Chemistry & Biochemistry Poster Fair Presenters Abstracts

Monday April 24, 2023
1:00 – 3:30
UArizona Bear Down Gym

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2024 CBC Senior Thesis/Capstone Presentations

Neel Ahmed – Biochemistry and Molecular Cellular Biology #25

Research Faculty Advisor: Nancy Horton, Molecular & Cellular Biology

Studying the functional roles of 7.5 kDa, 9 kDa, and 11 kDa proteins and the helicase activity of the NS1 protein from the human parvovirus B19.

Human Parvovirus B19 (B19V) is responsible for both benign and severe diseases in humans. Herein I describe several biochemical and biophysical investigations of the main replicative protein NS1 from B19V, as well as its three small proteins with unknown function and predicted to be intrinsically disordered (7.5, 9, and 11). The investigations characterize the native molecular weights of the small B19V proteins, their RNA binding activity, and DNA helicase activity of NS1. Methods include analytical ultracentrifugation, mass photometry, timed kinetic assays, and gel shift assays. An interesting oligomerization of the 11 protein was discovered which involved disulfide bonds which are particularly difficult to reduce. The helicase assay will be used to test point mutations identified by our collaborator to disrupt NS1 oligomerization and nuclear targeting. These studies further our understanding of B19V biology and inspire new approaches to treat the various diseases caused by B19V infection.

Tressa Baker – Biochemistry #34

Research Faculty Advisor: Arun Dhar, Animal & Comparative Biomedical Sciences

The Efficacy of RNAi Gene Silencing of VP28 in WSSV Exposed P. vannamei Shrimp

White spot disease (WSD) is an increasing epidemic that is impacting shrimp farms internationally and in turn hurting economies. WSD is caused by the white spot syndrome virus (WSSV), a systemic double stranded DNA virus. In order to combat the spread of WSSV, it is necessary to develop an efficient and affordable way to build up immunity in shrimp to WSSV. RNA interference (RNAi)-based therapeutics have been successful in laboratory settings using a reversed engineered Macrobrachium rosenbergii nodavirus (MrNV) viral vector in Penaeus vannamei shrimp. Building off of the success of engineered MrNV viral vectors, we created a similar MrNV viral vector for this study. The RNA-dependent RNA polymerase (RdRp) gene naturally found in MrNV was replaced with protein-coding genes for green fluorescent protein (GFP) and for the structural viral protein 28 (VP28) of WSSV. The VP28 gene was made to produce a loop-hairpin dsRNA of VP28 (lhVP28) when transcribed. We synthesized and analyzed the effectiveness of a MrNV-GFP-lhVP28 viral vector in silencing the VP28 gene in WSSV. Our data shows that the viral vector, MrNV-GFP-lhVP28, when injected intramuscularly into P. vannamei shrimp successfully triggers an RNAi response and expression of the lhVP28 within myocytes that in turn protected theses shrimps from developing WSD when exposed to WSSV. The University of Arizona's Aquaculture Pathology Laboratory's overall objective, of which this thesis is a part of, is to develop shrimp feed capable of stimulating a RNAi response in shrimp after consumption to inhibit WSSV infection and ultimately prevent WSD from spreading. Prior to developing feed, the viral vector must be developed and thoroughly tested for its effectiveness beforehand. This is only a continued steppingstone in the development of shrimp feed capable of delivering antiviral therapeutics against WSD that can be mass produced and distributed. All the same, the data is a promising progression to this goal.

Olivia Bertuca – Biochemistry #42

Research Faculty Advisor: Judith Brown, Plant Sciences

Gene knockdown and Mortality in Potato Psyllid by RNA Interference Toward Biopesticide Development

'Candidatus' Liberibacter solanacearum (Liefting) is a bacterial plant pathogen that causes yield-limiting diseases of potato, tomato, and other solanaceous crops, transmitted by the potato psyllid Bactericera cockerelli (Sulc). Pesticides used for controlling the psyllid vector to reduce pathogen spread are costly and environmentally unsustainable, so the potential for RNA interference (RNAi) biopesticides are under investigation as an alternative management approach. RNAi is a cellular mechanism that surveys for the cellular presence of double-stranded RNA and downregulates expression of the corresponding mRNA. Exogenous dsRNA introduced to a host cell can silence gene expression by cleaving the mRNA. Double-stranded DNA biopesticides are specific to the gene and organism targeted, minimizing harm to other organisms, unlike most other synthetic pesticides. Here, experiments were conducted to knock down the expression of V-ATPase subunits D and E, and inhibitor of apoptosis 5 (IAPP5) genes, known to regulate cell metabolism, homeostasis and apoptosis. Because these genes are involved in multiple metabolic pathways, silencing of these genes is hypothesized to cause mortality in the potato psyllid. Replicated mortality bioassay experiments were conducted in which dsRNA was presented to psyllids in a 20% sucrose solution for a 48-hour ingestion-access period (IAP). Approximately 120 3rd-instar nymphs were evaluated, per gene target, along with the water and luciferase non-target, negative control treatments. Mortality was monitored for 9 days, post-IAP. Total RNA was isolated from surviving 5th-instar psyllids. Gene knockdown was quantified by real-time reverse transcriptase polymerase chain reaction. Mortality was greatest when all three genes were targeted simultaneously, compared to lower mortality which resulted from knockdown of single gene targets. Gene expression analysis showed no statistically significant effect on gene expression post-treatment.

Yoneri Bueno-Diaz – Biochemistry #39

Research Faculty Advisor: Luisa Ikner, Environmental Sciences

Adenovirus Wastewater Treatment Analysis with qPCR Methods

Through the usage of qPCR methods, various samples of wastewater were analyzed to determine the amplification and effect of cell cultures on lysates. This was done through building a standard curve and using quantitative qPCR methods.

Lara Burhans – Biochemistry #14

Research Faculty Advisor: Minying Cai, Chemistry & Biochemistry

Molecular binding between opioid receptor subtypes and 9 newly developed synthetic opioids

Opioids are a class of natural or synthetic drugs used primarily for pain relief and sedation. They act on opioid receptors (ORs), a class of G protein-coupled receptors (GPCRs), through a signaling pathway initiated by G proteins. Once the G protein is activated, it causes a downstream signaling cascade, resulting in differing effects on the body. Desensitization can happen when a membrane-bound protein is exposed to an agonist for an extended period of time and the receptor is endocytosed to regulate the downstream effects on the cell. This is the same mechanism by which insulin dependency and addiction to substances, including opioids, occurs. ORs can be desensitized and endocytosed when a signaling protein, B-arrestin, allosterically binds to the GPCR and negatively inhibits G-protein signaling. In ORs, this process can lead to addictive and life-threatening side effects that vary greatly from the intended uses of the drug (Mafi et al., 2020).

Dr. Minying Cai, from the University of Arizona, developed a series of 9 synthetic opioids with varying molecular structures. In this study, three classes of ORs were extracted from the bilipid membrane via centrifugation. The concentration of each protein was determined by Pierce BCA Protein Assay. Lastly, an aliquot of Kappa-OR,

Delta-OR, and Mu-OR membrane-bound protein samples were each placed on the surface of a poly-lysine coated prism and subjected to plasmon waveguide resonance (PWR) spectroscopy. The intention of this study was to determine the strength of the intermolecular interactions between each receptor subtype and all 9 compounds. This lays the foundation for further studies on the activation and initiation of B-arrestin upon C1-9 binding.

Julio Camacho – Biochemistry #28

Research Faculty Advisor: David Margolis, College of Medicine, Orthopedic Surgery Department of Surgery

Osseosurface electronics for evaluation of fracture healing.

Long bone segmental fractures, typically resulting from traumatic injuries or cancer resections, currently don't have optimal treatments. Recent studies are focusing on the use of 3D printed scaffolds seeded with adipose-derived stem cells (ASCs) supported by metal rods to promote bone regeneration. This study aims to advance bone regeneration techniques through the development of Osseosurface Electronics, sensors designed to adhere to bone surfaces and measure bone strain, providing insights into the healing process and potentially predicting healing outcomes. The study employs a controlled experiment involving six rats, divided into control and experimental groups, to monitor bone healing and pain through new sensor technology and traditional pain assessment methods. The results are pending, but this technology promises a novel way to gauge the effectiveness of bone healing strategies and pain management in segmental bone injuries.

Alejandra Carreon Torres #4

Research Faculty Advisor: Bernardo Lemos, Pharmaceutical Sciences

The impact of heavy metals: arsenic, chromium, and cadmium exposure on Beas-2b nucleolus fragmentation

The long-term exposure to heavy metals is known to cause serious problems such as cancer and genomic instability by damaging the DNA and the DNA repair homeostasis. Acute exposure to hexavalent chromium is known to increase ribosomal DNA (rDNA) copy number and also increase nucleolar fragmentation. The increased rDNA copy number observed from acute exposure contrasts what is observed from occupationally exposed human subjects who show a reduced rDNA copy number. We investigated the relationship between heavy metal exposure and ribosomal DNA regulation in human cells, focusing on the changes from more chronic exposure and what sensitization chronic exposure has to acute response to hexavalent chromium. Human lung epithelial cells (BEAS-2B) were chronically exposed to low concentrations of As, Cd, and Cr for one month. After establishing a chronic exposure to these metals we observed their response to acute 1.25 uM hexavalent chromium. We observed that chronic exposure to arsenic caused an increase in the nucleolar fragmentation. We also observed that for our passage-matched controls, the response to acute chromium exposure was predominantly an increase in the number of cells with 2 or 3 nucleolus foci. The response to acute chromium exposure for chronically exposed Cr and Cd are less distinct and further replicates are needed to observe the effect.

