Chemistry & Biochemistry
Poster Fair
Presenters Abstracts

Monday April 24, 2023
1:00 – 3:30
Student Union Memorial North Ballroom

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2023 CBC Senior Thesis/Capstone Presentations

Vanessa Addison – Biochemistry #27

Research Faculty Advisor: John Ross Buchan, Molecular and Cellular Biology

Rsp5/NEDD4 facilitates the endolysosomal clearance of TDP-43 in ALS pathology.

Amyotrophic Lateral Sclerosis (ALS) is a devastating and terminal neurodegenerative disease. A key pathological hallmark in >97% all ALS cases is the cytoplasmic mislocalization and aggregation of a nuclear RNA binding protein, TDP-43. Driving clearance of cytoplasmic TDP-43 reduces toxicity in various ALS models, though how TDP-43 clearance is regulated remains controversial. To address this, we conducted an unbiased yeast genome-wide screen using high-throughput dot blots to identify genes that affect TDP-43 levels. Our screen identified ESCRT complex factors, which induce membrane invagination, and K63-linked ubiquitination factors (particularly the E3-Ubiquitin ligase Rsp5/NEDD4) as key facilitators of TDP-43 endolysosomal clearance. In both yeast and HEK293 models, we have established that TDP-43 co-localizes and physically interacts with Rsp5/NEDD4 and the ESCRT complex and that perturbations to either affect TDP-43 accumulation. TDP-43 is ubiquitinated by Rsp5/NEDD4, and overexpressing Rsp5/NEDD4 suppresses TDP-43 toxicity in both yeast and human cell models. Following Rsp5/NEDD4 over-expression, TDP-43 protein solubility is increased, and its stability is concomitantly reduced. Taken together, these results affirm the role of endolysosomal flux in mediating TDP-43 cytotoxicity and suggest that Rsp5/NEDD4 is critically implicated in this pathway. Our findings provide further insights into proteostasis and may have broader implications in the identification of novel therapeutic strategies for ALS and other TDP-43 proteinopathies.

Taiya Alvarez-Williams – Biochemistry #54

Research Faculty Advisor: Dennis Lichtenberger, Chemistry and Biochemistry

Infrared Region Engineering and Analysis on Substituted Styrene Molecules for Investigating Long-Wave IR Window Transparency

Optical technologies in the long wave infrared region incentivized the development of high-resolution components for thermal imaging. These components consist of organic comonomers that are screened using several computational chemistry interfaces, such as Spartan ‘18 and AMS in order to perform Density Functional Theory (DFT) calculations to predict IR properties for improved LWIR window transparency. In this study, the comonomers of interest were several styrene analogs. These substituted styrene type molecules were observed to study trends that have an overall effect on LWIR window transparency.

Jonah Balsa – Biochemistry, Molecular and Cellular Biology #28

Research Faculty Advisor: George Sutphin, Molecular and Cellular Biology

3-hydroxyanthranilic acid immune activity in Caenorhabditis elegans

The roundworm *Caenorhabditis elegans* is a model organism with the ability to demonstrate impact on immunity and cellular mechanistic interactions. The kynurenine pathway metabolite 3-hydroxyanthranilic acid (3HAA) has previously had little knowledge surrounding its role in the immune system maintenance of the roundworm *C. elegans*. Preceding research indicates that the inhibition of the enzyme 3-hydroxyanthranilate dioxygenase (HAAO) metabolizes and decreases levels of 3HAA in *C. elegans.* By blocking HAAO, this increases intracellular 3HAA levels resulting in the extension of lifespan in *C. elegans*. Mass spectrometry data conducted throughout the age of *C. elegans* displays a gradual increase in 3HAA levels with a max difference occurring on day 8. HAAO inhibited worms have increased immune function, leading to the belief that iron could potentially play a critical role in immune pathogen response due to its link to bacterial growth, oxidation of 3HAA, and pro-inflammatory activity in mammals. Inhibition of Ferroportin (FPN) has shown that an

increased labile iron pool contributes to an increased lifespan as well, displaying iron transport has an interaction with 3HAA resulting in lifespan extension. In addition to this, our lab has developed a system known as systematic imaging of *C. elegans* killing organisms (SICKO) that allows for quantification and visualization of pathogens in the host to gain a better understanding of the pathogen-host interaction within the *C. elegans.*

Elizabeth Browne – Biochemistry, Philosophy #52

Research Faculty Advisor: John Jewett, Chemistry and Biochemistry

Development of Aryl Diazonium Ion (ADI) Probes to Study Biological Systems

Aryl diazonium ions (ADIs) are small molecules that react with biomolecules. ADIs are known to degrade nucleic acids via aryl radical formation. ADIs are also known to form covalent bonds with amino acid residues (tyrosine and histidine) on proteins via electrophilic aromatic substitution. Altering the chemistry of biological structures can elucidate and alter their functions, and ADIs' targets are relevant to several essential processes. Tyrosine is abundant at sites of protein-protein interaction and is a site of post-translational modification. Histidine contributes to enzyme activity (e.g. serine proteases) and acts as a proton shuttle. Nucleic acids act as a template for synthesis of proteins.

Despite their potential as chemical probes, the reactivity of ADIs has not been fully characterized. It is unknown how ring substitutions and reaction conditions impact their reactivity. It is unknown which positions on amino acid residues react with ADIs, as well as how many ADIs bond to a single residue. It is unknown whether ADIs react to a greater extent with tyrosine or histidine. The speed, extent, and mechanism of reactions with nucleic acids are underexplored.

The first aim of this project is to fill these gaps in knowledge by systematically characterizing ADI reactivity with biomolecules. These data will help determine appropriate applications of ADIs. A set of ADIs with substitutions that varied steric and electronic effects were synthesized. To address unknowns about reactivity with proteins, the products formed when an ADI is allowed to react with either p-cresol (a tyrosine mimic) or 4-methylimidazole (a histidine mimic) were characterized via NMR. Then, reactions under varying biologically relevant conditions with a 1:1:1 molar ratio of ADI:p-cresol:4-methylimidazole were conducted. The total and relative yield of products were quantified via NMR. To address unknowns about reactivity with nucleic acids, ADIs with different substitutions were combined with DNA and the reactions were quenched at different times. The quantity of DNA remaining was measured using ethidium bromide fluorescence. The primary chemical aim of these experiments is to determine how readily different ADIs form aryl radicals; the primary biological aim is to determine whether ADIs are applicable to DNA as probes or drugs.

In the future, we will characterize the interaction of ADIs with proteins to determine whether the principles outlined in small molecule studies apply to macromolecules. We will finish optimization of the protocol of DNA experiments, then compare the results of ADIs with different substitutions. When all of these data are correlated to physical organic properties, we hope to elucidate a set of principles to predict ADI reactivity with biomolecules to facilitate their use as chemical probes in complex biological systems.

Preston Buttery – Biochemistry #29

Research Faculty Advisor: Brian Enquist, Ecology and Evolutionary Biology

The Influence of Elevation Change on Phosphorus Composition of Peruvian Plants

The element phosphorus is a foundational component that is necessary to facilitate growth, sustain biological processes, and encourage replication across all life forms on the planet. In particular, phosphorus is integral to plant life as it allows for them to perform necessary biochemical processes in the organism such as the manufacturing of nucleic acids, helping to accomplish cellular regulation, and undergoing photosynthetic processes. As the Earth experiences an increase in global greenhouse gasses in the atmosphere, plants are able to thrive due to the fact that their respiration is dependent on carbon dioxide intake. In turn, this creates a demand for a larger phosphorus concentration in the soil in order to keep up with the accelerated plant growth. There exists a finite amount of usable phosphorus in the soil for plants to use and as the demand for it grows, it leads to depletion of nutrients necessary for plant sustainability in the soil. In Peru during March of 2018, plant samples from a variety of genuses and species were taken and dried in order to perform an analysis for phosphorus concentration found in the plant specimens. The samples collected from the plants in Peru span from a variety of elevations at the collection site. These samples were then broken down by a series of chemical processes and analyzed for their phosphorus concentration. By averaging the phosphorus concentrations of the samples stemming from the same genus as well as averaging their respective elevations from which they were taken, it was determined that as the elevation of a plant increased, the concentration of phosphorus found in the sample decreased. This is indicative that the demand for phosphorus is higher among plants at lower elevations due to a variety of factors such as proximity to urban development as well as weather patterns that allow for lower-elevation soil to become more nutrient dense.

Cristian Chavira – Biochemistry #44

Research Faculty Advisor: Joann Sweasy, Cellular and Molecular Medicine

A collapsed fingers subdomain is the basis for DNA Polymerase β I260M mutator activity

DNA Polymerase β (Pol β) fills single nucleotide gaps as a part of the base excision repair pathway (BER); thus, deficiencies in Pol β can lead to increased mutation frequency in the cell, which can result in genomic instability and cancer. Our lab has previously shown that the I260M somatic mutation of Pol β, which was first identified in prostate cancer, has reduced nucleotide discrimination in a sequence context-dependent manner. I260M incorporates the incorrect G opposite A in this context more readily than WT. To identify the molecular mechanism of the reduced fidelity of I260M, we studied incorporation using single turnover kinetics, and conformational changes using steady-state fluorescence and stopped-flow FRET. Our data indicates that the I260M mutation affects the fingers region of Pol β by creating a “collapsed” state in both the open (in the absence of nucleotide) and closed (prior to chemistry) states. Importantly, we show that the incorrect incoming nucleotide binds more tightly to I260M when compared to the wild-type 3.4-fold. Based on this data, we found that the collapsed fingers subdomain state of I260M may decrease nucleotide discrimination in I260M, illustrating the importance of a correct “fingers closing” conformational change for polymerase fidelity. A model is being developed to compare the rate of the “fingers closing” conformational change and the reverse reaction of nucleotide release between I260M and the WT.

