenic, increasing their probability of developing arsenic-related diseases such as cancer, diabetes, and cardiovascular disease. While it is known that arsenic causes these diseases, the exact mechanisms are still uncertain. One hypothesis involves the nuclear factor erythroid 2-related factor 2 (NRF2) signaling pathway. NRF2 is a transcription factor that plays a role in proteostasis, DNA repair, mitochondrial function, and more. Normally, the NRF2 system is activated to restore baseline metabolism during increased oxidative stress, as NRF2 downstream genes are designed to mitigate reactive species production and restore normal homeostasis. However, the Zhang lab has shown that chronic exposure to arsenic results in prolonged activation of the NRF2 pathway, significantly altering cellular metabolism, which may drive the progression of certain diseases, including diabetes. To test this hypothesis, we treated muscle myoblasts with arsenic for three months. Our results indicate that the levels of NRF2 and a number of its target proteins are significantly higher in arsenic-treated cells compared to control cells. These target proteins are involved in the antioxidant response, glucose metabolism, the TCA cycle, and autophagy, indicating that NRF2 may be driving arsenic pathology. Future studies will determine if prolonged activation of NRF2 is causing the diabetic effect observed in muscle during arsenic-linked diseases.

Jimiyah Carter

Fort Valley State University, Biology

Mentor: Dr. Noshene Ranjbar – Psychiatry

Development and implementation of integrative psychiatry curriculum into residency and fellowship training

ASTRACT: **Educational Objective(s):** 1. To describe an elective curriculum that targets resident knowledge in integrative medicine; 2. To delineate aspects of the curriculum which also meet common program requirements for physician well-being; 3. To discuss how this integrative design curriculum has developed based on feedback from trainees over a four-year period. **Methodology:** Residents (n=7) and fellows (n=3) participating in Integrative Psychiatry 1st year Curriculum (IPC I) and the Integrative Psychiatry 2nd year Curriculum, were interviewed using standardized questions. The first and second year cohorts were separated, and the answers analyzed based on overarching themes and trends. **Results:** The first-year cohort, participants engaged in an in-person experiential curriculum, an online curriculum, and had supervision for the outpatient integrative medicine clinic. Participants had a positive experience and were able to implement the course material into their personal life, clinical care, and for educating their colleagues and peers. Participants largely benefitted from the experiential portion. The online modules were useful as a resource, but often too time-consuming and detail-oriented. Examining these topics to identify high-yield concepts could be effective.

For the IPC II trainees, the year-long elective consisted of continuing care for their existing patients in the integrative psychiatry clinic and receiving clinical supervision. Advantages included strengthening concepts learned in Psych IMR 1, and refining skills. All participants highly recommend the curriculum to other residents, and believe this course should be a partial requirement for all residents. Conclusion: The pilot IPC program at the University of Arizona has been feasible to implement, rated highly among residents/fellows, improved every year based on feedback, and addresses components of well-being both for patients and residents/fellows

Shontrice Coleman

California State University San Bernardino, Physics

Mentor: Dr. Samantha Harris, Nathaniel Napierski and Kevin Granger – Cellular & Molecular Biology

cMyBP-C Removal in Spy-C Mice Induces Prolonged Spontaneous Oscillatory Contractions (SPOC) in Cardiac Cells Treated with Ryanodine