Jackie Choi – Biochemistry #15

Research Faculty Advisor: Oliver Monti, Chemistry & Biochemistry

Utilization of a Molecule/Electrode System in Breaking Anticorrelation Between IE and RNE

The renormalization energy (RNE) complicates the connection between the gas phase molecular structure and conductance. Changes in the renormalization energy and vacuum level shift counteract the change in ionization energy (IE), limiting the range of conductance. As the ionization energy increases, the renormalization energy decreases. Such opposing correlations represent new “design principles”, allowing us to predict the relative magnitude of observed conductance trends. We explore a supramolecular design, in which the ionization energy and renormalization energy can be modified independently. Due to the Van der Waals interactions

within the supramolecule, new functionals and DFT methods were researched. Upon creation of this construct, different substituent groups were placed at separate positions (X and Y situated) on the macrocycle. Running these as Gaussian calculations, the IE and RNE were plotted to test the aforementioned molecular designs. Results show that between a functional without long-range interactions (B3LYP) and that corrected for dispersion (wB97XD), there were conflicts with the IE and RNE for the latter. However, the exact cause could not be determined.

Devin Collins – Biochemistry #6

Research Faculty Advisor: Rui Xiong, Pharma/Tox

Empowering Virtual Screening with Computational Chemistry

This paper will discuss the computational methods and process by which drug discovery occurs, and how it can be used to find drugs for novel targets. Even with the numerous resources that exist today, drug discovery cannot be entirely computational as significant physical validation is required to create accurate models. In this paper, I rely heavily on virtual screening as it is a powerful tool that is used in the drug discovery process to filter through vast areas of chemical space and then I use the results to predict how ligands will physically bind. I find that by increasing the number of protein models, the docking results become more accurate. Because proteins have many different conformations, combining these can result in a model that can better predict how well a molecule will bind. I show that for MLH1, a protein that regulates mismatch repair, computational methods can significantly aid the drug discovery process. Ultimately, I find multiple hits that bind in the micromolar range.

Rylee (Rei) Ellsworth – Biochemistry #43

Research Faculty Advisor: Hillary Mehl, School of Plant Sciences

Impact of nutrient scarcity on competition between aflatoxigenic and non-aflatoxigenic biocontrol strains of Aspergillus flavus

Aspergillus flavus is a fungus notable for producing highly carcinogenic aflatoxins. One of the most effective tactics for reducing aflatoxin in crops is the application of biocontrol products (biopesticides) containing non-aflatoxin producing strains of A. flavus that outcompete aflatoxin producers in soils and crops. These non-aflatoxigenic strains of A. flavus are selected from fungi isolated from field samples, which have naturally occurring mutations resulting in a loss of aflatoxin production. Deeper understanding of the factors influencing competition between aflatoxigenic and non-aflatoxigenic genotypes is critical to improving existing biocontrol products and better protecting crops from aflatoxin contamination. Experiments were conducted in which a variety of micro- and macronutrients were limited to evaluate how nutrient availability influences competition between pairs of aflatoxigenic and non-aflatoxigenic isolates. Nutrient scarcity is meant to mimic soils in field environments, which similarly might offer nutrient-poor environments where non-aflatoxigenic biocontrol isolates would ideally still outcompete aflatoxigenic strains of A. flavus. While any impacts of micronutrient (Cu, Fe, and Zn) scarcity were heavily dependent on the pairs of inoculated isolates and too specific to make any generalized conclusions, more broad trends were noticeable in the manipulation of available macronutrients carbon (C) and nitrogen (N). Changing the C:N ratio resulted in greater changes in outcomes of competition between aflatoxigenic and non-aflatoxigenic isolates than keeping that ratio constant while manipulating the absolute quantities of them present. Furthermore, a scarcity of N had a greater effect than scarcity of C, and non-aflatoxigenic isolates were more competitive than aflatoxigenic isolates at low concentrations of N. Future research is needed to study the changes in genotypic competition across a broader range of macronutrient scarcity with the C:N ratio kept fixed instead of being variable, as preliminary results suggest non-aflatoxigenic isolates may have an advantage over aflatoxigenic genotypes at a level of moderate macronutrient scarcity. If some amounts of macronutrient scarcity give non-aflatoxigenic biocontrol strains of A. flavus an advantage over aflatoxin producers, these conditions can be helpful when informing growers of aflatoxin-susceptible crops of best biocontrol practices to minimize the risk of aflatoxin contamination.

Michael Foster – Biochemistry #8

Research Faculty Advisor: Jon Njardarson, Chemistry & Biochemistry

Towards a Total Synthesis of Apomorphine: Novel Structures for the Treatment of Parkinson's Disease

Parkinson's disease is a neurological disorder characterized by the progressive destruction of dopaminergic neurons in the brain. Destruction of dopaminergic neurons diminishes neural connectivity of pathways that utilize dopamine as the primary neurotransmitter. Treatment of motor symptoms of Parkinson's disease focuses on maintaining dopamine levels in the brain or replicating the effect of dopamine in neuronal synapses. Apomorphine is a non-narcotic structural derivative of morphine that has been used for decades as a treatment option for Parkinson's disease but remains underutilized due to synthetic limitations preventing access to pharmacological analogs. A total synthesis of apomorphine is in progress, building the molecule from available starting materials, utilizing carbon-carbon bond forming chemistry, chiral auxiliaries to allow selectivity for stereoisomers, and cyclization reactions to complete the tetracyclic structure of the molecule. A new method of synthesizing apomorphine will allow the attachment of physiologically significant functional groups to the molecular structure to improve drug-like properties.

Joshua Goldring – Biochemistry #11

Research Faculty Advisor: Christopher Hulme, Pharmacy

Investigating the structure-function relationship of end-capping groups on a selective DYRK1A inhibitor

Dual specificity tyrosine-phosphorylation-regulated kinase 1A (DYRK1A) is implicated in the progression of neurodegenerative diseases such as Alzheimer's Disease. The Hulme group has developed proprietary small-molecule inhibitors of DYRK1A and optimized them for high specificity and efficacy. Still, there remains unintended binding of these inhibitors to Phosphodiesterase 3A (PDE3A), which may result in dysregulation of cardiac and vascular contraction. This work details the further optimization of our inhibitors for the elimination of PDE3A binding, as well as the structure-function relationship between additional functionalization of these ligands and the observed effects on their binding to DYRK1A and PDE3A.

Marcus Gomez – Biochemistry #31

Research Faculty Advisor: Noel Warfel, Cellular & Molecular Medicine

Autophagy Induced Chemoresistance

In order to cancer to progression, tumor cells must find ways to survive in the harsh tumor microenvironment. PIM kinase is one pathway that cancer cells hi-jack to enhance cell proliferation and survival, making PIM an appealing target to increase the efficacy of chemotherapy. However, drugs that target PIM kinase have not had the success that was anticipated. We recently discovered that kinase-dead PIM is capable of increasing resistance to chemotherapy. RNAseq data indicates a new role for PIM in inducing autophagy in dependent of its kinase activity. Autophagy is a process that recycles organelles and other cellular structures to produce energy, and increased autophagy is associated with resistance to chemotherapy. I will use immunofluorescence, western blotting, and cell viability assays to show that autophagy is increased by kinase-dead PIM as a mechanism of chemoresistance in prostate cancer.

Brandy Hadley-Nihiser – Biochemistry #44

Research Faculty Advisor: Ravishankar Palanivelu, Plant Sciences

Heat Stress Response in Tomato Reproduction: Investigating Thermotolerant and Thermosensitive Pollen Tube Growth Phenotypes

Rising temperatures pose challenges to crop cultivation, emphasizing the need to understand plant responses to heat stress. This study investigates the impact of heat stress on pollen tube growth in tomato varieties and to have a better understanding of the thermosensitive and thermotolerant phenotypes. Initial findings suggest that thermotolerant varieties exhibit greater resilience to heat stress, and when using thermotolerant pollen on a thermosensitive pistil it can help aid the growth of pollen tubes under heat stress.
Self-pollination and cross-pollination assays were done in growth chambers at control temperature 25°C and heat stress temperature 37°C. To visualize the pollen tube growth, pistils were stained using Aniline blue dye.

Elizabeth Harper – Biochemistry #23

Research Faculty Advisor: Pascale Charest, Molecular & Cellular Biology

Investigation of Calmodulin Binding Partners in D. discoideum Chemotactic Pathways

In the single-celled phase of its life cycle, Dictyostelium amoebae will perform chemotaxis towards cAMP in a calcium-dependent manner, facilitated by the G-protein coupled receptor cAMP receptor cAR1. However, it is not known how calcium-dependence affects chemotaxis. The highly ubiquitous calcium-binding protein calmodulin is a calcium signaling integrator, and its function in Dictyostelium amoebae is not well-characterized. Sequence analysis of cAR1 shows a potential calmodulin binding domain. We hypothesize that calmodulin binds active cAR1 to promote cell migration. In the future, we will perform bioluminescence resonance energy transfer (BRET) as well as co-immunoprecipitation experiments to determine if an interaction occurs between Calmodulin and cAR1. We performed a calmodulin pulldown to determine possible calmodulin binding partners in chemotactically competent Dictyostelium cells. The interactions will be analyzed with mass spectrometry. Understanding the role of calmodulin in Dictyostelium migration can help us understand the role of calcium and calmodulin in migration of other eukaryotic cells.