Wesley Chiu – Biochemistry, Systems Engineering #47

Research Faculty Advisor: Roberto Guzman, Chemical Engineering

Development and Modeling of Chitosan Nanoparticles for Antidepressant Drug Delivery

Antidepressants are some of the most prescribed medications in the US. However, they often come with significant side effects. New drug carriers have been developed to help aid in the specificity and duration of drug release, including nanoparticles. Chitosan is a glucosamine polymer that has been used across a wide range of nanomedicine drug delivery applications. This project aims to prepare chitosan nanoparticles to encapsulate antidepressants, model the release of the drug, and consider the effects of chitosan modifications. Chitosan nanoparticles were successfully formulated through ionic gelation to encapsulate antidepressants venlafaxine and paroxetine. In vitro drug release studies were performed and mathematically modeled to characterize release stages. PEGylation of chitosan improved drug loading and altered release profiles.

Kaitlyn Chung – Biochemistry, Microbiology #30

Research Faculty Advisor: Walter Betancourt, Environmental Science

Evaluation of Viral Indicators of Advanced Physical Treatment for Potable Reuse

Advanced treatment processes for potable reuse are indispensable to mitigate microbial and chemical contaminants in recycled water. Viruses pose a particular risk due to their small size, low infectious dose, and resistance to disinfection. Understanding virus concentrations and their reductions through advanced treatment trains is essential for safe water reuse. While research has extensively studied virus rejection mechanisms by membrane processes at bench and pilot scales, full-scale studies are scarce, especially for reverse osmosis membranes, which are considered complete barriers for pathogens in the United States, with limited regulatory credit.

This study was conducted at a full-scale integrated membrane system in Arizona to evaluate multiple viruses as indicators of advanced physical treatment. The viruses investigated included human enteric viruses (Enterovirus, Reovirus, Norovirus Genogroups I and II, Adenovirus) and virus surrogates (Somatic and male-specific coliphages, crAssphage). Viruses were concentrated by centrifugal ultrafiltration and by absorption-elution methods. Digital polymerase chain reaction assays were used to quantify virus genomes for all viruses except for coliphages that were enumerated by the single-agar layer method. The study revealed virus breakthrough after full advanced treatment for both coliphages and two human enteric viruses (Norovirus GI and Adenovirus) highlighting the importance of continuous monitoring of advanced treatment trains to ensure the safety of water for potable reuse.

Madison Cook – Biochemistry #22

Research Faculty Advisor: Carol Dieckmann, Molecular and Cellular Biology

5' tRNA Processing in Yeast Mitochondria

RPM2 is a protein in yeast (Saccharomyces cerevisiae) mitochondria that provides charge shielding for an RNA/protein complex called RNase P, which is used to cleave the 5’ leaders of all pre-tRNAs encoded by the mitochondrial DNA. It was previously believed that lipoic acid (a product of the FAS II pathway) modified RPM2, as this would provide precise control. However, using anti-lipoic acid antibodies in previous studies showed that there in fact is no lipoic acid attachment in RPM2. Our hypothesis is that a precursor to lipoic acid, called octanoic acid, or a longer derivative of octanoic acid, is attached to the protein instead. We are hoping to discover where the fatty acid(s) modifies the protein, and eventually, whether it is octanoate or some other product of the FAS II pathway. The protein can be split into two halves: an N-half and a C-half, of

which the C-half function can be lost without causing death of the cells (N-half essential function is separate from RNase P activity). It is believed the fatty acid attachment occurs on lysine residues in the C-half. Thus, our method was to systematically modify lysine residues to arginines in order to preserve the positive charge function but prevent fatty acid attachment. The change in yeast growth, lack of Lys modification (gel shift assay), or loss of mitochondrial DNA (if P activity is completely defective) when the RPM2 protein is modified shows us whether cellular respiration is occurring and to what extent. This indicates the importance of the modified residues and their possible role in fatty acid attachment.

Alexis Cruickshank-Taylor – Biochemistry #23

Research Faculty Advisor: Nancy Horton, Molecular and Cellular Biology

Creation of SgrAI Dimer Construct to Form a Binary Complex

Enzyme filamentation is a novel discovery with its mechanism being widely unexplored. SgrAI, a type II restriction endonuclease, is utilized to further the understanding of enzyme filamentation. Computational modeling suggests that the SgrAI filamentation mechanism is superior to other mechanisms because it protects host DNA from aberrant cleavage by sequestering activated SgrAI on DNA containing the activating primary sequences. A SgrAI binary complex, where only two copies of SgrAI assemble rather than an open-ended filament, can also perform this protective mechanism. However, modeling also suggests that the filament mechanism is much faster at activating SgrAI than a binary complex. To test this prediction, a SgrAI construct was designed with one wild-type subunit and one mutant subunit per dimer, which should assemble with only one other similar heterodimer. However, coexpression of wild-type and mutant SgrAI chains form wt-wt and mt-mt homodimers, as well as the desired wt-mt heterodimer. Different purification tags were placed on the wt and mt chains allowing for isolation of only the heterodimer; however once isolated, the heterodimer may re-equilibrate to form a mixture of homo and hetero dimers. To prevent re-equilibration, crosslinking of the SgrAI dimer subunits prior to purification is required. In this study, BM(PEG)3 is used to crosslink the SgrAI heterodimer subunits. Various purification methods and crosslinking conditions such as SgrAI and BM(PEG)3 concentration, reaction time and temperature, and reaction buffers were assessed. SgrAI crosslinking was identified in multiple crosslinking reactions and current efforts are being made to improve the reaction's yield. After further purification, future tests will analyze the effect on SgrAI activity activation of forming a binary complex versus open-ended filaments.

Kyla Ditoro – Biochemistry #53

Research Faculty Advisor: Craig Aspinwall, Chemistry and Biochemistry

Lipid Bilayer based Ion Selective Electrodes

Lipid bilayer-based ion selective electrodes (ISEs) are a new type of electrochemical sensor that combines the advantages of ISEs with the versatility of lipid bilayer membranes. In this study, we demonstrate the use of lipid bilayer-based ISEs for the electrochemical analysis of calcium ions in aqueous solutions. Our results show that these electrodes are able to accurately and selectively measure ion concentrations, with good sensitivity and stability. In addition, we show that lipid bilayer-based ISEs are compatible with living cells, opening up the possibility of using these electrodes to study ion transport in cells. Overall, our results suggest that lipid bilayer-based ISEs are a promising new tool for electrochemical analysis.

Lipid bilayer-based ion selective electrodes (ISEs) are a promising tool for electrochemical analysis. In this study, we demonstrated the use of lipid bilayer-based ISEs for the measurement of calcium ion concentrations in aqueous solutions. The electrodes consisted of a lipid bilayer membrane containing ionophores, which selectively bound and transported the ions of interest. We found that the electrodes were able to accurately and selectively measure the concentrations of calcium ions over a range of 10-1000 micromolar. The electrodes showed good sensitivity and stability, and were compatible with living cells. These results suggest

that lipid bilayer-based ISEs have potential applications in chemical analysis, environmental monitoring, and biotechnology.

Lipid bilayer-based calcium ion selective electrodes (CaISEs) are a type of electrochemical sensor that is used to measure the concentration of calcium ions in aqueous solutions. These electrodes consist of a lipid bilayer membrane containing ionophores, which selectively bind and transport calcium ions across the membrane.

CaISEs have several advantages over traditional ion selective electrodes. For example, they are more selective and sensitive, allowing for the detection of low levels of calcium ions. They are also compatible with living cells, which makes them useful for studying calcium ion transport in biological systems.

CaISEs are commonly used in a variety of applications, including chemical analysis, environmental monitoring, and biotechnology. For example, they can be used to measure calcium ion concentrations in water samples to assess water quality, or to study the role of calcium ions in cellular signaling and other biological processes.

In conclusion, lipid bilayer-based calcium ion selective electrodes are a valuable tool for the electrochemical analysis of calcium ions. They offer improved sensitivity and selectivity, and are compatible with living cells, making them useful for a wide range of applications.

Julie Fan – Biochemistry #25

Research Faculty Advisor: Samantha Harris, Cellular Molecular Medicine

Reduced expression of cMyBP-C protein across left heart chambers for mice and cat models

Cardiac myosin binding protein C (cMyBP-C) exerts its role on larger structural heart proteins in the sarcomeres of heart muscle to regulate contractions. Current studies have not yet measured whether or not there is variable distribution of cMyBP-C between the atria and ventricles, which would be expected as these two chambers produce different forces to achieve their function in the circulatory system. Investigating this may also shed more light regarding this protein's functional impact on associated heart pathologies and our foundational understanding of this protein's role in the heart muscle. The A31P mutation on cMyBP-C is also a common mutation associated with hypertrophic cardiomyopathy in domestic felines, but the mechanism for this is not fully clear. Here we determine with western blots that the expression of cMyBP-C is increased in the left ventricle compared to the left atria in both mice and cat models. We also conducted western blots that determined that there is no difference in cMyBP-C expression for wildtype cats and those with the A31P mutation, suggesting that the mechanism of heart failure associated with this mutation is not related to an alteration in the relative distribution of this protein across heart chambers.