ASTRACT: Cardiac myosin binding protein c (cMyBP-C or C-protein) C is a sarcomeric protein necessary for regular cardiac function. It has 11 domains starting at the N-terminus (called the C0 domain) and finishes at the C-terminus at C10. Mice were engineered to contain a tobacco etch virus protease (TEVp) recognition cleavage site located between domains C7 and C8. Additionally, these mice were engineered to express a SpyTag (st) recognition sequence located at the N-terminus of C8 of cMyBP-C. This would covalently bond with a consensus sequence known as SpyCatcher. When cardiomyocytes from these mice are permeabilized and subsequently treated with TEVp, N-terminal domains C0-C7 (γC0C7) are cut and removed from the sarcomere leaving st-C8-C10 bound to the myosin containing thick filament. As a consequence of removal of γC0C7, spontaneous oscillatory contractions (SPOC) were induced that continued after force reached steady state. These results provide evidence that SPOC is regulated by C-protein. In this project, we wanted to do a simple characterization of SPOC induced by removal of γC0C7. Characterization included: 1) how long SPOC can last in a cell without stopping when activated under fixed conditions (i.e.: between a motor and transducer pin)? 2) Does SPOC occur when not fixed by the motor and transducer? and 3) can SPOC occur in the presence of ryanodine, a Ca2+ channel blocker. We show that SPOC continues after reaching steady state for periods between 15-45 minutes. SPOC was also maintained for up to 60 minutes after γC0C7 was phosphorylated. It was undetermined if SPOC can occur in a non-fixed position since the cell folded itself until we could not visually see SPOC. Finally, SPOC occurred even in the presence of ryanodine revealing that SPOC was not due to Ca2+ cycling from release/uptake by the sarcoplasmic reticulum.

Alyssa Cordova

University of Arizona, Physiology

Mentor: Dr. Erika Eggers - Physiology

Analysis of bNOS in the Early Stages of Diabetes in the Retina

ASTRACT: Diabetes is a common disease among populations in the U.S., where 30.3 million people have been diagnosed with the condition (CDC, 2017). In being diagnosed with diabetes, it has been shown that 40-45% of individuals in the U.S. are more susceptible to experience diabetic retinopathy (DR) (NEI, 2015). Previous studies have analyzed the effects of diabetes on the retina and how it leads to visual deficits. Moore-Dotson (2016) found that there was a decreased inhibition of the rod bipolar cells by amacrine cells in the diabetic retina which leads to visual impairments. In another study, Giove and Deshpande (2009) saw an increase in neuronal Nitric Oxide Synthase (nNOS) activity resulting in the increase of nitric oxide itself. The increase of nitric oxide has been found to be associated with the early stages of diabetic retinopathy. More so, Pang (2010) found that antibodies used against brain Nitric Oxide Synthase (bNOS = nNOS) in mouse retinas show bNOS-specific staining in all layers of the inner retina. In this study, we looked at the ganglion cell layer (GCL), inner nuclear layer (INL), and inner plexiform layer (IPL) to identify the bNOS+ intensities in all three layers to see if their presence was different between control and diabetic retinas. The purpose of this study was to identify early changes in diabetic retinas to find therapeutic targets before any vision loss occurs.

Cyonna Gibson

University of Arizona, Physiology

Mentor: Dr. Klearchos Papas, Dr. Leah Steyn and
Dr. Nathaniel Hart – Surgery and Physiology

Establishment and Characterization of Islet-Like Aggregates as a Model System for Diabetes Research

ASTRACT: Diabetes, a disease that impairs the body's ability to regulate blood glucose homeostasis, afflicts hundreds of millions of people worldwide. The islets of Langerhans are a group of endocrine cells in the pancreas that help regulate blood glucose levels. One cell type within islets is the β cell, which produces and secretes the hormone insulin. Type 1 and type 2 diabetes are both characterized by β cell dysfunction and/or loss. Our group is developing β cell replacement strategies to treat diabetes. However, primary β cells from rats, pigs, and humans are difficult and expensive to isolate, and do not survive long in culture. We sought to create an islet-like model that was readily available and inexpensive. We used a rat INS832.3 β cell line to establish a suspension cell culture system that lead to the formation of islet-like aggregates. We then characterized aggregate size, viability, and function. We determined that the optimal time to use these cells was within 2-3 days of suspension culture. Based on our analyses we concluded these islet-like aggregates are a beneficial model for advancing β cell research.