Clare Hotze – Biochemistry #22

Research Faculty Advisor: Thomas Tomasiak, Chemistry & Biochemistry

Investigating the Molecular Basis of Glutathione Transport by Yeast Cadmium Factor I

The ABC transporter superfamily is comprised of active membrane transporters that facilitate the flux of solutes across membranes through ATP catalysis. Yeast Cadmium Factor 1, or Ycf1, is a vacuolar ABCC subfamily transporter in Saccharomyces cerevisiae. Environmental heavy metal pollutants that are absorbed by yeast cells can induce significant oxidative stress that is harmful to the cell. Ycf1 plays a major role in protecting the cell from oxidative damages by sequestering electrophilic heavy metals like cadmium, arsenic, and lead into the vacuole. It does this through conjugation with glutathione, the most abundant intracellular antioxidant, prior to transportation by Ycf1. However, the molecular mechanism for substrate recognition and transport of these glutathione-metal complexes remains unknown. Using a novel cryo-EM structure of Ycf1 bound to oxidized glutathione and cellular survival assays, we tested twelve amino acids that we predicted to be binding determinants that allow Ycf1. Our findings suggest that glutathione complex recognition utilizes a “flex-pocket” mechanism that has specificity for the glutathione moiety while maintaining the flexibility to accommodate complexes of diverse sizes.

Anna Jaison – Biochemistry #13

Research Faculty Advisor: Robin Polt, Chemistry & Biochemistry

Utilizing Minimally Competent Lewis Acids for Glycosylation

This study investigates the optimization of minimally competent Lewis acids (MCLAs) for effective glycosylation reactions. The effectiveness of ZnI2 and InBr3 as catalysts with two different glycosyl donors, Glc(OAc)5 and Lact(OAc)8, under consistent conditions was explored. The approach used various methodologies, including the Gutmann-Beckett, Child's Method, and Fluoride Ion Affinity techniques, to evaluate Lewis acid minimally competence based on changes in energy and yields. The findings reveal significant variations in reaction outcomes, highlighting the importance of catalyst-donor pairing. ZnI2 demonstrated high yields with Lact(OAc)8, while InBr3 showed high yields with Glc(OAc)5. However, InBr3's combination with Lact(OAc)8, despite showing the most negative energy change, resulted in a lower yield. This study contributes to advancing science, particularly in drug development and precision medicine, by providing a framework for the tailored selection of catalysts to achieve desired glycosylation profiles.

Honor Jang – Computer Science, Biochemistry #24

Research Faculty Advisor: Kamel Lahouel/Christian Tomasetti, Translational Genomics Research Institute (TGen, outside UofA)

Batch effect correction in cfDNA fragmentation data using deep generative models

The fragmentation patterns and endpoints of cell-free DNA (cfDNA) depend on several factors, such as the nucleosome's organization or chromatin structure. Tumor-derived DNA similarly result in unique patterns, which analyses thereof can provide development in early cancer detection. Using amplicon-based sequencing to detect cancerous patterns in cfDNA show promise as a cheaper and more sensitive alternative to current options. However, the sensitivity also leaves results vulnerable to a variety of batch effects, such as primer lots used in the polymerase chain reaction (PCR), genomic DNA contamination, and other unknown external sources of variation. Previously, a linear dimensionality reduction approach found some success, but required knowledge of the batch effect sources to properly function. In addition, this linear approach struggles to preserve the complexity and features of the approximate 350,000 amplicons considered. A generative model shows promise in reconstructing the high-dimensional amplicon counts vector, preserving the relevant fragmentation information, and removing any batch related source of variation without prior knowledge of possible batch effects. Basing the generative model on autoencoders, the amplicon counts vector can be assumed to be generated from a simple source, allowing its signal to be transformed through a deep structure to fit complex data.

Eliza Johnson – Biochemistry #35

Research Faculty Advisor: Sean Limesand, Animal & Comparative Biomedical Sciences

Glucose Responsiveness of a Novel Synthetic Ovine Super Promoter

Prior research indicates that constructs containing the endogenous ovine insulin gene promoter have little to no activity in pancreatic beta cells. Our objective was to develop an ovine insulin promoter that is both glucose-responsive and beta-cell specific. To do this, we concatamerized the proximal promoter region of the ovine insulin gene to create a sheep insulin super promoter (SISP). We cloned SISP into two adenovirus constructs with a CMV promoter driving the fluorescent protein ZsGreen and SISP promoting either the fluorescent protein mCherry or luminescent protein luciferase. These constructs were tested in MIN6 cells to determine the promoter's specificity and glucose responsiveness in an insulinoma cell line. Results indicate that SISP had a high infection efficiency in MIN6 and was responsive to higher glucose concentrations. The addition of the antioxidant N-acetyl cysteine did not affect promoter responsiveness. The next steps for this super promoter include testing in ovine islets and directly comparing its activity to the endogenous ovine insulin promoter. SISP

can be used as a tool for beta cell isolation, monitoring glucose-stimulated insulin secretion, and targeting gene expression in beta cells.

Sai Julakanti – Biochemistry #29

Research Faculty Advisor: Anisha Apte, Surgery

THE EFFECT OF ORAL DELIVERY OF CNP-MIR146A IN THE COLON IN MURINE CROHN'S MODEL

Crohn's Disease (CD) is a chronic inflammatory intestinal disease first described as regional ileitis by Crohn, Ginzburg, and Oppenheimer in a case series presented at the American Medical Association annual meeting in 1932. CD inflammation affects the entire intestine, with the distal ileum being the most frequently affected part. Patients experience periods of flares and remissions during the disease course. The pathogenesis involves interactions between environmental factors, the immune system, susceptibility genes, and changes in the host's microbiome, leading to disruption of the intestinal mucosa. Inflammatory cells play a significant role in maintaining active disease, with most therapies targeting the cascade of inflammatory and pro-inflammatory cytokines. Treatment of CD is multidisciplinary, with medical treatment focusing on mucosal healing and symptom reduction, while surgery plays a key role in treating complications such as stenosis, perforations, fistulas, and abscesses. However, surgical recurrence affects over 80% of operated patients. Various surgical strategies have been investigated to improve outcomes, including the introduction of laparoscopic techniques, although they have not succeeded in reducing recurrences. In light of the persistent challenges in treating Crohn's disease, we have pursued an alternative approach aimed at attenuating the inflammatory response. Our focus has shifted towards utilizing CNP-miR146a, a novel therapeutic agent comprising cerium oxide nanoparticles (CNP) conjugated with microRNA-146a (miR-146a). This review focuses on CD inflammation and discusses potential strategies to prevent recurrences, particularly novel approaches on reducing the inflammation that maintains this disease.

David Jurkowitz – Biochemistry #1

Research Faculty Advisor: Travis Wheeler, Pharmacy Practice and Science

Conservation-Based Prediction of Protein Binding Pockets

Proteins interact with their environments (ligands, other proteins, etc.) at cavities their targets bind to called binding pockets. To design drugs that affect a protein's function, it is necessary to know the location and architecture of its binding pockets. Traditionally, binding pockets have been identified through experimental structure-determining methods such as X-ray crystallography, NMR, or cryo-electron microscopy of protein-ligand complexes. However, this data is sparse and expensive and time-consuming to produce. Two common computational methods are running molecular dynamics simulations and exploring the surface of a known or predicted protein structure and predicting where the pockets may be. The former option is also time consuming and requires a known ligand. Programs that use the latter option, such as fpocket and to a lesser extent, P2Rank, will return many unlikely pockets along with the more probable pockets for a given protein. This project's goal is to identify the true binding pockets for all human proteins from the collections produced by fpocket and P2Rank. This improvement is made by incorporating calculations of sequence conservation, which neither fpocket or P2Rank yet do. If a position or region of a protein is conserved across homologous sequences, it is likely to be necessary for maintaining the protein's structure or for accomplishing one of its functions. Therefore, one of the identified amino acids would be more likely to be the center of a binding pocket. Multiple sequence alignments (MSAs) of homologous proteins were created from PANTHER protein family sequences. From the MSAs, relative entropy values were calculated for each amino acid of the human protein. These values served as a proxy for measuring sequence conservation. Potential binding pockets were computed using fpocket and P2Rank, and the relative entropy values were mapped to the amino acids involved in the pockets to arrive at the improved set of high probability binding pockets. These rankings were compared with those of P2Rank, and their accuracy was evaluated by using a dataset of known binding pockets. Currently,

more fine-tuning of the conservation-based scoring method is needed to produce a meaningful improvement over P2Rank's algorithm.