Nicole Ferguson – Biochemistry, Neuroscience & Cognitive Science # 38

Research Faculty Advisor: Erika Eggers, Physiology

Impacts of a High-Fat Diet on the Neurovascular Unit of the Inner Retina

A high-fat diet (HFD) can recapitulate the pathogenesis of metabolic disorders (including diabetes) in rodent models, which can impact retinal function and health, impairing vision. Stained retinal images from 18 male and female C57Bl/6J mice fed a HFD (60% saturated fat) or a normal mouse chow diet (4% fat) for 18 weeks were analyzed in ImageJ/FIJI to elucidate physiological changes across both sexes. The proportion of vessels covered by astrocytes (anti-GFAP stain) was greater for female HFD than female Control ($p=0.013$), and greater in HFD groups combined compared to Controls ($p=0.012$). Morphological features of astrocytic processes were quantified; the proportion of astrocytes with frayed ends was greater for male HFD than the male Control ($p=0.005$), and for HFD groups combined compared to Controls ($p=0.005$). Both HFD groups show a trend of increased thickened astrocytic processes compared to their prospective Control groups, an indicator

of astrocytic activation. The thickened processes correlate with blood glucose, which was significantly higher in the female HFD group compared to female Control at the end of the study. Pericyte (anti-NG2 antibody stain) area in the Inner Nuclear Layer (INL) was greater in the HFD groups of both sexes compared to respective Controls (p<0.001 for males and p=0.002 for females), and in HFD groups combined compared to Controls (p<0.001). The proportion of capillaries covered by pericytes in the INL was greater in the HFD groups of both sexes compared to respective Controls (p<0.001 for males and p=0.026 for females) and in HFD groups combined compared to Controls (p<0.001). The HFD-induced changes to the neurovascular unit including increased proximity between vessels and astrocytes, morphological changes in astrocytes, increased number of pericytes and increased proximity between pericytes and capillaries may indicate early physiological effects in prediabetic conditions.

Carson Freeling – Biochemistry # 19

Research Faculty Advisor: Thomas Tomasiak, Chemistry and Biochemistry

Bioinformatic Identification and Analysis of Candida glabrata Ybt1 as a Putative Vacuolar ABC Transporter

The fungal species Candida glabrata has demonstrated azole resistance in clinical isolates. This resistance is likely conferred by the species' increased expression of ATP-binding cassette (ABC) transporters at the vacuolar and plasma membrane. Using BLAST searches and multiple sequence alignments, C. glabrata yeast bile transporter 1 (CgYbt1) was identified as an ABC transporter involved in either cellular detoxification or stress response. By optimizing the expression of CgYbt1 in Saccharomyces cerevisiae, further in vitro and in vivo studies may be conducted to experimentally determine its structure and function.

Parker Geffre – Biochemistry, Molecular & Cellular Biology #32

Research Faculty Advisor: Laura Meredith, Natural Resources and Environmental Resources

Real-time Online Analysis of Soil Isoprene Diffusion: Drivers of Biotic Consumption and Implications for Biogenic Volatile Organic Compounds as Biomarkers of Soil Health

Soil volatile organic compounds (VOCs) play a promising role as biomarkers due to their diverse roles as signaling molecules, metabolic intermediates, secondary metabolites and even sole carbon sources to certain surrounding microorganisms. However, as VOCs remain an oft overlooked subset of the soil metabolome, the overall dynamics and impact of microbial VOC cycling within soil and on soil health remains to be understood.

To study this, we performed a series of in-situ-isoprene-dosing soil column experiments that utilize real-time online mass spectrometry to measure the biotic consumption of isoprene overtime as it is released from a subsurface doser. A proton-transfer-reaction time-of-flight mass spectrometer (PTR-TOF-MS) measured isoprene, carbon tetrachloride as a control chemical, and isoprene oxidation products to track the dynamics of isoprene uptake upon subsequent dosings. We removed soil core samples from the columns before and after isoprene dosing periods. From these soil cores, we will evaluate metagenomic and metatranscriptomic results from the beginning and end of a dosing period, investigating shifts in overall microbial population, diversity, and gene regulation to further estimate the microbial impact on biogenic (BVOC) cycling.

We hypothesize that an observed increase in isoprene retention corresponds with increased microbial consumption and higher abundances of bacteria that consume BVOCs. Specifically, we expect either significant shifts in overall microbial community diversity, specific gene upregulation related to isoprene consumption, and or increased populations of certain isoprene-degrading community members to be responsible. Microbial metabolites produced post-consumption and their fates within the soil will also be discussed.

By examining biotic consumption of isoprene in a controlled soil system, our work presents a novel measurement setup that provides key insights into how BVOCs could be used as a predictive biomarker in overall soil health by examining metagenomic, metatranscriptomic, and metabolomic shifts in tandem.

Sidney Haigler – Biochemistry #48

Research Faculty Advisor: Adam Printz, Chemical and Environmental Engineering

Silane Surface Modifications and their Influence on Perovskite Solar Cell Films

The interaction of a silane self-assembled monolayer (SAM) has been shown to improve the power converting efficiency (PCE) of perovskite solar cell devices (PSCs). The SAM can interact with the SnO2 electron transport layer (ETL) through Si-O bonds and with the perovskite through electrostatic bonds, coordination, or hydrogen bonds of its terminal groups. Using different silane terminal groups, we aim to find a silane monolayer that will produce higher quality perovskite films while maintaining the structure and function of the perovskite. We found that once deposited on the substrate, the silanes do not change the crystallinity or structure of the perovskite evidenced by X-ray diffraction, photoluminescence, microscope imaging, and ultraviolet absorption. We used photoluminescence to assess the quality of the films and concluded that the silanes with halogen terminal groups will work best when moving forward with silane SAM perovskite solar cell devices.

Rachel Hurley – Biochemistry #33

Research Faculty Advisor: Todd Schlenke, Entomology

Characterization of vitellogenin-like leader sequences for trafficking Cas9 into developing parasitoid embryos

Parasitoids are insects that live on or in the bodies of other arthropods during their juvenile life stages. They are diverse and ubiquitous in nature and infect most insect species. Hosts attempt to kill the parasitoid eggs/larvae via encapsulation, a process in which thousands of blood cells bind to the foreign object and make a tight capsule around it. Encapsulation is similar to the granuloma responses of vertebrates, and thus host-parasitoid interactions serve as a good model for how animals fight off macro-parasites in general. However, many aspects of the encapsulation response, and the parasitoid ability to suppress or evade this response, are uncharacterized. I am working on a parasitoid wasp species, Leptopilina heterotoma, that infects the lab fruit fly Drosophila melanogaster. D. melanogaster is a genetic model system, but it is currently very difficult to genetically manipulate parasitoids like Leptopilina. Their small size makes it difficult to inject dsRNAs for RNAi knockdown without seriously injuring them, and it is also difficult to inject their embryos with Cas9-gRNA complexes to make CRISPR knockouts because their eggs are often laid into hosts and require the host environment to survive. Our goal is to develop a new and efficient approach to produce CRISPR knockout mutations in parasitoids by modifying a method called “ReMOT control” (Chaverra-Rodriguez et al). In this method, Cas9-gRNA complexes are injected into adult female wasps and are trafficked into developing embryos in the ovary due to a recombinant vitellogenin-like motif appended to Cas9. This way, Cas9 is delivered directly to eggs before they leave the mother. We have identified ‘leader sequences’ from the gene encoding the major L. heterotoma yolk protein lipophorin (a homolog of vitellogenin) that we will test to determine their ability to deliver proteins into ovarian embryos. This will reveal which lipophorin leader sequences mediate embryonic uptake, and they can then be used to deliver Cas9 to embryos in future CRISPR experiments.

Terese Kulangara – Biochemistry #35

Research Faculty Advisor: Richard Simpson, Nutritional Sciences

The Effect of Aging on Military Readiness in a Retired Elite Soldier - A Case Study

The Backpack Treadmill Running Protocol has previously shown to be an excellent predictor of military readiness. More specifically, the analysis of blood lactate thresholds and walking/running economy associated with this protocol allows for evaluation of an individual's physical fitness. Although this protocol has been shown to predict military success, it has not been evaluated among the retired military soldier population. In 2020, the Department of Defense requested that the limit of re-recruiting 1000 retired military soldiers in the case of a national emergency be lifted. It is therefore of great interest to determine the reasonableness of this request by utilizing the Backpack Treadmill Running Protocol to analyze and compare the physiological differences in metabolic response during the protocol between active military service and after a substantial time since retirement. The participant was one 44-year-old male with a background in competitive endurance sports. This participant was previously involved in a military readiness study in 2006. Consequently, this specific case study compares the participant's physiological responses to the Backpack Treadmill Running Protocol in 2006 and in 2022. Specific analyses of interest were respiratory gas measures, heart rate, rate of perceived exertion, blood lactate, and catecholamine responses to exercise at every stage of the protocol. Through breath-by-breath calorimetry, the 2-CAT ELISA, and the Lactate Assay kit, all relevant measures were collected and analyzed. Results from this study indicate that a higher VO2 is seen at every stage in the protocol and that the Blood Lactate Threshold is seen to be reached significantly earlier in the protocol. These findings are indicative of the confirmation of the hypothesis that aging and retirement are seen to negatively impact military readiness. However, during the course of the study, training measures were beginning to be implemented. Based on the initial results, we anticipate that a retired military soldier could ultimately progress via training in such a way as to quickly be reconditioned to achieve military readiness status. However, further investigation is necessary to determine if elite retired soldiers can indeed be efficiently trained in such a manner as to result in complete military readiness.

Brent Lee – Biochemistry, Neuroscience and Cognitive Science #21

Research Faculty Advisor: Matthew Cordes, Chemistry and Biochemistry

Investigating Sphingomyelinase Activity of Sicarius Beta-1-F proteins

Phospholipase D (PLD) toxins are found in recluse spider venom and known for their neurotoxic effects to prey and dermonecrotic effects to humans. These toxins bind and catalyze cleavage of lipid head groups, and cyclization of the lipid backbone to a variety of sphingolipids and lysophospholipids with various headgroups. These toxins are differentiated by their preference for specific head groups allowing for easy categorization within a phylogenetic tree. For example, some only act on lipids with a choline head group (alpha-clade), ethanolamine head group (beta-1-ABC clades), while others have not yet been functionally characterized (beta-2 and beta-1-EF clades). We use a representative of the Beta-1-EF clade from Sicarius. In general, sphingomyelinase activity is lower in Beta-1-EF variants as compared to alpha variants when studied under enzyme-coupled choline/ethanolamine release assays. Previous studies have shown very little sphingomyelinase activity but indicate some potential for hemolytic and necrotic activity. This current investigation indicates the possibility of Beta-1-EF variants possessing mild activity against choline containing lipids like sphingomyelin. This finding may indicate possible sphingomyelinase activity in the species of Sicarius despite the lack of any alpha clade representatives. However, with the additional presence of ethanolamine containing lipids, there shows an increase in sphingomyelinase activity compared to choline only samples. These results combined may show that Beta-1-EF representatives may have some sphingomyelinase activity but may be dependent on allosteric activation. This is the first known isolated Beta-1-EF representative that shows some levels of sphingomyelinase activity, indicating that, under certain conditions, these variants can act as sphingomyelinases. This activity may explain the presence of sphingomyelinase activity in these spiders in some studies, as well their dermonecrotic and hemolytic potential in venom.