Tianna Graham

University of Arizona, Molecular & Cellular Biology

Mentor: Dr. Lisa Nagy – Molecular & Cellular Biology

Body Building for Insect Embryos: A Workout Guide by Tropomyosin isoforms

ASTRACT: Throughout the animal kingdom, many organisms form their body plan by developing segments. In insects like *Tribolium castaneum*, these segments, or repeating units of the body, are regulated by a segmentation clock. The segmentation clock is a 3-gene oscillator that is activated by a signaling molecule called Wnt in the growth zone of the embryo. However, the way in which the segmentation clock regulates segmental growth and elongation is unknown. When the expression of Wnt is knocked down in *Tribolium* embryos, there is a 6-fold upregulation of tropomyosin 2. Tropomyosin is an actin-binding protein that has previously been shown to be a master regulator of the cytoskeleton in both muscle and non-muscle cells. It functions in muscle contraction, cell crawling, cell division, and most recently, it was found to have a role in localizing mRNA to the poles in early *Drosophila* embryos. How tropomyosins function in segmentation is unknown. I found homologs for tropomyosin 1 and 2 in the *Tribolium* genome, with multiple isoforms. I cloned small fragments from three different tropomyosin isoforms and analyzed their expression in early embryos. I found mRNA expression along the mesoderm/ectoderm boundaries, along the midline of the later embryo, as well as along the outer edges of the embryo. This expression along tissue boundaries in the embryo implicates tropomyosin function in the development of the midline and other morphogenetic events.

Justin Hooks

University of Arizona, Pre-medical Biology

Mentor: Dr. Shaowen Bao - Physiology

Development of auditory temporal processing

ASTRACT: Neural changes constantly occur in a developing brain, with one specific aspect being levels of neural inhibition and excitation throughout the progression of the critical period of learning. The research conducted was intended to analyze how neural plasticity is affected by changes in inhibition and excitation which are correlated with age, and how these changes in plasticity ultimately affect auditory perception. To do so, FVB mice were exposed to an auditory exercise known as GAP detection at two separate ages, allowing for the presence different levels of plasticity at different ages. Performance on GAP detection was measured by showing a ratio of mouse physical response to cued auditory stimulus versus uncued auditory stimulus, where a lower ratio represented better performance on the exercise. Results showed that the younger age group averaged a ratio of 0.88087 while the older age group averaged a ratio of 0.701037, showing significant improvement on GAP detection performance for older mice which had greater inhibition and less excitation than at younger ages. These results imply that a balance of neural inhibition and excitation may be necessary for improved auditory perception, a change which naturally occurs as aging ensues and the critical period of learning progresses and eventually closes.

Kevin Hurtado

Northern Arizona University, Biological and ecological Sciences

Mentor: Dr. Bill Montfort and Dr. Sarah Young – Chemistry & Biochemistry

Pursuing Full-Length CD47 Structure: A Step Towards Improving Cancer and Cardiovascular Disease Treatment

ASTRACT: Cluster of differentiation 47 (CD47), an immune checkpoint protein, is a key player of the immune system involved in preventing phagocytosis of cells by macrophages as a "don't eat me" signal. Cancer cells exploit this process by overexpressing CD47 at the cell surface, thereby escaping detection and clearance by the immune system. Blocking the "don't eat me" signal elicited by CD47 is a therapeutic target for drugs in clinical trials; however, only a small number of patients respond to treatment. CD47 signal mechanism is largely unknown; a greater knowledge of CD47 function and structure will help improve therapies targeting CD47 signaling, the scope of this project. CD47 is a ~50-kDa transmembrane protein that is composed of an extracellular Ig domain, five transmembrane helices, and one short cytosolic tail of unknown function. Signal regulatory protein alpha (SIRPα) and thrombospondin-1 (TSP-1) are the only known ligands of CD47. SIRPα binding to CD47 prevents phagocytosis, a mechanism that is well-studied and characterized. TSP-1 binds CD47 and inhibits nitric oxide (NO) signaling through soluble guanylyl cyclase (sGC) which subsequently inhibits angiogenesis, the formation of blood vessels from pre-existing vessels. The mechanism of TSP-1 binding, however, is not known and not well-characterized. Thus far, TSP-1 binding to the CD47 ectodomain alone is not detectable and furthermore, TSP-1 loses binding to aged cells in culture and mature erythrocytes. Currently, there is no full-length structure of CD47 to characterize the TSP-1/CD47 signaling axis. To characterize this interaction, we expressed and purified full-length CD47 in Sf9 cells using the baculovirus system. Purified CD47 from detergent and nanodiscs ¬¬¬¬— artificial lipid bilayers — were loaded onto negative stain carbon grids and imaged to determine sample quality for future cryo-electron microscopy experiments. SDS-PAGE analysis of CD47 was used to verify sample quality for x-ray crystallography experiments and crystal screens were performed.