Pulari Kartha – Biochemistry #41

Research Faculty Advisor: Brian J. Enquist, Ecology & Evolutionary Biology

Fluctuations in Plant Nitrogen and Carbon across Elevation Gradients in the Rocky Mountains

Across elevation gradients, plants can be observed to have a wide variety of traits, despite being in the same geographical area. Elevation gradients can cause physical changes in flora, but also have an impact on the chemistry of the plant, due to the decreases in temperature and vapor pressure deficits, which are the driving forces behind these changing physical qualities. In the Rocky Mountains, subalpine ecosystems are distinct due to the presence of a drought season following snowmelt in May, which is then perpetuated by less frequent monsoon rains. With climate change and global warming, snowmelt occurs earlier and earlier each year, leading to a longer period of time during which the flora in these ecosystems are subjected to drought. This time period is characterized by a decrease in nutrient availability and ecosystem productivity. In order to understand the effect of drought on these ecosystems, I compared plant chemical traits across an elevation gradient, sourcing samples from subalpine meadows, as well as from their higher elevation alpine counterparts, which do not experience these same environmental conditions. Fluctuations in carbon and nitrogen content within leaves samples across elevational gradients are apparent, giving insight into the effect of environmental conditions on plant stoichiometry. Using samples sourced from the Rocky Mountain Biological Laboratory (RMBL) in Gothic, Colorado, not only can the presence of microclimates as a result of differences in elevation can be observed through stoichiometric analysis, but also highlight the effect of drought on plant metabolism. Carbon percentage, nitrogen percentage, and the ratio of carbon to nitrogen within leaf samples sourced from different sites were measured and analyzed. Plant traits gathered from drought-affected sites appeared to have significantly lower nitrogen content compared to their high elevation counterparts. The variation of carbon and nitrogen levels obtained from the assessment of leaf samples gathered across the elevational gradient studied gives insight into the impact drought has on plant metabolic activity, as well as the dynamics of an ecosystem.

Brennan Kennedy – Biochemistry #33

Research Faculty Advisor: Konrad Zinsmaier, Neuroscience

Characterize Phenotypic Effects of Deletion in the CS Domain of CSP

CSP is a neuroprotective protein found in the secretory vesicles of neurons. Mutations in the CSP gene can cause neuronal ceroid lipofuscinosis (NCL). This is a debilitating and ultimately deadly disease characterized by the buildup of lipofuscin in the lysosomes of cells. Given CSPs neuroprotective properties and the potentially deadly consequences of its misfunction CSP is a protein of interest. To understand better how CSP works a deletion in the linker region of the CSP gene was created in fruit flies. Data was collected by measuring the amount of CSP by using a confocal microscope to image the neuromuscular junctions (NMJ) of 3rd instar fly larvae. Using the computer program Fiji images were analyzed showing a significant decrease of CSP in flies with the linker region deletion relative the control flies.

Heather Kwapeszeski – NSCS and Biochemistry #21

Research Faculty Advisor: Marielle Walti, Chemistry & Biochemistry

Studying the Structure of Hsp10 and its Interaction with the Alzheimer's Peptide

Alzheimer's Disease (AD) is the most common form of dementia, impacting millions of people and their families. Amyloid beta 42 (Aβ42), the Alzheimer's peptide proposed to be directly involved in AD, has been studied for several decades given its importance in various pathways and connection to disease states. Although there is no current treatment for AD, various approaches to prohibiting these plaques from forming are being researched. One avenue is through chaperone proteins, which are responsible for aiding the proper folding of other proteins and inhibit the formation of lethal aggregates. The heat shock protein 60 (Hsp60) and its co-chaperone 10 (Hsp10) are an example of such a chaperone system. Here we implement the expression and purification protocol of Hsp10. We are working towards solving the structure of apo Hsp10, that is currently not known. Further, by chance, we found that Hsp10 in absence of Hsp60 inhibits the formation of the toxic Aβ42 fibril. Using solution-state nuclear magnetic resonance (NMR) spectroscopy we investigate the binding site of Hsp10 and Aβ42, and found that the binding site spans over the entire Ab42 peptide and is not restricted to specific residues. We are currently determining the kinetics of this interaction. Further research may indicate possible therapeutic pathways.

Angela Mankin – Biochemistry #27

Research Faculty Advisor: Hahn Soe-Lin, College of Medicine

Characterization of vascular patency and impact of anatomic variation on flow modeling in a novel high-fidelity whole-body donor cadaveric model for simulated surgical and procedural training

A lack of standardized learning platforms utilizing cadaveric models creates a disconnect between hands-on experience with anatomically correct training platforms and the real life demands of comfort with medical procedures. The Knowledge Donor program bridges this gap by providing medical learners with specially preserved whole-body donors that can be utilized in surgical simulations, without the risk of complications to live patients. This program uniquely ventilates the lungs and perfuses expired human blood products - that cannot be used in living patients and otherwise would be discarded - to simulate the breathing and blood flow of a live patient, but in a non-living cadaveric specimen. The program then provides learners with the opportunity to perform simulated procedures and surgeries in environments that closely resemble that of a fully functional operating room.

The quality of tissue preservation underlying the whole-body donor model relies heavily on the anatomy and patency of the donor's vascular system. Since the vascular system is significant in both the program's preservation techniques and in the simulation of blood flow, understanding the limitations of the vascular system may inform the current preservation and perfusion processes and can help perfect the Knowledge Donor training model.

The use of angiographic imaging allows for the direct visualization of a Knowledge Donor's vasculature in a minimally invasive, non-destructive fashion that does not impair subsequent utilization of the donor for surgical procedures. We have concluded that the arterial system remains eminently intact, while the distal venous system is subject to significant vascular collapse leading to incomplete perfusion of the venous system. These angiographic findings, providing an understanding of the support as well as limitations of the vascular system, propose future directions in refining the preservation and perfusion processes to obtain a more complete preservation that allows for a more anatomically functional model.

Allison Mason – Biochemistry #36

Research Faculty Advisor: Kacey Ernst, Epidemiology and Biostatistics

Perceptions and Attitudes Surrounding COVID-19 Prevention Strategies and Risk Perceptions

The perceptions and attitudes surrounding COVID-19 and the prevention strategies effectuated have varied and caused widespread controversy in the media. The purpose of this study was to determine the individual perceptions of COVID-19 prevention strategies from the perspectives across age groups within the state of Arizona. This was a randomized qualitative study where Arizona residents 18 years of age and older were eligible for participation. Qualtrics, the web-based software, was used to distribute the online survey to qualifying participants. Participants were stratified according to age (18-34, 35-44, 45-59, 60-74, and 75+) and were asked a series of questions pertaining to ongoing COVID-19 prevention strategies, with responses recorded using 5-point Likert scales. Results were collected from April 2023 to July 2023. A total of three thousand two hundred ninety-four responses were collected, with 3117 (96.4%) agreeing to participate. One thousand five hundred twelve participants responded to our inquiry about previous COVID-19 diagnoses, with age group 18-34 having the highest percentage (53.23%) of a confirmed COVID-19 diagnosis and age group 75+ having the lowest percentage (31.58%) of a confirmed COVID-19 diagnosis. When asked how likely the participant is to get tested for COVID-19 after being exposed to someone with COVID-19, age group 18-34 had the highest percentage (40.15%) of "extremely likely" responses while age group 75+ had the lowest percentage (25.53%) of "extremely likely" responses. Responses indicated that the youngest age group (18-34) was more accepting of COVID-19 prevention strategies and demonstrated more cautious behavior compared to the oldest age group (75+). Immunocompromised individuals remain at a higher risk for severe COVID-19. With this study, researchers and healthcare professionals can monitor the future behavior and likelihood of treatment of different age groups by using their perceptions of prevention strategies of various diseases.

Eleanor McBride – Biochemistry #18

Research Faculty Advisor: Veaceslav Coropceanu, Chemistry & Biochemistr7

Electronic structure of efficient circularly polarized emitters based on organic chiral molecules

Chiral molecules exist as a pair of left-handed and right-handed mirror images (enantiomers) that cannot be super-imposed. Chiral molecules interact selectively with the right and left circularly polarized light resulting in chiro-optical properties such as electronic circular dichroism (CD) and circularly polarized luminescence (CPL). In this project we use electronic structure calculations to identify chiral molecules with strong CPL effect and large dissymmetry (g) factors. We focus on two groups of DOBNA based closed-shell thermally activated delayed fluorescence (TADF) molecules and. The g factor can range from -2 to +2, but only a few molecules with g factors about 10-2 been reached so far. In this project we investigate how the g factor could be tuned by chemical molecular design.

Gal Melman – Biochemistry #10

Research Faculty Advisor: Jon Njardarson, Chemistry & Biochemistry

New Frontiers of the Anionic Amino-Cope Cascade

After discovering a way to synthesize chiral sulfinyl imine phosphonate reagents in one step instead of four and running Horner-Wadsworth-Emmons reactions to get an Ellman-imine product, the anionic amino-cope cascade can be used with different substituents to make chiral heterocycles. Those heterocycles that include a cyclohexanone that can be oxidized to give the phenol and then be protected by a triflate group. They can later be transformed into structures that include pyridine rings, which are necessary for a multitude of FDA approved drugs. New heteroatomic substituents, including phenyl sulfide, were tested to determine if the anionic amino-cope cascade works on them as well. In the future, these substituents will be scaled up and pushed further to make pharmaceuticals that can treat autoimmune diseases.