Melissa Lim – Biochemistry #46

Research Faculty Advisor: Jeong-Yeol Yoon, Biomedical Engineering

Handheld, Autofluorescence Identification of Soil Microbiome

The archaea, bacteria, viruses, fungus, and protists found in soil, as well as their genes, make up the soil microbiome. By examining soil pH levels, soil water content, and bacterial composition, this study seeks to forecast soil health. The soil microbiome is crucial for nutrient cycling, decomposition, and promoting plant growth. Healthy soil is essential for supporting living ecosystems that support people, animals, and plants. Particularly, bacteria are crucial for the productivity and health of soil, maintaining vital ecosystem functions including denitrification, mineralization, and nitrogen fixation.

Shayna Maddern – Biochemistry, Molecular and Cellular Biology #41

Research Faculty Advisor: Chris Hulme, Pharmacology and Toxicology

The design and synthesis of Proteolysis Targeting Chimeras towards degradation of Dual-Specificity Tyrosine-Regulated Kinases

Dual-specificity tyrosine-regulated kinases (DYRK) are involved in pathways throughout the body, with orthologs in all eukaryotic organisms. Members of the DYRK family, DYRK1A and DYRK1B, are implicated in the progression of several neurodegenerative diseases and cancers. Previous work in this lab has discovered potent and selective small molecule DYRK1A inhibitors that demonstrate a reduction of key Alzheimer's hallmarks, amyloid plaques and neurofibrillary tangles, in vivo and are moving forward in clinical trials. Current work explores the use of proteolysis targeting chimeras to induce degradation of DYRK proteins. PROTACs are bifunctional molecules that have made strides in targeting previously considered "undruggable" proteins through a molecular glue-like mechanism. This could allow for more effective reduction of DYRK1A/B activity and disruption of protein-protein interactions that are not affected by inhibition on its own. PROTACs targeting DYRK1A/B combine the structure of our lab's small molecule inhibitor that binds in the ATP binding pocket of DYRK1A/B with a linker chain connecting it to an E3 ligase-targeting ligand. This recruits the proteasome to induce degradation via existing cellular pathways. The design and synthesis of three series of PROTAC structures have been herein explored. In vitro data returned on degradation and binding for these molecules shows a path forward towards optimization and clinical trials.

Madeleine Milner – Biochemistry #20

Research Faculty Advisor: Thomas Tomasiak, Chemistry and Biochemistry

Investigating the Role of Zn2+ Dependent Immune Regulation

Intracellular zinc concentration is a major regulator of inflammation within the lungs and has been implicated in the onset of viral respiratory symptoms. In particular, zinc homeostasis within the airway epithelium is essential for the catalytic activation of zinc-metalloenzymes like the Angiotensin Converting Enzyme (ACE) family, positioning zinc transporters as crucial to immune response activation through regulation of processes like the pro-inflammatory cytokine response and viral entry into the host cell. Of particular interest is the Golgi-bound zinc efflux transporter, ZnT7, which is primarily expressed in lung epithelial cells. Mass Spectrometry analysis suggests interaction with a protein component of the causative agent of Covid-19, the SARS-CoV-2 membrane protein (M Protein). Formation of the ZnT7-M Protein complex may serve as the basis of zinc-mediated immune regulation by SARS-CoV-2. As such, identifying various molecular mechanisms by which the ZnT7-M Protein interaction modulates zinc homeostasis in the human host may prove valuable in the development of SARS-CoV-2 targeted therapeutics. Using bioinformatics, computational modeling, structural studies, and biochemical approaches we show that ZnT7 and M Protein are interaction partners,

likely through a transmembrane interface that preferentially stabilizes a ZnT7 conformation state thereby disrupting endogenous cytosolic zinc levels.

Nicholas Mortimore – Biochemistry, Molecular and Cellular Biology #26

Research Faculty Advisor: John Ross Buchan, Molecular and Cellular Biology

Developing a Screen for 3' UTR Scaffolding of Protein-Protein Interactions in S. cerevisiae

Protein interactions are fundamental to all cellular processes. However, relatively little is known about how specific protein interactions and complexes are established in the natural cellular environment, given limits on protein diffusion and a multitude of potential "off target" protein binding partners. Recently, a novel mechanism for facilitating nascent protein interactions was discovered, termed "3' Untranslated Region (3' UTR) Scaffolding." 3' UTR Scaffolding occurs when one protein binds to the 3' UTR of the mRNA encoding for its interaction partner and waits for the mRNA to undergo translation. Once translated, the two proteins are in proximity and efficiently interact with one another. To date, only a few examples of 3' UTR Scaffolding have been found. Here we describe a screen in S. cerevisiae (baker's yeast) to identify the role of many genes' mRNA 3' UTRs in mediating the interactions of their protein products. A better understanding of the prevalence of 3' UTR Scaffolding could have implications throughout all aspects of cellular biology and may identify novel means to alter protein interactions via targeting of mRNA 3' UTRs.

Victoria Munoz – Biochemistry #55

Research Faculty Advisor: Dennis Lichtenberger, Chemistry and Biochemistry

Computational vs. Experimental Window Transparency Values for Chloroform and Thiophene

Accurate and cost effective computational methods are needed for the prediction of bulk optical properties of hypothetical new materials. In this study, computational methods for predicting infrared spectra were tested against experimental infrared spectra of a test set of molecules to determine the window transparency (wT%) across the long wave IR region (LWIR) for each molecule. The basis set 6-31G* used with the Density functional theory (DFT) functional B3LYP was determined to be accurate and fast for predicting wT values when compared to other Pople, Dunning, and Alrich/Weigend type basis sets. Various computational methods were tested as well for expediency and accuracy of vibrational spectra prediction using the 6-31G* basis set where applicable. The results showed that PBE0 and B3LYP are both accurate and fast options for predicting vibrational spectra and wT%.

Sami Muslmani – Biochemistry, Neuroscience and Cognitive Science #45

Research Faculty Advisor: Marvin Slepian, Biomedical Engineering

COVID-19-Associated Cytokine Storm in Mechanical Circulatory Support: An In-Vitro Study

Catheter-based mechanical circulatory support (MCS) systems are increasingly utilized for therapy in advanced heart failure patients. The need for MCS has grown in parallel with COVID-19-associated heart dysfunction. Following a COVID-19 infection, there is a rapid increase in levels of circulating pro-inflammatory cytokines referred to as a "cytokine storm". This "cytokine storm" has been shown to disrupt the immune system drastically. Proteins (e.g. cytokines) are sensitive to their biochemical environment, undergoing conformational changes that can ultimately affect biological function. It is well recognized that MCS impart shear stress on the blood and circulating components. However, there remains a lack of understanding as to the impact of MCS devices on cytokines, particularly COVID-19-associated cytokines. Here, we utilized an Impella 5.5 to circulate a cytokine mixture (IL-6, IL-8, TNFα, IL-1β) representative of the COVID-19 "cytokine storm". We hypothesize that MCS-induced flow alterations - i.e turbulence and shear stress, will alter cytokine structure and binding ability as indicated by gel electrophoresis and ELISA binding. We found a significant

increase in cytokine-antibody binding via ELISA after 1 hour of shear exposure, compared to the resting sample. Non-native gel electrophoresis of samples allowed for evaluation of molecular mass against protein standard (2-25 kDa). Notably, single bands of IL-6 and TNFα were visible in the resting samples; however, sheared samples showed double bands at the same location, indicating influence of shear on a portion of IL-6 and TNFα population size. Our findings suggest MCS could play a role in cytokine function and ultimately inflammation in a wide range of diseases. With further translation and defining mechanisms involved, these findings could help to inform improved MCS therapy.

Christopher Nabong – Biochemistry #42

Research Faculty Advisor: John Streicher, Pharmacology

Creation of Fluorine-18 Radiotracer for Positron Emission Tomography in neurological disease

Pet Imaging is a critical tool for the quantification and detection of the biological processes and metabolic functions of tissues and organs with the use of radiotracers. Specifically for all neurological diseases, the Translocater protein (TSPO) is highly expressed in the mitochondrial membrane of glial cells in the brain. Our goal is to create a radio tracer with Fluorine-18 labeling technology which is radiolabeled to a small fragment of the Diazepam Binding inhibitor (DBI), which is known to interact with the TSPO ligand. It must be small enough to enter through the blood brain barrier (BBB) and interact with the TSPO protein to be visible through PET imaging. Current results show the creation of 6 preliminary amino acid fragments with the purification of the protein.