Daniela Liera

Harvard University, Neurobiology

Mentor: Dr. Martha Bhattacharya - Neuroscience

Investigating the Role of TMEM184b in Axon Degeneration In Vivo

ASTRACT: Abstract Pending

Shanoa Nez

University of Arizona, Molecular & Cellular Biology

Mentor: Dr. Robin Harris – Epidemiology & Biostatistics

The Prevalence of Gallstone Disease Among an American Indian Community in the Southwest

ASTRACT: Introduction: Gallstone disease is considered to be the most prevalent gastrointestinal disease among women and is rarely found in children or infants. There are two forms of gallstones, cholesterol or pigment (black or brown) stones, both of which are formed in the gallbladder or biliary tract. The highest rates of gallstones occur among the American Indian population in the United States, with rates between 50% and 80%. Risk factors associated with the development of gallstones include obesity, certain genetic diseases, rapid weight loss, female, or being of American Indian or Mexican American race/ethnicity. Methods: In the Summer of 2018, a cross-sectional survey was conducted from a random sample of households from three Southwest American Indian communities. The questionnaire included three questions relating to gallstone disease. Questions were also asked about lifestyle and other health conditions. Prevalence of gallbladder disease was calculated for men and women. R programming was used to analyze the associations between gallbladder disease and potential risk factors.Chi-square was used to test associations between gallbladder disease and potential risk factors. Results: A total of 105 people were recruited from 72 households. A total of 22 women reported prior gallstone disease (34.9%) andmen (7.1%). Women who were >50 years old had higher prevalence compared to who were >50 years old. No associations were observed between self-reported gallbladder disease and diabetes and smoking. Conclusion: Gallstone prevalence is high among the Southwest American Indian Tribe. However, there is a gap in knowledge on diet and how it affects the formation of gallstones. Further research is needed on how these factors vary by type of gallstone formation.

Annabella Opoku

Rider University, Health Sciences

Mentor: Dr. Heidi Brown and Dr. Martha Rocio Ruiz – Epidemiology & Biostatistics

Is Adaptation Mal-adaptation: an Assessment of Mosquitoes and Water Harvesting

ASTRACT: Green infrastructure (GI) has been known to provide a variety of benefits to a community. Some include stormwater mitigation, air quality control, and possibly rendering cities to be climate-change resilient. Despite this, GIs have been linked to being sources for mosquitoes to breed, posing preconceived health risks. Mosquitoes are disease vectors, carrying pathogens that can increase a person's risk of getting a life-threatening infection when they feed on humans. There is little known about whether GIs attract mosquitoes. This study investigates whether well-maintained GI design strategies have the greatest impact on conservation while limiting the negative consequences of mosquitoes. GI sites were identified around the University of Arizona and a day following a rain event the sites were checked to see if there standing water. If so, a sample of the water was collected to determine whether there were mosquito larvae present. The mosquito was then identified in the lab using a dichotomous key. The species that was expected to be found were Culex quinquefasciatus, Culex tarsalis, and Aedes aegypti.