Andriy Myloserdnyy – Biochemistry #12

Research Faculty Advisor: Robin Polt, Chemistry & Biochemistry

*A **Synthesis of a Glycosylated Oxytocin Derivative for the Treatment of Opioid Use Disorder***

Oxytocin is an endogenous cyclic neuropeptide that has important effects in the uterus, brain, and throughout other systems in the body. It is used today clinically as an i.v. infusion to induce labor, prevent post-partum bleeding, and to stimulate lactation. However, this hormone is limited in other therapeutic applications due to its low half-life in serum and poor blood-brain barrier (BBB) penetration. Glycosylated oxytocin derivatives have been designed to avoid these issues and are of interest for many therapeutic applications. One key application of oxytocin derivatives is for the treatment of pain. Currently opioids are the main class of drugs used for the treatment of pain, but these drugs carry dangerous side effects. Opioid use can lead to constipation, dependance, opioid-induced respiratory depression (OIRD), and overdose. Opioid use disorder (OUD) is a growing issue and prescription opioids are one of the most misused drugs in the U.S. Glycosylated oxytocin derivatives can potentially be used for the treatment of pain and can be potentially used as a safer alternative to opioids. In addition, glycosylated oxytocin derivatives can also be used as another tool in the treatment of OUD and could help reduce the prevalence of OUD in the U.S.

Marie Ojeh – Biochemistry #45

Research Faculty Advisor: Rebecca Schomer, Plant Sciences

Isolation and phenotypic characterization of chemotactic Methylotrophs from arid-environment agricultural site

We are interested in the genotypic and phenotypic trends that separate methylotrophs isolated from arid environments from those that are isolated from temperate environments Here we isolated 45 Methylotrophs from Sorghum grown in Maricopa, Arizona. We characterized these strains based on 16S rRNA sequencing, their chemotaxis to methanol and on rich media, and their growth using Methanol as a sole carbon source. We found diverse genotypes were represented in the library of isolates. Most of the strains exhibited some level of chemotaxis to methanol and some level of growth on methanol. In the future, we will sequence the complete genomes of these isolates to understand the relationship between methylotrophs and host plants in water limited environments.

October Owen – Chemistry #17

Research Faculty Advisor: Michael T. Marty, Chemistry & Biochemistry

Removal of artifacts from Hadamard Transform Multiplexing of coupled online SEC with CD-MS

Identification of large, complex analytes such as heterogeneous biomolecules using mass spectrometry is improved by using charge detection mass spectrometry (CD-MS) and separation using liquid chromatography (LC). CD-MS requires many spectra to produce adequate ion statistics, and the number of spectra acquired from a single LC injection is typically insufficient. We have recently pioneered the use of Hadamard Transform (HT) multiplexing to resolve this. However, HT demultiplexed spectra are known to contain significant spectral artifacts arising from deviations between real chromatographic data and the binary input expected by HT algorithms. We explored two methods of artifact removal: masked multiplexing and inverted sequence injections.

Data from a SEC LC system coupled with CD-MS using a 31-digit (0000100101100111110001101110101) injection sequence was collected for the enzyme β-galactosidase. The resulting chromatogram indicated elution at the predicted times and was demultiplexed using UniChromCD, revealing artifacts in the form of small peaks up to 5% of the intensity of the analyte peak. Several algorithms have been developed to remove

such artifacts from similar ion mobility spectrometry data and are here being applied to remove artifacts from the collected CD-MS data.

The first method of artifact removal investigated was “masked multiplexing” introduced by Clowers et. al. This process involved randomly introducing artifacts into the S-matrix used for HT demultiplexing. This process is repeated to produce multiple chromatograms, each with a unique set of introduced artifacts, which are then compared. Regions of the chromatograms with large variance in intensity are flagged and deweighted, and analyte peaks—which ideally have little to no variation—are identified. This method successfully reduced artifacts in the collected β-galactosidase data.

A second method being investigated was the “Inverted HT Sequence” reported by Naylor et. al. This method requirede two chromatographic runs, with the second injection sequence being inverted to the first (i.e. 1 changed to 0 and vice versa). Ideally, after demultiplexing these two chromatograms would contain artifacts that are similar to each other but opposite in sign. Both demultiplexed chromatograms were averaged together reduce to reduce artifacts.

The relative benefits of these artifact removal methods were compared and analyzed for their ability to improve data from online SEC coupled with CD-MS. Factors being considered include the validity of assumptions made during processing (for example, analyte peak intensities will be uniform during masked multiplexing), if one method removes artifacts more completely than another, and time and effort required to implement the method.

Grace Parekh – Biochemistry #3

Research Faculty Advisor: Todd Vanderah, Pharmacology

Reversal of Oxycodone Opioid-Induced Respiratory Depression

Opioid use can lead to severe side effects, including opioid-induced respiratory depression (OIRD), which poses a significant risk to patient safety. This thesis explores the potential of CBR2 receptors in mitigating OIRD through mouse models and respiratory measures. The study aims to understand the mechanisms underlying respiratory depression induced by acute opioid exposure and investigate the efficacy of CBR2 receptor modulation in reversing this phenomenon. The study involves the acute intraperitoneal (IP) injections of oxycodone in mice and the subsequent administration of a CBR2 receptor antagonist, AM2301. Whole Body Plethysmography (WBP) was used to measure respiratory parameters: respiratory rate, minute volume, and tidal volume. Our results demonstrate that the CBR2 antagonist, AM2301, cannot fully mitigate opioid-induced respiratory depression by modulating basal breathing patterns and the WBP data. These findings may shed light on the potential therapeutic role of CBR2 receptors in managing OIRD and highlight the importance of further research in this area.

Chloe Park – Biochemistry #32

Research Faculty Advisor: Anita Koshy, Neurology, Immunobiology

Role of a Hypothetical Protein (TGME49_207210) in Toxoplasma gondii Persistence and Latency

Toxoplasma gondii, an obligate intracellular parasite, infects a wide range of warm-blooded animals and causes the disease toxoplasmosis. Key to T. gondii’s pathogenesis is its ability to transition from the rapidly-multiplying tachyzoite stage during acute infection to the dormant bradyzoite stage found within tissue cysts, which are the hallmarks of a chronic infection. Bradyzoites within cysts can reactivate to cause serious pathology and mortality in the immunocompromised. Encysted bradyzoites also play an important role in transmission between intermediate hosts. Given the critical role of this stage conversion in disease progression and transmission, this study aims to identify proteins that regulate differentiation in a T.gondii strain-specific manner. Using a recently generated RNA-seq dataset from infected murine neurons, we pinpointed a

hypothetical gene TGME49_207210 as being significantly upregulated in type II strains, which encyst more efficiently compared to type III strains. Utilizing CRISPR-Cas9, we deleted this gene from a wild-type type II strain and found decreased encystment in neurons for the knockout strain compared to the wild-type counterpart. Reintroducing TGME49_207210 into the knockout strain partially restores encystment. Future studies will focus on elucidating the interactions between TGME49_207210 and other parasite proteins to further enhance differentiation.

Nguyen Pham – Biochemistry: Physiology & Medical Sciences #19

Research Faculty Advisor: Craig A. Aspinwall, Chemistry & Biochemistry

Evaluation of the Membrane Permeability of Nitroxyl and Its Implications for Novel Drug Design

In recent years, reactive nitrogen species (RNOs) gained significant attention for their diverse biological roles of redox signaling, vasodilation, and chemical modification of enzymes. Nitroxyl (HNO), due to its unique pharmacological properties, has emerged as a promising agent in the treatment of myocardial infarction and cancer. The application of HNO in medicine can be further advanced through the capability to assess diffusion and membrane permeability. Leveraging the reactivity of the thiol functionality in glutathione (GSH) as an effective trapping agent for HNO enabled monitoring membrane translocation. Here, we utilized GSH-encapsulated large unilamellar vesicles (LUVs) of defined lipid composition and size as an alternative to cell membranes. Upon the addition of an HNO donor, Angeli's Salt, the depletion of free thiol groups was quantified by a highly sensitive, fluorogenic GSH assay. Membrane permeability of HNO, as a result, was characterized as a function of time, concentration gradient, and LUV size. Our findings offer valuable insights into the pharmacokinetics of HNO and may have broader implications in the novel drug delivery systems.

Niko Racciato – Biochemistry #40

Research Faculty Advisor: Wendy Moore, Entomology

UCEs as a method of inferring phylogeny in Bombardier Beetles

Prior to the development and increased accessibility of molecular techniques, phylogeny has been traditionally inferred using comparative morphology. However, members of the ground beetle subfamily Brachininae are very similar morphologically, and other methods may be necessary to infer their phylogeny. We applied the program PHYLUCE to assembled genomes from 11 brachinine specimens to extract regions of DNA highly conserved between taxonomic groups, also called ultraconserved elements (UCEs) and the regions flanking them. We then created phylogenetic trees, which we then compared to phylogenetic trees generated from morphology and a legacy gene. We found that UCEs returned evolutionary relationships similar to those found morphologically, although with less confidence at higher taxonomic levels. We found it is necessary to use combined data from several UCEs to obtain the most accurate phylogenetic information.

Anna Ramsook – Molecular & Cellular Biology #20

Research Faculty Advisor: John Jewett, Chemistry & Biochemistry

THE EFFECT OF pH ENVIRONMENTS ON ARYL DIAZONIUM ION RELEASE FROM TRIAZABUTADIENES ON DNA

Triazabutadienes (TBDs) are organic compounds that can serve as a scaffold for aryl diazonium ions (ADIs), which have high levels of reactivity and can damage DNA. Based on organic chemistry mechanisms, triazabutadienes can be introduced into varying pH environments for controlled release of the ADI. Based on previous literature, it is hypothesized that TBDs release ADIs under neutral and acidic conditions. This project focused on two sets of TBDs and ADIs: an unsubstituted set (H-ADI/H-TBD) and a Br-substituted set (Br-ADI/Br-TBD).