Jack Nichols – Chemistry #49

Research Faculty Advisor: Stephen Kukolich, Chemistry and Biochemistry

Rotational Spectra of Deuterated Isotopologues of 2-aminopyridine and Microwave Spectrometer Development

Our lab uses high-resolution microwave spectroscopy to measure rotational spectra and structures of small molecules. Analogs of DNA bases, like 2-aminopyridine, can be investigated with ease in isolated systems. The analysis of 2-aminopyridine can provide insight into the structures of DNA bases, which are difficult to examine in biological environments. The purpose of this project was to use microwave spectroscopy to determine the structures of three isotopologues of 2-aminopyridine with varying degrees of deuteration of its amino group. In addition, a LabVIEW-based program was created to control the microwave spectrometer used to measure rotational transitions for this experiment. Calculations were performed using density functional theory (DFT) and Møller-Plesset Perturbation Theory (MP2) to predict rotational transitions for each isotopologue. These transitions were used to determine the rotational constants and quadrupole coupling constants for the 14N and deuterium atoms in the isotopologues. These findings can be used in the future analysis of complexes containing 2-aminopyridine, such as the heterodimer of 2-aminopyridine and formic acid.

Andre Oropeza – Biochemistry #31

Research Faculty Advisor: Zhongguo Xiong, Plant Science

Engineering a Pepino mosaic virus mutant lacking the N-terminal 18 amino acids of the capsid protein

Plant viruses are useful expression vectors for producing large amounts of recombinant protein in plant tissues. Pepino mosaic virus (PepMV) was chosen for this study because it accumulates highly in the host and causes mild symptoms. To enable the expression of larger foreign proteins/peptides in this vector, we engineered an N-terminal truncation mutant in the capsid protein (CP) of PepMV. Here we report the engineering of a PepMV mutant lacking the N-terminal 18 amino acids of the CP (PepMV□18), and tested its

ability to infect Nicotiana benthamiana plants. We created PepMV□18 by performing Inverse PCR on an infectious cDNA clone of PepMV using a high fidelity DNA polymerase and a pair of specific primers. The forward primer was identical to the 5' end of the CP gene but contained an 18 amino acid deletion, and the reverse primer was complementary to the sequences upstream of the CP gene. After purifying and ligating the resulting DNA fragments, we transformed the circular DNA plasmid, pPepMV□18, into Escherichia coli. Once we confirmed the deletion in the purified pPepMV□18 by PCR amplification of a small region surrounding the 5' end of the CP gene, we digested the plasmid with BamHI, which released the entire infectious cDNA of PepMV□18 from the plasmid backbone. We then used T7 RNA polymerase to make RNA transcripts from the infectious cDNA for plant inoculation experiments. Two types of N. benthamiana plants were inoculated: a wild type and a variant containing a transgenic movement protein (MP) from Red clover necrotic mosaic virus. The MP dilates the size of the plasmodesmata in the cell wall of plants which assists the movement of PepMV□18 across neighboring cells. The results of this experiment showed that the PepMV□18 mutant was more infectious and spread faster in the plants that contained the MP. The next steps of this project would be to integrate the gene of the SARS-CoV-2 spike protein into the PepMV□18 vector and determine if it can be successfully replicated in the host plant and create recombinant virus-like particles that can stimulate an immune response in humans.

Emmie Ortizo – Biochemistry #43

Research Faculty Advisor: Edward Gelmann, Medicine

NKX3.1: Multifunctional Homeodomain Protein and Prostate Tumor Suppressor

NKX3.1 is a developmental regulatory protein required for tissue differentiation. During development, NKX3.1 is expressed from the earliest stages of prostate formation. In adults, NKX3.1 controls normal differentiation and protects against oxidative damage by regulating gene expression through interactions with other transcription factors. The loss of this protein leads to carcinogenesis, and studies have provided insight to the mechanisms in which NKX3.1 loss of function linked to cancer mechanisms.

In cancer conditions, NKX3.1 protein is markedly reduced. The reduction can be attributed to mechanisms that lead to the disruption of the gene where NKX3.1 is encoded or by degradation of the protein. Down-regulation of NKX3.1 protein has significant effects on the proliferation, differentiation, and polarity of prostate epithelial cell proliferation. Furthermore, the loss of NKX3.1 increases incidence of DNA damage, which increases oncogenic risk. A proposed mechanism that leads to NKX3.1 degradation is DYRK1B phosphorylation in the serine 185 residue. A potential therapy to reduce NKX3.1 loss is the inhibition of the kinase.

Giang Pham – Biochemistry, Computer Science #51

Research Faculty Advisor: Minying Cai, Chemistry and Biochemistry

Design of novel human MC4R selective ligands

The human melanocortin 4 receptor (hMC4R) has been a focus for drug development due to its roles in appetite inhibition, blood pressure increase, and sex drive. Despite the creation of numerous hMC4R ligands, few exhibit strong binding selectivity for hMC4R over other subtypes with high potency. This is because the relationship between ligand type and hMC4R activation pattern was not well understood, leading to unexpected side effects and the failure of many potential drug candidates. To address this issue, we designed and synthesized a new class of peptides for selective hMC4R activation. One of the peptides showed excellent potency, and this peptide demonstrated both remarkable selectivity and potency for hMC4R over other MCR subtypes, which can be compared with previously known agonist MTII.

Krista Potter – Biochemistry #37

Research Faculty Advisor: Fiona McCarthy, Animal and Comparative Biomedical Sciences

Chicken Gene Nomenclature for Olfactory Receptors

Olfactory receptors (ORs) are G-protein-coupled chemoreceptors responsible for the transmission of information to sensory regions of the brain and are also known as a large and complex gene family across a variety of species. The goal of this research is to assign nomenclature to chicken OR genes and to assess how the loss or expansion of OR genes in chicken reflects the function of ORs in chicken. Potential OR genes were identified from NCBI gene annotations and each chicken gene was compared to human OR genes using the HORDE BlastP tool. Phylogenetic analyses were then conducted to approve or reject the chicken gene subgroup, subfamily, and member using human, mouse, and rat orthologs. Additionally, the human ortholog of the chicken gene's current nomenclature was included to approve or reject the subgroup, subfamily, and member. Additional BlastP searches were done to obtain human OR proteins with the greatest percent identity outside the HORDE library. Phylogenetic analyses were then completed using human proteins to approve the components of the gene nomenclature. A total of 92 chicken OR genes were provided with proposed nomenclature including a gene name and gene symbol. Of the 92 chicken OR genes, 73 genes were provided with nomenclature matching the HORDE Blast results, proving to be a reliable tool in determining human orthologs to provide chicken gene nomenclature. Gene loss and expansion were observed among the chicken OR genes when compared to the human OR genome, likely related to loss of function or conservation of proteins and evolution due to adaptation of the domesticated chicken. A notable expansion of chicken OR genes was observed among the subfamily 14, likely suggesting an expansion of an olfactory function in domesticated chicken.

Eric Primack – Biochemistry #50

Research Faculty Advisor: Michael Brown, Chemistry and Biochemistry

A Biochemical Perspective on Rhodopsin

G-protein coupled receptors (GPCRs) are an abundant protein superfamily found in a variety of cell types, making it a high-valued pharmaceutical drug target. Extensive research is necessary to provide deep understandings on the protein's interactions and functions, in efforts to provide more effective treatments to pathologies involving GPCRs. Rhodopsin is a model GPCR, found in mammalian retina rod cells, that we analyzed spectroscopically. Upon light activation and photoisomerization of the retinal cofactor from 11-cis retinal to all-trans retinal, rhodopsin conformationally transforms into a myriad of intermediate states including the metarhodopsin I (MI) and metarhodopsin II (MII) states. There is a known pH and temperature dependent equilibrium between the MI and MII states as well as an understanding that an intracellular protein pocket forms and that hydration of this pocket positively influences the MII state's stability. After purifying rhodopsin from bovine retina and utilizing UV-Vis spectroscopy, our goal was to observe the time-dependence of the MII state at various pH and to mathematically analyze the data recorded to fully understand the transformations that rhodopsin undertakes. We found that the MII state is time-dependent and the MII fraction varies with pH over time. When analyzing the data recorded, we found that the singular value decomposition method of analysis may have to be modified to prove to be a reliable method to analyze our time-dependent experiments. However, when we applied the least squares, linear regression still provided a basic analysis of the samples. We hope our work will provide insight into the specific molecular mechanisms of GPCRs to further the advancement of treatments or cures for cases involving abnormal GPCRs.

Hillary Schiff – Biochemistry, French #40

Research Faculty Advisor: Scott Boitano, Physiology

Biased proteinase-activated receptor-2 antagonists preferentially limits allergen-induced airway hyperresponsiveness and inflammation while allowing for bronchorelaxation

Biased signaling in G-protein coupled receptors (GPCRs) has emerged as a target for drug development. Protease-activated receptor-2 (PAR2) is a GPCR present in the airway epithelium with biased signaling that has been shown to trigger both detrimental effects [airway hyperresponsiveness (AHR), inflammation, mucus overproduction] and beneficial effects (bronchorelaxation) associated with allergen-induced asthma. These dual effects have been shown to be dictated by the two primary signaling pathways downstream of PAR2 activation: Gαq/Ca 2+ signaling is associated with bronchorelaxation, and β-arrestin/MAPK signaling is associated with AHR, inflammation and mucus overproduction. We have developed full (C391 which antagonizes Gαq/Ca 2+ and beta-arrestin/MAPK signaling) and biased (C781 which antagonizes beta-arrestin/MAPK signaling) antagonists of PAR2 and tested their efficacy in acute allergen-induced asthma mouse models. Full and beta-arrestin/MAPK signaling compounds attenuated AHR and inflammation in mouse models, and to a lesser extent mucus overproduction. In a human bronchial model, the full PAR2 antagonist C391 prevented PAR2-dependent bronchial relaxation while the biased PAR2 antagonist C781 did not. Antagonism by C781 and other biased PAR2 antagonists can fine tune and effectively improve safety profiles for drug development in asthma treatment.