Brayan Pagan

University of Puerto Rico Cayey, General Science

Mentor: Dr. Hua Xu – Children's Research Center

Validation of DLL1/NHE8/Best2 antibodies

ASTRACT: The Na+/H+ exchange proteins from the SLC9A gene family are proteins that have an important role in the homeostasis of the human body. A specific member from this group is the NHE8 protein. It has the functions of fluid absorption, intracellular pH homeostasis and volume regulation. This protein is very important and depending of the tissue can have two location within the cell as a plasma membrane or as an organelle. There are problems that have been discovered in animal models when this protein is at a decreased level. Those issues are male infertility due to an abnormality in the LH receptor and disorder in the testosterone level, less protection in the intestinal mucosa layer and an increased rate of colitis- associated cancer. Because of these reasons the validation of proper antibodies is a necessity to understand better the role that NHE8 can have in different systems of the body. This study focuses in the research to test different antibodies in tissues originated from spleen, distal, and proximal colon. Different conditions like dilutions, time per washes, techniques, and samples were utilized to understand what are the most stable for NHE8, DLL1 and Best-2 antibodies. Some of the antibodies had great results concerning the size and intensity of detection while others need further testing to get the exact procedure to utilize the antibodies for future research concerning the NHE8 protein.

Devin Saunders

Morgan State University, Nutritional Science

Mentor: Dr. Ann Skulas Ray and Dr. Mallory Reed

Effects of Prescription Omega-3 Fatty Acid Multi-Therapy on the Inflammatory Response to Stroke in Mice

ASTRACT: Currently, there are no therapeutic treatments for stroke patients that target post-stroke chronic inflammation to enhance recovery of cognitive and motor function. Administration of long-chain omega-3 polyunsaturated fatty acids (LC-PUFAs) have been shown to be protective in animal models of neuroinflammation.1 Specialized pro-resolving lipid mediators (SPMs), bioactive derivatives of essential LCPUFAs docosahexanoic acid (DHA) and eicosapentaenoic acid (EPA), may regulate the immune response and suppress pro-inflammatory eicosanoids. In most existing animal models of stroke, omega-3 interventions are given within 6 hours of ischemic onset. We hypothesize that this research will reveal a novel therapeutic strategy, and that increased exogenous omega-3 intake 1 week after ischemic onset will decrease neuropathological and biochemical deficits. We further hypothesize that SPMs play an important role in the resolution of inflammation following stroke.

Ohiyah Shirley

Ft. Lewis College, Exercise Physiology

Mentor: Dr. John Konhilas and Melissa Lopez Pier –
Biomedical Engineering

Gender differences in Hydration Status and Exercise Performance with Kona Deep Water

ASTRACT: Dehydration is caused by prolonged exercise, which impairs thermoregulation, endurance, and exercise performance. Meanwhile, prompt rehydration is restoration of water loss, and imperative whenever dehydration occurs. A previous study in our lab involved these two concepts and determined that Kona Deep Water, a deep ocean mineral water, is the most compatible hydrator for rehydration compared to regular spring water and Gatorade. The purpose of this study is to understand how dehydration and immediate rehydration will impacts performance. We hypothesize that that prolonged exercise dehydration will impact females and males adversely, and that rehydration will return both females and males to their baseline euhydrated state. Body mass measurements and hydration status (determined by Urine Specific Gravity) were collected from participants from the beginning to end. Participants were exposed to the dehydrating and rehydrating exercise protocols. Participants also took two psychological tests post-exercise and post-rehydration. Biological samples were collected halfway through the dehydrating exercise protocol. After reaching 3% body mass loss (BML), biological samples were collected and a dehydrated VO2 max was performed. Post-dehydration protocol participants consumed an equal BML amount in Kona Deep Water, spacing half the amount out with a 30-minute rest period. The participant final test was a euhydrated VO2 max test. There were no significant differences between the female and male participant for morphometrics and VO2 max performance measurements, except for systolic blood pressure and time to reach 3% BML. Additionally, salivary osmolality and plasma osmolality demonstrate that hydration is returned to baseline with Kona post-exercise. Kona is the best rehydrating strategy compared to sports drink and spring water for both men and women.