The TBD/ADI experiments involved a two-fold process: synthesis of compounds and DNA experiments with these compounds, beginning with synthesizing the two sets of diazonium salts and triazabutadienes. Diazonium salts were made in open-air conditions at a temperature of 0 ºC. Triazabutadienes were synthesized under inert conditions at room temperature using a Schlenk line. Triazabutadienes were then protected to prevent ADI release with ethyl chloroformate as a protecting group. These compounds were then introduced into Lambda ("λ") DNA as part of the DNA experiments in either acidic (pH 4) or neutral buffer (pH 7.4). The DNA experiments were run under conditions of 37 ºC, no light, for 30-minute constant time-points. Then, gel electrophoresis was used to visualize the results.

The pre-release of the ADI from the TBD was completed using the half-lives of the compounds, which were determined via kinetics experiments. The varying effects of the TBDs and ADIs differed based on the pH of the environment. Results show that, as hypothesized, the TBD released the ADI under acidic conditions. Further, introducing DNA led to some protection of ADI release from the TBD. The ability to control the release of an ADI from a TBD is useful in pharmaceutical studies of drug delivery and target discovery. Future directions include studying the impact of substitutions of TBDs and ADIs with varying electron-donating and electron-withdrawing groups.

Asia Richardson – Biochemistry #9

Research Faculty Advisor: Jon Njardarson, Chemistry & Biochemistry

Exploring New Avenues and Applications of the Underutilized Anionic Amino-Cope Rearrangement

Heterocyclic compounds are frequently found in US FDA approved drugs. New synthetic pathways to different heterocycles are therefore important to investigate in the endeavor to stream-line synthesis towards an array of new small molecules. As a part of this endeavor, we currently detail our expansions of our previous discoveries regarding the asymmetric anion-accelerated amino-Cope rearrangement. From our first report on the use of this anion accelerated amino-Cope rearrangement in 2017, the reaction has since evolved into an extensive platform. Through further explorations of the anionic amino-Cope rearrangement products, we have developed a new reaction that forms densely substituted chiral pyridines - the 2nd most common nitrogen heterocycle found in US FDA approved drugs.1 Besides the newly developed pyridine forming reaction, a number of new, interesting nucleophile and electrophile partners are being currently tested in this rearrangement. Previously, only carbon substituent containing nucleophiles were synthesized and tested in this cascade. However, the use of a sulfur-containing α-β unsaturated ester nucleophile has been an exciting investigation, revealing possibilities of installing additional heteroatoms onto the chiral cyclohexenone products, aiding in an ongoing synthesis of the medication, apomorphine. In addition to the investigation of new nucleophiles, we are currently synthesizing allenyl imines as new electrophile substrates to test. A probe into allene-containing electrophiles is a promising endeavor, as it could introduce new functionality to the cyclohexenone Cope products that could expand the use of the developed platform. Ultimately, we are optimistic about advancements in Cope chemistry, and will continue to explore its uses in drug discovery and the synthesis of natural products.

Kristen Roehling – Chemistry, Applied Mathematics #16

Research Faculty Advisor: Stephen Kukolich, Chemistry & Biochemistry

Internal rotation analysis and calculations of the ammonia-formic acid complex

Our lab uses high-resolution microwave spectroscopy to determine the structure and dynamics of small molecules. Hydrogen-bonded complexes involving oxygen and nitrogen can be used as analogs to better understand DNA base pairs. In this project, the rotational spectrum of ammonia-formic acid was analyzed from 7-22 GHz using direct measurement and double resonance microwave spectroscopy. Analysis of the spectrum revealed that ammonia acts as a low-barrier internal rotor in this complex. The XIAM5 program was utilized to obtain an excellent fit for 20 A state transitions and 16 E state transitions. The fit yielded rotational constants, 14N quadrupole constants, and internal rotor parameters. The barrier to internal rotation (V3) was found to be 195.18(7) cm-1.

Jakob Sera – Biochemistry #6

Research Faculty Advisor: Dennis Lichtenberger, Chemistry & 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.

Brian Shaw – Biochemistry #2

Research Faculty Advisor: Haining Zhu, Pharmacology & Toxicology

Hexavalent Chromium Induces Stress Granules and Malignancy in a G3BP1 Dependent Manner

Hexavalent chromium [Cr(VI)] is a toxic heavy metal associated with severe environmental health risks. Low-level environmental exposure to Cr(VI) has been implicated in health conditions including cancer. Stress granules (SGs) are dynamic membraneless organelles influencing multiple cellular pathways including cell survival, proliferation, and malignancy. However, the relationship between Cr(VI) exposure and SGs remains unclear. We aim to elucidate the impact of Cr(VI) exposure on SG dynamics and the potential role of SGs in Cr(VI)-induced malignancy. Human bronchial epithelium cell line BEAS-2B was exposed to acute high concentration and chronic low concentration of Cr(VI) to test whether Cr(VI) induced SGs. BEAS-2B cells were exposed to low concentrations of Cr(VI) for an extended period of time to induce malignant transformation, generating transformed cells (CrT). SG formation in response to oxidative stress was evaluated in BEAS-2B and CrT cells. Moreover, the SG core component G3BP1 was knocked out in CrT cells to investigate the role of SGs in Cr(VI)-induced SGs and malignancy. Acute exposure to high concentration of Cr(VI) and prolonged exposure to low concentration of Cr(VI) both induced SG formation. Pre-exposure to Cr(VI) potentiated a robust SG response as compared to cells without pre-exposure. Chronic Cr(VI) exposure induced malignant transformation, resulting in an up-regulated SG response as well as increased proliferation, sphere formation, and transformation markers. Knocking out the SG core protein G3BP1 in CrT cells may have contributed to reduced SG formation and various malignant properties. Cr(VI) exposure induces SGs at low and high concentrations. An up-regulated SG response in cells chronically exposed to low concentration Cr(VI) is associated with increased malignant properties. The core SG protein G3BP1 plays a role in mediating Cr(VI)-induced malignancy, representing a novel mechanism and a potential therapeutic target.

Skyler Tilden – Biochemistry; Molecular and Cellular Biology #37

Research Faculty Advisor: Charles Gerba, Environmental Sciences

Mechanism of action of natural products' inhibition of viral activity

Viruses have always been a cause for health concerns, but they recently have been brought to the forefront in society. Viruses can contaminate hard surfaces as well as many other locations in everyday life. Natural disinfectants, such as salicylic acid, have long been used as antiviral agents to combat viruses and present less safety concerns compared to their synthetic counterparts. Capsids function as the protein shells of viruses that encapsulate the virus's genetic material. One way that antiviral agents in disinfectants inhibit viral activity is through disruption of the capsid. Viruses MS-2, Phi X174, and PR772 are propagated in their respective E. coli bacteria strands prior to introduction of disinfectants. 0.5% salicylic acid in 40% EtOH is placed into each vial of host strands and shaken on an orbital shaker at 200 RPM for 1 minute and 10 minutes. Both 1-minute and 10-minute experiments are plated using the agar overlay procedure. Colonies from all experiments are placed into two separate conical tubes. These are then treated with an azo dye, Propidium Monoazide. Half of the experiments will be exposed to UV light to induce the dye-genome complex. To determine the ability of natural disinfectants, in natural products, to disrupt viral capsids, capsid integrity quantitative PCR is run.

Raydon Tran – Biochemistry and Pharmaceutical Sciences #8

Research Faculty Advisor: Bernardo Lemos, Pharmacy

The effects of Cadmium on BEAS-2B bronchial cells

Cadmium (Cd), a known toxic metal readily bio-sequestered in plants, is exposed to the human population mainly through inhalation of tobacco smoke and ingestion of food grown in Cd-containing soils. In North America, the ingestion amount is generally minimal and within acceptable limits, but the concern for Asia remains. In North America, the primary route of exposure to the general public is tobacco smoke due to the tobacco plant's strong uptake of Cd from the environment. Because smoking is a high-exposure route for Cd, we studied the effect acute Cd exposure has on human bronchial cells (BEAS-2B). We first observed the toxic dose of Cd on BEAS-2B cells to find a sub-cytotoxic dose that these cells could tolerate. We then exposed BEAS-2B cells to this dose and observed the dose-dependent change in the copy number of ribosomal DNA (rDNA). Because nucleolar fragmentation has been linked with rDNA copy number changes, we further investigated the effect of acute Cd toxicity on nucleolar fragmentation in BEAS-2B cells. Our results show that exposure to higher concentrations of Cd decreases BEAS-2B viability. Cd doses as high as 2 μM maintained a minimum of 60% viability after acute exposure. Cells exposed to 1 and 2 μM Cd did not increase the nucleolar fragmentation after 24 hours of exposure.

Vara Vungutur – Biochemistry #30

Research Faculty Advisor: Ningning Zhao, Nutrition

ZIP8, ZIP14, and ZnT10 expression in mouse testes

Manganese (Mn) is an essential trace metal in the body and it is involved in metabolism, neurological development, and antioxidant defense. Three manganese transporters have been identified thus far: ZIP8, ZIP14, and ZnT10. Research has been done on both cellular homeostasis in terms of kidney and intestinal epithelial cells as well as systemic homeostasis in the lung, liver, and small intestine, concerning these three Mn transport proteins. However, little is known about the role of these transporters in Mn metabolism within the male reproductive system. To investigate the roles of Mn transporters in testes, we used western blotting to identify Mn transporters within the whole tissue. We identified that ZIP8 is the only manganese transport expressed in the testes. To further determine how ZIP8 is regulated by Mn in the testis, we used two Mn overload mouse models, ZIP14-deficiency and ZnT10-deficiency mice. We performed Inductively Coupled Plasma Mass Spectrometry (ICP-MS) analysis to determine Mn concentrations in the testes of models. We

further isolated different cell populations from the testis of wild-type mice to study ZIP8 protein expression in specific cell types, including germ, sertoli and leydig cells. Overall, this project provides insight into the roles of ZIP8 in testicular function and physiology, and helps to elucidate the mechanism of manganese metabolism in the male reproductive system.