Allison Steedman – Biochemistry #39

Research Faculty Advisor: Felicia Goodrum, Immunobiology

Human Cytomegalovirus Induced Changes in Low-Density Lipoprotein Receptor Expression and Trafficking

Human Cytomegalovirus (HCMV) is a beta-herpesvirus that establishes latent infections in humans, reactivating and causing disease in those who are immunocompromised. It has a broad tropism allowing it to infect a wide variety of cells, and can manipulate a variety of pathways to establish a successful infection. In unpublished data collected by the Goodrum lab, low-density lipoprotein receptor (LDLR) was found to be strongly downregulated in HCMV infection in fibroblasts. LDLR is a cell surface receptor responsible for the uptake of cholesterol-rich ligands. Through the use of immunoblotting, immunofluorescence, and the creation of a CRISPR LDLR KO, we aimed to gain more insight into how LDLR is trafficked in a latent versus replicative state among a variety of different cells types. In a cell type mimicking latency, THP-1 monocytes, there was very little change in LDLR between mock and WT infected cells. However, in a replicative infection, mature LDLR (mLDLR) is driven to the lysosome for degradation, and immature iLDLR (iLDLR) accumulates in the ER and is targeted for ERAD. A knockdown of LDLR increases the cleavage of SREBP, a transcription factor for lipogenic proteins. This may indicate that downregulating LDLR helps the virus increase levels of proteins related to lipogenesis, providing a potential reason for the virus to degrade and block the formation of LDLR. Future experiments are needed to further understand the workings of the mechanism, and the implications and consequences of HCMV manipulating ERAD to degrade host proteins.

Megan Teramoto – Biochemistry #24

Research Faculty Advisor: Nancy Horton, Chemistry and Biochemistry

A preliminary investigation of the interaction between Human Parvovirus B19's NS1 protein and various human proteins

Human Parvovirus B19 (B19V) is a small, non-enveloped DNA virus with significant clinical manifestations. While best known for causing Erythema Infectiosum, a mild affliction common in children called Fifth's Disease, this virus is potentially devastating for those with pre-existing conditions like sickle-cell anemia or

acquired immunodeficiency syndrome (AIDS) and those who are pregnant, among others. Interestingly, B19V has also been implicated in the onset of several autoimmune diseases. Non-structural protein 1 (NS1) is one of the few proteins encoded by B19V's small genome, and it is known to have a variety of diverse activities including helicase, nuclease, and transactivation activities. While some aspects of NS1 have been studied more extensively, little is known about the C-terminus domain of the protein, which is thought to be responsible for the transactivation activities of the protein. The transactivation role of NS1 is explored further here, as a variety of pull-down assays were optimized and conducted in efforts to show direct binding interaction between NS1 and human proteins including Specificity Protein 1 (Sp1), GTPase-activating protein-binding protein 1 (G3BP1), and Ring Finger protein 2 (RNF2). Preliminary results suggest possible binding between NS1 and RNF2, while no binding is observed between NS1 and Sp1, in contrast to previous findings in the literature. The interaction between NS1 and human proteins has the potential to elucidate the pathways and mechanisms through which B19V, and NS1 specifically, is able to trigger autoimmune disease and this research furthermore opens the possibility of addressing some of the serious physiologic effects of the virus.

Grace Thatigiri – Biochemistry #36

Research Faculty Advisor: Purnima Madhivanan, Public Health

Family adaptation to COVID-19 stressors on the US-Mexico Border

The COVID-19 pandemic has impacted Latinos in the United States, both personally and in terms of their loved ones. The urban underprivileged and minority communities with little access to healthcare have been most adversely impacted by the virus. Nearly half of Latino Americans say that the coronavirus poses a hazard to daily living, and 1 in 4 say that the COVID-19 has significantly harmed their mental health. The COVID-19 pandemic's effects on recent Mexican immigrants to the United States and their mental health are not well understood. The goal of this study is to better comprehend the various coping strategies and viewpoints held by the Hispanic communities in Arizona regarding the virus and COVID-19. There are numerous factors that cause stress in a border community's households. the following paper examined the relationship between a person's place of birth and their willingness to
receive the COVID vaccine.

Methods: Data was gathered using tablets to administer in-person surveys in English and Spanish. The information was gathered at several public and cultural events with a Hispanic population in Tucson, Arizona. The poll participants have to be Hispanic adults over the age of 18 and be able to sign an informed consent form. The data was analyzed using McCubbin and Patterson's ABCX Model.

Results: The data shows that the Hispanic population born in the USA is 1.94 times more likely to receive the vaccination than the population born in Mexico. The p-value of USA-born Hispanics is 0.019 in reference to the Mexican-born population. This demonstrates that there is a significant correlation between the place of birth and vaccine willingness. Most of the participants had received vaccinations and believed the shot to be safe.

Hayley Wondra – Biochemistry #34

Research Faculty Advisor: Kirsten Limesand, Nutritional Science

Targeted Yap Disruption in Aquaporphin Cells

Head and neck cancers are unfortunately common today, alongside detrimental side effects that diminish one's quality of life. Radiation, a popular treatment method, damages salivary glands, making the Aquaporphin cells located there unable to make saliva. Hypo-function of salivary glands can result in cavities, sores, infections, and increased risk of certain diseases and malnutrition. Previous research demonstrated that loss of salivary function is associated with decreased apical polarity and increased localization of transcriptional co-activator Yap. Yap levels have been the highest in irradiated salivary gland tissues that are

unable to revive normal function. Contrastly, Yap is needed for the regeneration of tissues–employing a delicate balance of Yap needed for homeostasis. Centralizing on acinar cell populations, Aqp5 is responsible for constructing proteins that contribute to amylase manufacture. A modification takes place in the specific mouse model utilized, where Cre recombinase cuts the Yap gene at specific LoxP sites in these acinar cells with the Aqp5 promotor. We found that it was significantly crucial in day 30 female mice, that Cre is absent alongside the injection of IGF1 in order to restore normal salivary flow rates after radiation. In comparison with day 30 males, IGF1 was able to restore salivary flow rates whether Yap was deleted by Cre or not. There was approximately a 20 percent positive amylase area increase with day 30 after radiation and insulin growth factor administration in comparison to irradiated tissues alone. These results suggest that Yap activity is responsible for radiation-induced loss of amylase, loss of normal polarity, compensatory proliferation in the acinar department, and the working ability of IGF1. Understanding the full magnitude of disruption of Yap in cells provides a new systematic understanding of the regulation of radiation-induced hyposalivation.

RESEARCH PRESENTATIONS

Janelle Amegatse – Chemistry #3

Research Faculty Advisor: Thomas Gianetti, Chemistry and Biochemistry

Stable Carbocation Helicenium Dimer and Trimers

Organic molecules possessing multiple positively charged centers have a variety of applications, including their ability to catalyze the reduction of oxygen without the presence of a metal. Furthermore, as they can be reduced to a neutral radical, they present a variety of oxidation states allowing them to serve as organic redox active molecules for symmetrical all-organic redox flow batteries. Here in we report the synthesis of two notably stable carbocation helicenes with two and three centers of positive charge, our novel dimer and trimer respectively.

Olivia Bertuca – Biochemistry #11

Research Faculty Advisor: Ravishankar Palanivelu, Plant Sciences

Screening for Thermotolerance in Wild Tomato Plant Accessions

Climate change diminishes crop yield by inhibiting pollen tube germination, transport of sperm to the ovary, and development of seeds and fruits. This then endangers global food security by limiting supply of foods that are the product of plant reproduction. This project studies this critical process using Solanum lycopersicum tomato plants. Some accessions, or varieties, of tomatoes produce similar fruits under extreme heat as those in ideal temperatures. To identify thermotolerant tomato accessions, this project involves screening wild accessions of tomato by measuring the fruit weight and seed yield of plants pollinated in 25 degrees Celsius vs. 37 degrees Celsius. To date, 38 accessions have been screened and 5 produced fruits at both conditions. The relative fruit weight and seed yield were calculated for each accession to evaluate control and experimental fruits. Accessions CW0027 and CW0110 had a larger experimental fruit than control fruit, which points to possible thermotolerance. Future work includes screening the remaining accessions, performing additional screens of high-performing accessions, and developing new assays to examine pollen grain viability at 25 degrees Celsius vs. 37 degrees Celsius. One such assay involves comparing levels of reactive oxygen species (ROS) of pollen grains stained and incubated at control and experimental temperatures. Excessively high or low ROS levels indicate inviable pollen and can help identify the thermotolerant accessions in addition to the fruiting experiment. Screening for thermotolerant varieties of tomato will help combat climate change-induced food insecurity.

Katelyn Boone – Biochemistry #16

Research Faculty Advisor: Kaveh Laksari, Biomedical Engineering

Characterizing the Kinematics of a Rotational Impactor to Study Traumatic Brain Injury in Small Animals

Traumatic brain injury (TBI) is a public health concern with 1.3 to 3 million cases reported annually in the United States. Generally, the dominant injury mechanism for most TBIs, especially mild and moderate variations, rotational motion of the head. However, the current devices used to replicate TBI in animal models mostly rely on direct hit to restrained exposed brain, or involve hitting the brain using an impactor with little control over the rotational motion of the head after impact. In our current study, we investigated a that motion of the head. The animal head is fixed to a cradle. Released air pressure shoots a slug in a restrained pipe to hit the bottom of the cradle from the side, turning it around approximately the center of the animal's head. The parameters we can modulate to affect the kinematics of the head motion are the pressure behind the slug and the placement of the slug inside the pipe. The rotation impactor will eventually be used to induce TBIs on animal models to study traumatic brain injury. The first set of data was created by varying pressures while keeping the slug at a neutral point. The second set of data was collected by varying the position of the slug inside the pipe while keeping the pressure at 30 psi. Three trials for each pressure and slug placement were completed. Each trial was filmed using a high-speed camera to capture when the impactor starts and ends the movement, the camera was set to a resolution of 336x240 pixels and 15941 frames/second. On the front of the impactor (where the animal's head would go) two markers were placed. By using a marker tracking script in MATLAB, the angle of the line passing through these markers, and subsequently rotational velocity, and acceleration of the cradle were calculated. Kinematic graphs of angle, rotational velocity, and rotational acceleration were created and analyzed. , corresponding to the moment the slug hits the cradle. The change in angle over time was then calculated by taking the slope of the Angle v Time graph from the minimum angle to the max angle. These values were averaged within their groups. From these slopes, the 30 psi pressure and 1 inch slug placement developed the greatest angle change. The next steps for this project include quantifying peak instantaneous velocity and acceleration to assess if those are high enough to induce TBI in small animals.