Regina Solomon

UT Houston, Biology & Chemistry

Mentor: Dr. Noel Warfel – Cellular & Molecular Medicine

Regulation of PIM Degradation in Cancer Cells'

ASTRACT: Prostate cancer is the most prevalent cancer diagnosed in American males and remains the second leading cause of cancer-related deaths. PIM kinases have been identified as a pro-survival kinase that show potential for clinical regulation due to the overexpression of this protein with more aggressive tumors. The characteristic of a hypoxic (low oxygen) microenvironment in tumors has also been found to regulate PIM expression and causes decreased effectiveness of PIM inhibitors currently in use in the clinical setting. The goal of this study was to shed light on how PIM expression is controlled in hypoxia as well as with targeted inhibition of neighboring oncogenic pathways. To conduct this study; PC3-LN4 (prostate cancer) and HCT-116 (colon cancer) cell lines were harvested in normoxia and in hypoxia conditions with the use of the lab's hypoxia chamber. Western blots were performed with cell lysates to visualize protein expression of cancer cells after experimental treatments. RNA extraction followed by qPCR analysis was used to visualize gene expression at the transcription level. PIM1 was found to be upregulated in hypoxia in conjunction with HIF1, GSK-ser9, and AKTser473, a pro-survival kinase similar to PIM. qPCR analysis revealed PIM is expressed in a HIF-1 independent manner at the transcriptional level. Treatment with a range of oncogenic protein inhibitors yielded differing results in regard to PIM expression, so future work must be conducted in order to solidify PIM kinases as a potential biomarker for hypoxic tumor cells and improve current PIM inhibitors that are sensitive to the effects of a low oxygen tumor microenvironment.

Brenden Wimbish

James Madison University, Chemistry

Mentor: Dr. Jeff Pyun and Dr. Lindsey Holmen – Chemistry & Biochemistry

Biomimetic Metallopolymers Produced via Controlled Radical Polymerization for Electrocatalytic H_2 Generation

ASTRACT: A significant problem faced globally is the effects, and limited resources, of fossil fuels on the environment. As a result, clean and sustainable alternative fuels and energy carriers, such as H2 gas, are a new focus to counter this issue. Unfortunately, there are not many clean, or carbon free, techniques to produce H2 that don't require the use of rare-Earth metals, such as Pt as an electrode. However, there are some microalgae that consist of an enzyme called [FeFe]-hydrogenase that has an active center which utilizes Earth-abundant metals to photolytically split water to generate H2 anaerobically. Multiple biomimetics, or artificial enzymes, have been synthesized in hopes of modeling the active site of the enzyme for optimized H2 production. Previously made biomimetics of just the enzyme active center have had drawbacks including low catalytic activity, short lifetime, and poor water solubility. One method to overcome these drawbacks is by creating a support system around the active site mimic, to simulate the protein, which our lab has done by constructing a series of biomimetic metallopolymers containing a [2Fe-2S] cluster by utilizing a controlled radical polymerization technique called atom transfer radical polymerization (ATRP). We have found that by changing the number of monomeric units added to the [2Fe-2S] metalloinitiator, otherwise known as the length or molecular weight of the polymer, we observe a difference in the catalytic activity of the metallopolymer grafted from [2Fe-2S] complex. We have shown that with a polymeric arm, the active site would be better isolated from dimerization resulting in longer catalyst lifetime, a large polymeric support which may limit the rate of electron and proton transfer to [2Fe-2S] core reduces the catalytic performance for H2 generation.