Michelle Wei – Biochemistry, Math #26

Research Faculty Advisor: Guang Yao, Molecular & Cellular Biology

Modeling the Depth of Cellular Dormancy from RNA-sequencing data

High-throughput transcriptome RNA sequencing is a powerful tool for understanding the dynamic process of cellular dormancy. Our recent work, which profiled transcriptomic changes over time in quiescent fibroblasts, suggests that quiescence deepening represents a trajectory from active proliferation to permanent senescence. To model this trajectory, we trained an elastic net that predicts "quiescence depth scores" (QDS). When tested on publicly available RNA-sequencing datasets, the model predicted QDS that accurately reflected the relative dormancy depth of a wide array of cell types. To streamline the dormancy depth analysis process, we created QDSWorkflow, an R package for predicting QDS using bulk and single-cell RNA-sequencing data. Here, we use QDSWorkflow to analyze dormancy depth in fibroblasts and neural stem cells.

Ashley Wellington – Biochemistry #38

Research Faculty Advisor: Roberto Guzman, Chemical & Environmental Engineering

Synthesis of Doxorubicin Liposomes as Nano-Carriers for Cancer Therapy

Doxorubicin hydrochloride (HCl) is a single agent, anthracycline that blocks the use of the topo-isomerase enzyme and therefore stops the development of cancer cells which when paired with these nanoliposomes creates a stronger drug therapy. Evaluation of the release study and initial drug encapsulation for this drug and derivations could prove to have more advanced elimination of tumors within the human body. Specifically, breast cancer is known to be the second most common cancer among women within the United States. Doxorubicin drug components combat against breast cancer, ovarian cancer, and even Kaposi sarcoma (AIDS patients). The utilization of dissolutions of the drugs in lipid suspensions, extrusions for preparation of nanoparticles, UV drug measurements, drug dialysis, and more techniques will assist in analysis of encapsulation efficiency, and final drug release data. This study should provide enlightenment on the efficiency of doxorubicin, its deviations, and even other comparative drugs which can be useful towards further cancer therapeutics and drug nano-carrier design.

THE UNIVERSITY OF ARIZONA
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Chemistry
& Biochemistry

RESEARCH PRESENTATIONS

Daniel Aranda – Chemistry #46

Research Faculty Advisor: Thomas Gianetti, Chemistry & Biochemistry

Synthesis, Characterization, and Application of Pyrene-Functionalized Carbenium

Stable carbenium ions like AzaDiOxaTriAngulenium (i.e. ADOTA) have a diverse range of applications. This family of organic molecule's properties can be fine-tuned by varying pendant arm ligands and core functionalization's. This combined with their ability to be easily synthesized adds to their promise in varying fields like catalysis and energy storage. Herein, we report a five-step synthesis of a pyrene-functionalized ADOTA (i.e. pyrene-ADOTA) starting from commercially available pyrene and 1,3-dimethoxybenzene. Moreover, we study the photophysical and electrochemical properties and potential applications of the target molecule.

Cole Bellomo – Chemistry #50

Research Faculty Advisor: Jeffrey Pyun, Chemistry & Biochemistry

Synthesis of novel sulfur-based polymers for IR imaging

Conventional methods for producing IR lenses involve the use of super-critical materials, such as germanium. Due to the high cost and demand of these lenses, especially for defense and automotive industries, the Pyun group has proposed an alternative method that involves the copolymerization of sulfur with an organic monomer, dubbed inverse vulcanization. Initial research showed that the mechanical properties of the sulfur-polymer were lacking. Unreacted sulfur remained in the lens, which affected the mechanical and thermal properties. In order to improve these properties, the Pyun group discovered the use of sulfenyl chlorides (i.e. sulfur-monochloride) as a way to react with the unreacted sulfur and improve the mechanical properties. For this research project, mechanical properties were compared of lenses with and without sulfenyl chloride, with varying compositions and thermal curing temperatures. After comparing the lenses, it was found that lenses polymerized with sulfur-monochloride had improved mechanical properties.

Anna Campbell – Biochemistry #65

Research Faculty Advisor: Matthew Cordes, Chemistry & Biochemistry

A comparison of venom and non-venom expressed phospholipase D homologs from recluse spiders

Phospholipase D enzymes are a major component of recluse spider venom which cause paralysis in insect prey or necrotic lesions in mammals. All spiders carry versions of this enzyme for non-venom functions, but recluses are the only spiders to have adapted them for venom use.Comparison of venom toxins with related non-venom enzymes may shed light on how this enzyme may have evolved in response to venom recruitment.To make the closest comparison, we plan to clone and express a non-venom variant that is also from a recluse, specifically Loxosceles rufescens. As venom proteins must function within prey organisms, and the specific lipid modifications they catalyze likely factor into their toxicity, one might expect changes in associated enzyme properties. Thus, we plan to compare the thermal stability, enzymatic activity, and substrate specificity of venom and non-venom examples.Non-venom enzymes, however, should avoid catalyzing unregulated toxic reactions,so we will also investigate the role of a potentially inhibitory C-terminal domain to see if non-venom variants have additional regulation. Overall, comparing these properties may improve our understanding of how the selective pressures surrounding venom use shaped phospholipase D toxins.

Sean Chen – Biochemistry #56

Research Faculty Advisor: Michael F. Brown, Chemistry & Biochemistry

Effect of Water and Lipids on GPCR Activation

Rhodopsin is an archetype for the largest family of G-protein-coupled receptors (GPCRs), which is in turn the largest family of proteins in the human genome. They are of particular interest in pharmaceuticals as GPCRs comprise more than one-third of pharmaceutical targets. In this study, we analyzed the net-zero exchange of free energy between the lipid membrane and rhodopsin, As we have previously demonstrated, rhodopsin activation is related to bulk in flux of water molecules [1]. Our work has further illustrated this phenomenon as well as provided evidence to support the flexible surface model (FSM). The FSM states that changes in the curvature and hydrophobic forces play a role in modulating rhodopsin activation [2]. We created recombinant membranes that coupled rhodopsin activation to changes in the membrane's intrinsic curvature as well as variations of the membrane curvature forces. The proportion of active rhodopsin was measured using UV-vis spectroscopy. We found that a greater ratio of lipids will tend towards greater proportions of active MII. ≈Zero intrinsic curvature favors inactive MI state while negative curvature favors active MII state. In addition, we varied the osmotic stress using hydrophilic polymers. Large osmolytes were excluded from the water pocket and dehydrated rhodopsin, shifting it towards inactive MI. Small osmolytes penetrated the water pocket and hydrated rhodopsin, shifting equilibrium towards active MII. The effects of osmotic pressure outweighed those of membrane curvature forces on activation of rhodopsin. 1. Fried, S.D., et al., Hydration-mediated G-protein–coupled receptor activation. Proceedings of the National Academy of Sciences, 2022. 119(21): p. e2117349119.
2. Brown, M.F., Curvature forces in membrane lipid-protein interactions. Biochemistry, 2012. 51(49): p. 9782-95.

Kay Do – Chemistry #60

Research Faculty Advisor: Elisa Tomat, Chemistry & Biochemistry

Synthetic Modifications and Coordination Chemistry of the Redox-active Tripyrrindione Scaffold

Tetrapyrrolic bile pigments have been a well-studied class of oligopyrroles since their initial isolation in the 19th century. In the structure of these naturally occurring oligopyrroles (e.g., biliverdin, bilirubin), the pyrrole rings are linked by methylene or methine bridges at the alpha position, and the terminal pyrrole rings feature carbonyl groups. Lower-order analogs, such as tripyrrin-1,14-diones and dipyrrin-1,9-diones, are an emerging class of redox-active ligands. The Tomat group has shown the tripyrrindione ligand, a tripyrrolic synthetic analog of the uroerythrin pigment, to coordinate divalent metals, such as palladium(II), as a dianionic radical. Synthetic modifications of the tripyrrindione scaffold are expected to modify the electrochemical profile and coordination chemistry of this ligand. This spring semester, we sought to study the effects of the incorporation of an azulene moiety in place of the central pyrrole ring. The ligand was synthesized through a multi-step procedure including protection, bromination, substitution, condensation, and deprotection. The coordination of palladium(II) within the new azulene-dipyrrolinone ligand was tested under a number of conditions. The structure and properties of the isolated palladium(II) complex are currently being investigated by optical absorption spectroscopy, X-ray crystallography, NMR spectroscopy, and cyclic voltammetry.