Yoneri Bueno-Diaz – Biochemistry #10

Research Faculty Advisor: Walter Betancourt, Environmental Science

Water Treatment and Filtration Methods

I am working in Dr. Betancourt's lab at the WEST center, focusing on methods to evaluate the removal of viral indicators (i.e., bacteriophages) by an advanced treatment process (ultrafiltration-reverse osmosis) for safe and sustainable water reuse applications. This is done through various lab techniques such as ultrafiltration-reverse osmosis, filtration, elution, bacteriophage assays, etc. The experiment is ongoing but so far the results are that the combined integrated membrane system (ultrafiltration-reverse osmosis) was capable of removing on average from 89% to 94% of coliphages.

Caroline Coppinger – Biochemistry #12

Research Faculty Advisor: Zhongguo Xiong, Plant Sciences

Efficiency of Self-Cleavage 2A Peptides in Fusion Proteins Expressed in a Plant Virus Vector

The self-cleavage 2A peptides from picornaviruses consist of 18-22 amino acids that can mediate expression of multiple proteins from a single open reading frame in eukaryotes. These peptides offer options to regulate the ratios between fusion proteins and cleaved proteins because of their variable cleavage efficiencies. However, there have been conflicting reports on their cleavage efficiency and side-by-side comparisons have been lacking in plant models. In developing a plant viral expression vector to display foreign proteins on the surface

of viral nanoparticles, we chose 2A peptides to regulate the ratio of fusion and free proteins. We tested 2A peptides from 4 picornaviruses: Equine rhinitis A virus (E2A), Foot-and-mouth disease virus (F2A), Porcine teschovirus-1 (P2A), and Thosea asigna virus (T2A). The 2A peptides link GFP to the N-terminus of the capsid protein (CP) of Pepino mosaic virus (PepMV), a single-stranded RNA virus with a 6.4 kb genome. PepMV particles are flexuous rods of 508 by 13 nm, made of 1290 copies of a single species of 24 kDa protein. To facilitate convenient in-frame insertion of foreign genes and 2A peptides at the N-terminus of the PepMV CP, three unique restriction sites were engineered immediately after its AUG initiation codon in the PepMV infectious cDNA clone. In various GFP-2A-CP fusion constructs made subsequently, the recombinant viruses were able to initiate infection, spread from cell to cell, and translocate long distance in Nicotiana benthamiana. The only exception was pPVF-GFP, which used F2A to mediate fusion protein expression and had impaired movement from inoculated to systemic leaves. Western blotting analysis showed variable efficiency of fusion protein cleavage, but all at levels much lower than those reported in human and animal cells. The fusion protein in pPVF-GFP was barely cleaved (<5% cleavage), explaining the inability of this recombinant virus to move systemically without the help of a movement protein. The PepMV CP is a multifunctional protein that is involved in the encapsidation of the viral genome, cell-to-cell movement, long distance movement, and suppression of RNAi. A high percentage of uncleaved GFP-2A-CP fusion protein would have a deleterious effect on the infectivity of the recombinant virus.

Anthony DiGirolamo – Chemistry #1

Research Faculty Advisor: Dennis Lichtenberger, Chemistry and Biochemistry

Novel [2Fe-2S] Metallopolymer Active Site Platforms for Electrocatalytic Production of H2 from Water

The electrocatalytic generation of H2 gas as an energy storage vector is relevant to advancements in renewable energy technology. We have previously studied both aryl and alkyl bridged [2Fe-2S] metallopolymer catalysts which have rates of >10^5 per second per site. Recently we have begun to synthesize and characterize "open" type [2Fe-2S] active sites where the thiolate ligands are not bridged by the functional groups connected to them. Using electrochemical techniques such as cyclic voltammetry, we aim to understand how these "open" system catalysts compare to previous generation catalysts in hopes that the differing geometry of the active site will result in either lower overpotentials, or higher catalytic currents.

Luke Fasse – Chemistry #4

Research Faculty Advisor: Thomas Gianetti, Chemistry and Biochemistry

Stable Carbocation Helicenium Dimer and Trimers

Organic molecules possessing multiple positively charged centers have a variety of applications, including their ability to catalyze the reduction of oxygen without the presence of a metal. Furthermore, as they can be reduced to a neutral radical, they present a variety of oxidation states allowing them to serve as organic redox active molecules for symmetrical all-organic redox flow batteries. Here in we report the synthesis of two notably stable carbocation helicenes with two and three centers of positive charge, our novel dimer and trimer respectively.

Jacob Fredman – Biochemistry #5

Research Faculty Advisor: Robin Polt, Chemistry and Biochemistry

Synthetic Methods and Optimizations of Serine Glycosides for Use in PACAP Drug Analogues

Utilizing minimally competent Lewis acids (MCLA's) A selective reaction is able to be developed for **β**-Glycosylation of Serine Glucosides and Serine Lactosides. These Serine Glycosides will be utilized as the

starting material for PACAP synthesis. The MCLA catalyzed reactions require further fine tuning to allow for better yields and lower costs for purification.

Madison Grams – Biochemistry #6

Research Faculty Advisor: Elisa Tomat, Chemistry and Biochemistry

Reactivity and uptake of an iron prochelator in the presence of N-acetylcysteine in cancer cells

Iron is an essential nutrient in cellular metabolism and for this reason cancer cells often upregulate iron import and storage proteins to meet their increased metabolic needs. Because of its redox chemistry, iron can also be toxic to cells, which therefore carefully handle its storage to avoid the generation of reactive oxygen species (ROS). Given the importance of iron in cell proliferation, several iron chelators have been shown to be effective antiproliferative agents, with many compounds undergoing clinical trials. Prochelators, which only bind to iron after undergoing intracellular activation, are investigated in strategies for targeting intracellular iron in cancer cells. Though iron deprivation alone is toxic to cells, chelation can either accelerate or diminish ROS production via Fenton-type chemistry. PH4 is a disulfide-based iron prochelator found to generate ROS when bound to iron both in vitro and intracellularly. MDA-MB-231 breast cancer cells treated with antioxidant N-acetylcysteine (NAC) and prochelator PH4 showed enhanced toxicity rather than cell rescue as would be expected. Seeking to understand the mechanism of increased toxicity, the redox state of the cell was investigated using a fluorescent probe to detect ROS. In this assay, the presence of NAC decreased the amount of ROS, suggesting that oxidative damage is not what makes the treatment more toxic. UV-visible absorption and mass spectrometry data indicate that NAC is reacting with PH4 to form a bioconjugate that facilitates uptake. An iron-binding fluorescent probe was then used to estimate the relative amount of PH4 taken up by cells in the presence or absence of NAC. The conjugate was then synthesized and isolated to assess its antiproliferative activity and verify that it is the active species in solution.

Aunita Hakimi – Bioinformatics #17

Research Faculty Advisor: Ross Buchan, Molecular and Cellular Biology

Investigating the role of stress granules in the cell cycle and DNA damage response

Stress granules (SGs) are cytoplasmic assemblies of non-translating messenger ribonucleoprotein complexes (mRNPs) that form in response to numerous stresses. It is unknown what functions SGs play in cells, but recent affinity purification and proximity labeling experiments assessing SG composition suggest that SGs may regulate many processes in cells, including the cell cycle and DNA damage response (DDR). The long-term objective of our research is to reveal whether and how SGs regulate the cell cycle and DDR. Prior lab data using a human cell culture model revealed that a SG-assembly mutant (G3BP1/2ΔΔ) displayed abnormal cell cycle phenotypes, with a small percentage of them failing to arrest following an S-phase block. Furthermore, following release from an S-phase block, G3BP1/2ΔΔ mutants exhibited more DNA damage, which indicates they may be more prone to DNA damage and/or have defects in DNA repair. In this project, we will comprehensively assess the role of SG assembly on cell cycle regulation and the DDR by utilizing various SG inhibitory drugs, other known SG assembly mutants and SG inducing stimuli, in combination with cell cycle and DNA damage assays. By analyzing the consistency of cell cycle or DDR phenotypes amongst SG inhibited (or induced) cells, we will determine if SG assembly per se, or protein/inhibitor specific effects underpin observed cell cycle/DDR phenotypes. Future research will look at whether SG-inhibited cells fail to arrest at other cell cycle checkpoints and whether distinct subsets of cell cycle and DDR proteins accumulate in SGs triggered by various types of stress. Targeted disruption of cell cycle/DDR protein localization in SGs will also be explored. Understanding how SGs regulate the cell cycle and DDR could lead to novel therapeutic approaches for diseases such as ALS and cancer, the pathology of which is linked to aberrant SG formation and/or persistence.

Veronica Hode – Biochemistry #14

Research Faculty Advisor: Edita Navratilova, Pharmacology

Exploring the Role of Prolactin in Endometriosis-Associated Pain

Endometriosis is a gynecological condition characterized by chronic pelvic pain and infertility. Endometriosis affects women in the 25-40 age range and occurs when the tissue lining of the uterus, the endometrium, grows outside the uterus, usually on or around the organs in the pelvis or abdomen. Endometriosis can cause excessively painful and heavy periods, pain during intercourse, and abdominal pain. Though underlying mechanisms of endometriosis have not been elucidated, clinical evidence suggests the involvement of prolactin, a neurohormone associated with female reproductive functions, pregnancy, and lactation. Preclinical studies in mice also showed that increased prolactin levels might promote or trigger pain development in females. Hence, we hypothesize that prolactin may play an important role in endometriosis-associated pain. To understand the linkage of prolactin to endometriosis, we induced an endometriosis model in mice by implanting a donor's uterus fragments into recipient mice. Implanted mice developed increased mechanical sensitivity in the abdominal region, indicative of pain. We used immunohistochemistry to confirm the presence of endometriosis lesions, and ELISA analysis to measure serum prolactin levels. Our results showed that endometriosis lesions in mice had histological characteristics similar to human endometriosis tissue. Levels of serum prolactin in the endometriosis model were found to be higher in comparison to the naive group. Moreover, levels of prolactin within the endometriosis lesions were significantly higher than in the uterus. These results suggest a probable association between prolactin levels and endometriosis-associated pain.

Clare Hotze – Biochemistry #18

Research Faculty Advisor: Thomas Tomasiak, Chemistry and Biochemistry

Investigating the substrate recognition of the human L-cystine/L-glutamate antiporter, xCT

Solute carrier (SLC) transporters are a superfamily of secondary carriers that play important roles in maintaining a constant balance of nutrients and toxins within the cell by regulating molecular flux across the cell membrane. One of the members of the SLC family, the system xc- transporter (xCT), is a heterodimer of the L-cystine/L-glutamate antiporter, SLC7A11, and the trafficking chaperone, SLC3A2 (or CD98). xCT supports redox homeostasis by importing L-cystine that will be used in the production of glutathione (GSH), the most abundant intracellular antioxidant, to neutralize cellular reactive oxidative species (ROS). In a disease state like cancer, xCT is overexpressed to combat the buildup of oxidative stress from upregulated metabolic activity. In addition to L-cystine and the GSH pathway, the kynurenine pathway is another method by which the cell utilizes to combat ROS buildup. Recently, L-kynurenine has been shown to be a substrate of xCT that when imported into cell, its metabolites serve as ROS scavengers to provide a secondary form of oxidative stress protection. However, the molecular mechanism by which xCT recognizes and transports L-kynurenine, a secondary substrate, remains unknown. As such, my research focuses on elucidating the molecular basis of secondary substrate recognition and transport in xCT to provide molecular insights that can further chemotherapy development. Given the substrate similarity between L-kynurenine and xCT native substrates, I hypothesized that Arg135, Arg396, and Tyr244 are responsible for recognizing L-kynurenine in the substrate binding pocket. To test my hypothesis, I mutated these residues to alanine and conducted cellular transport assays to determine if these residues are essential for transport function.

Isaac Kailat – Biochemistry #7

Research Faculty Advisor: Michael Taylor, Chemistry and Biochemistry

Design of pH-sensing pyridinium probe

The goal of this project is to synthesize a pH-sensitive pyridinium probe. The probe's initial design is guided by the research group's existing successes with modifying pyridinium salts for bioconjugate chemistry as well as by adding inductive substituents to improve the pH recognition of the probe. A four-step synthesis is proposed to design the baseline pH-sensitive pyridinium probe. The synthesis involves the Grignard reaction, a modified Baeyer pyridine synthesis, and deprotection of the aryl ether. The results of each step of the reaction are characterized through mass spectrometry and nuclear magnetic resonance spectrometry.

Benjamin Koppe – Chemistry, Computer Science #9

Research Faculty Advisor: Veaceslav Coropceanu, Chemistry and Biochemistry

Vibronic Theory of Stark Effect in Donor-Acceptor Systems

In organic solar cells, the charge- transfer (CT) electronic states that form at the interface between the electron-donor (D) and electron-acceptor (A) materials have a crucial role in exciton- dissociation, charge-separation and charge- recombination processes. CT absorption and emission spectra can provide information about electronic coupling, electron-vibrational coupling and driving force, i.e., microscopic parameters that describe the electron-transfer processes. Additional information can be derived from electro-absorption (Stark effect) data. For instance, in comparison to simple CT absorption, electro-absorption can provide an estimate of the electron-transfer distance. In this work we developed a vibronic model for electro-absorption and applied this model to describe the Stark effect on the CT absorption in model D/A interfaces. The results of the vibronic model simulations are compared with those obtained in the framework of the mixed quantum-semiclassical Marcus–Levich–Jortner model.

Ronald Palmenberg – Biochemistry #8

Research Faculty Advisor: Michael Taylor, Chemistry and Biochemistry

Synthesis of Quinolinium Probes for Bioconjugation Applications

Protein conjugation can have significant impact in scientific fields, including biomaterials, synthetic biologics, cellular imaging, and chemical mapping. Functionalizing protein molecules can have its challenges but creating a probe that is highly reactive and selective can push these fields forward. Photochemistry can be used to increase the selectivity of probes by opening up the aromatic residues, which have much lower abundance than other amino acids. The poster focuses on the work put in towards making a methoxy-substituted quinolinium probe to conjugate proteins.

Briana Pomales – Chemistry #2

Research Faculty Advisor: Dennis Lichtenberger, Chemistry and Biochemistry

The Modification of Modern Electrolysis Cells to Catalyze Hydrogen and Characterize Metallopolymers

It is becoming necessary to align energy needs with climate goals as fossil fuels account for the majority of the carbon dioxide emissions. The electrolytic production of hydrogen offers the potential to replace current fuel sources with a cleaner and high-density energy source without carbon dioxide emission as hydrogen can be produced from renewable energy, like wind and solar. Current hydrogen production through flow cells and electrolysis uses extreme conditions in acidic or alkaline solutions and when these systems are scaled to match energy needs, it introduces a hazardous workplace and area. Another issue is that platinum is currently the

standard for use in electrolysis cells because it efficiently produces hydrogen, but platinum is a scarce element thus, expensive. To produce hydrogen through electrolysis a cheaper catalyst with comparable performance to platinum is desired. Our metallopolymer catalysts combine metals with a polymer framework and have proven to be effective hydrogen catalysts and have multiple benefits, such as the ability to function at neutral pH, the use of earth-abundant elements and its comparability to platinum on a small scale. To better understand how metallopolymers perform over longer periods, we designed a flow cell to determine a turnover number for catalysis and to study the metallopolymers for a larger set-up. Our flow cell allows for the metallopolymer to be activated while isolated from the anode side, preventing the deactivation of the active site from oxidative interactions. Currently, the flow cell design has shown the metallopolymer is comparable to platinum at pH 7 and retains consistent activity longer than platinum.

Caleb Seekins – Biochemistry #15

Research Faculty Advisor: John Streicher, Pharmacology

Intermittent Fasting Boosts Opioid Antinociception by Enhancing SRC Kinase Signaling in the Spinal Cords of Male Mice

The use of opioids in the treatment of pain is widespread but comes with many drawbacks, including side effects like tolerance and addiction. Our previous research indicates that intermittent fasting (IF) can increase the efficacy of pain relief in morphine treatment while decreasing side effects like reward and tolerance. This pain relief was observed in male and female CD-1 mice that were subjected to 7 days of IF, with daily 18-hour periods of fasting, followed by 6-hour periods of feasting on standard chow. Our current research is aimed at characterizing the molecular pathways behind this phenomenon. We thus performed a proteomic study in the spinal cords of IF mice, which implicated the SRC kinase pathway as a possible modulator of pain relief. Following this, mice were subjected to the standard IF protocol then treated them with the SRC kinase inhibitor Src-1I (10 nmol, intrathecal injection) or Vehicle, followed by morphine (3.2 mg/kg subcutaneous injection), and were assessed for anti-nociception using the tail flick assay. The previously seen IF-induced increase in antinociception was eliminated by SRC inhibition in male mice though this effect was not observed in females. Further, mice having undergone the IF regimen and treated with the strong μ-opioid agonist DAMGO (10 nmol, intrathecal injection) displayed an increase in phosphorylated SRC in the dorsal horn of the spinal cord that was substantially higher in male mice than female. Despite this, Western Blotting on the spinal cords of mice having undergone the IF regimen and treated with DAMGO (10 nmol, intrathecal injection) showed an increase in phosphorylated SRC/total SRC in fasted mice that did not vary between the sexes. Combined, these results suggest that while fasting increases SRC phosphorylation in both male and female mice, the localized increase in SRC activation found in the dorsal horn of the spinal cord enhances morphine pain relief in male mice solely. Further discoveries in this mechanism could result in the development of improved pain management therapies, as well as uncover novel molecular circuits that link diet to opioid pain relief.

Emma Slenkovich – Biochemistry, Spanish Linguistics #13

Research Faculty Advisor: Aneta Kielar, Speech, Language and Hearing Science

The methods, neuromechanism, and applications of tDCS in treatment for neurological disorders

Transcranial direct current stimulation (tDCS) is a neuromodulation technique used to enhance neurorehabilitation. A weak current is applied via two electrodes of opposite polarity placed on the scalp. tDCS instantaneously modulates neuronal excitability and when used in multiple sessions has shown to strengthen synaptic connections to promote relearning. Past research has shown positive results when pairing tDCS to targeted behavioral tasks during rehabilitation treatment for neurological disorders. We evaluated the efficacy of tDCS as an adjuvant treatment to language therapy targeting the Logopenic variant of Primary Progressive Aphasia (lvPPA), a language disorder that affects phonological skills and can lead to deficits in written language skills. The treatment coupled phonological manipulation tasks to stimulatory anodal tDCS targeting the left inferior frontal gyrus of a 71-year-old woman in the early stages of lvPPA. The participant showed robust improvements in written performance that were maintained for several months after completing treatment (Nickels et al., 2023). This presents strong evidence of the efficacy of pairing tDCS with behavioral intervention and prompts further exploration of the use of tDCS in treatment of other PPA variants and other neurological disorders.

Nickels, K., Beeson, P. M., Rising, K., Jebahi, F., & Kielar, A. (2023). Positive changes to written language following phonological treatment in logopenic variant primary progressive aphasia: Case report. Frontiers in Human Neuroscience.