Aranea Dunckley - Biochemistry and Molecular & Cellular Biology #63

Research Faculty Advisor: Marielle Walti, Chemistry & Biochemistry

Investigating the Structure and Function of Hsp60

Heat shock protein 60 (Hsp60) functions as a molecular chaperone, playing a vital role in maintaining protein homeostasis by regulating protein folding and preventing protein aggregation. Hsp60 has been implicated in many well-known diseases such as Alzheimer's disease and Type 2 Diabetes. It is crucial to understand what conformations and functions Hsp60 obtains within its folding cycle to determine Hsp60's role in disease pathology. First, we sought to visualize Hsp60's folding mechanisms using advanced techniques, including nuclear magnetic resonance (NMR) spectroscopy and cryo-electron microscopy (cryo-EM). In contrast to its bacterial counterpart GroEL, which is always a stable tetradecamer, Hsp60 can adopt various states and the absence of oligomeric species structures remains a notable gap in our current understanding. Second, we determined the role of the folding cycle structures through functionality assays recording the folding of its natural substrates and ATPase activity. Surprisingly, Hsp60 is also active without its co-chaperone, Hsp10, although to a lesser extent. Understanding the complete folding cycle of Hsp60 will provide valuable insight for developing much-needed biomarkers and eventually drugs for these devastating diseases.

Samuel Durfee – Chemistry #51

Research Faculty Advisor: Jeffrey Pyun, Chemistry & Biochemistry

Molding, processing and analysis of novel optical polymers from Sulfenyl Chloride Inverse Vulcanization

In response to worldwide sulfur production, 60 million tons of sulfur produced annually, sulfenyl chloride inverse vulcanization (SC-IV) was a system developed in the Pyun Group that employs this feedstock for the development of novel materials. One of the most promising candidates from SC-IV is a material dubbed disulfide glass, which shows facile fabrication methods, inexpensive base chemicals, and displays interesting optical, thermomechanical, and chemical properties. We have thereby demonstrated a myriad of processing techniques, such as molding, diamond turning, PDMS casting, and thin film spin coating. From these processing techniques, these samples can be leveraged for many optical purposes with robust properties.

Sam Ellis – Biochemistry and Molecular & Cellular Biology #57

Research Faculty Advisor: Michael Taylor, Chemistry & Biochemistry

Photo-induced Proximity Labeling of Mitochondrial Permeability Transition Pore

This project seeks to investigate the molecular compositions of the mitochondrial permeability transition pore (mPTP) under high Ca 2+ levels. Since the present molecular biology toolbox alone, for example, genetic manipulation, seems to be insufficient to elucidate the components of mPTP and introduce many controversies; thus, we decide to utilize the chemical approach, especially photochemistry and proximity labeling, to identify the overall mPTP configuration. In particular, Trp121 of cyclophilin D (CyPD) will be functionalized with a synthetic hetero-bifunctional pyridinium probe upon irradiation with LED green light to install a reactive warhead that can be used in subsequent photo-proximity labeling. After initiating mPTP with adenine nucleotide translocase (ANT) inhibitor, carboxyatractyloside, its overall configuration will be captured in a single snapshot upon irradiation with UV light as the activated warhead moiety on CyPD will conjugate to any proteins in very close proximity. The cross-linked proteins will be pulled down and identified via tandem mass spectrometry, Western Blot, and/or co-immunoprecipitation.

Luke Fasse – Chemistry #47

Research Faculty Advisor: Thomas Gianetti, Chemistry & Biochemistry

Separation of Helical Enantiomers

Helical molecules have demonstrated a spin selectivity effect when used as an electron transport medium. The helical conformation of these molecules favors a spin state of the electron and has presented a promising avenue for spintronics applications. To fully understand and harness the chiral-induced spin selectivity effect it is essential to separate helical enantiomers. This separation allows for a focused study of how the distinct chirality of these molecules influences the spin polarization of charge carriers. Herein, we report the synthesis and characterization of a racemic quinacridinium with the potential to be separated through column chromatography.

Madison Grams – Biochemistry #61

Research Faculty Advisor: Elisa Tomat, Chemistry & Biochemistry

Prooxidant ligand improves the antiproliferative activity of glycoconjugated iron prochelators in ovarian cancer cells

As an important cofactor to many cellular processes, iron plays a crucial role in cancer progression. Depriving cells of iron prevents further growth and leads to cell death. In this work, we describe a new series of iron prochelators with the goal of depriving the cells of available iron and causing oxidative damage. Our studies in ovarian cancer cells show that the lead compound, PH4 binds intracellular iron and alters iron regulatory proteins ferritin H and TFR1. Fluorescence-based assays indicated the increased production of reactive oxygen species (ROS) in cells treated with PH4, and the toxicity of the iron complex of PH4 was found to be dependent on intracellular glutathione concentration. Lastly, we employed a glycoconjugation strategy with our ligand to target cancer cells more directly via the glucose transporter GLUT1, which is overexpressed in many cancer phenotypes. The combination of a prooxidant chelator with a carbohydrate moiety is expected to produce cytotoxic agents of high tumor selectivity.

Megan Hahn – Chemistry and Biochemistry #52

Research Faculty Advisor: Jeffrey Pyun, Chemistry & Biochemistry

Development and Fabrication of High Verdet-Constant nanoparticle-polymer colloid materials for use in magnetic-optic devices.

A main focus of the Pyun group is the development of magneto-optic active materials for use in optical isolators and high-sensitivity magnetometers. Current project efforts are focused on developing cobalt nanoparticle colloids with increased Verdet constant by varying particle size and inorganic content loading. This colloid consists of polymethyl methacrylate (PMMA) grown from the surface of ferromagnetic cobalt nanoparticles, in a process known as surface-initiated atomic transfer radical polymerization (SI-ATRP), to disperse and stabilize the particles. Linear polymer is then doped into the material before spin-coating, in order to control the inorganic loading content. Films have previously been heavily limited by transparency at higher levels of inorganic loading and made with polystyrene. Increased particle sizes, and subsequent magnetic properties, has allowed for greater inorganic loading while retaining transparency. Additionally, switching to PMMA and improved polymerization off of the particles has streamlined the fabrication process by controlling the interparticle distance and inorganic loading in a singular step via SI-ATRP. The use of PMMA, as opposed to polystyrene, in these films with higher inorganic loading due to larger particle size has allowed for the fabrication of spin-coated thin films with Verdet constants in the 106 range, 800x higher than the current industry standard.

Joseph Jung – Chemistry #55

Research Faculty Advisor: Jeffrey Pyun, Chemistry & Biochemistry

Synthesis and Fabrication of Transparent Optical Components for IR Imaging

The polymer poly(S-r-(NBD)2), synthesized from elemental sulfur (S8) and NBD2, has a high IR % transmission in the Long Wave Infrared region (LWIR) compared to current industrially available polymers. It can replace high-cost infrared transparent materials, such as germanium, with affordable plastics that can be used for thermal imaging, night vision, in cars for safety as IR transparent lenses. In this project, the IR % transmission was measured using two different FTIR spectroscopy detectors, Deuterated Triglycine Sulfate (DTGS) and Mercuric Cadmium Telluride (MCT), to compare the signal strength of different IR regions. DTGS is more effective for detecting large elements and a wider spectral region than MCT, however, MCT has a higher specific detectivity ($D*$). High sulfur content poly(S-NBD2) was observed to have the highest % transmission, around 50%, but was unstable, as over time the sulfur crashed out of the sample. Decreasing thickness was also shown to increase transparency. As the amount of sulfur decreases, the IR % transmission was observed to also decrease. The IR % transmission can be predicted because of this relationship. Based on this relationship, the IR % transparency could be controlled by altering the sulfur composition, or reducing the thickness, to have better IR % transmission.

Isaac Kailat – Biochemistry #58

Research Faculty Advisor: Michael Taylor, Chemistry & Biochemistry

Activity-based Lysosomal Sensing

Chemical probes are an effective way to ask questions about how a target protein behaves and functions. This is particularly useful in the context of drug discovery to methodically measure the roles of targeted proteins in healthy and diseased cells. However, the utility of chemical probes depends on being highly selective, not causing deleterious side effects to its target molecule, and detecting a useful change in the neighboring biological environment. Lysosomes, once thought to be solely the cell's recycling center, have been recently implicated in complex signaling cascades that regulate cellular metabolism, homeostasis, and longevity.

My project is to detect intracellular lysosomal activity through fluctuations in the cellular proton gradient, pH. To this end, I have analyzed non-linear laser dyes, namely pyridinium phenoxide betaines, and have adapted these dyes to bioconjugate proteome modification. I have applied organic chemistry techniques, ranging from organometallic chemistry to reverse-phase chromatography, to synthesize these compounds. Subsequently, I have tested the photophysical properties of these probes using UV-visible light spectroscopy. I have performed protein photoproximity labelling experiments that validated that my compounds can detect intracellular pH through deconvolution of protein mass chromatograms. Future work will involve building more sophisticated structure-activity relationship models and in vitro cellular studies, including fluorescence imaging and chemoproteomic analysis.

A possible application of these probes will be to study lysosomes in healthy and diseased cells through activity-based protein profiling. The goal of these probes is to investigate the "dark proteome", i.e.: proteins with poorly defined and understood structure or function. Specifically, this project could be used to better understand diseases with abnormal basal lysosomal activity, such as pancreatic adenocarcinoma, as well as the mechanism of lysosome-targeting therapeutics, including siramesine and next-generation antibody-drug conjugates.

Caleb Konecek – Biochemistry; Molecular & Cellular Biology; Spanish #67

Research Faculty Advisor: Pascale Charest, Molecular & Cellular Biology

Role of Rap1 in Regulating mTORC2 Function in Breast Epithelial Cells

Chemotaxis is a fundamental cellular process that plays a critical role in immune responses to external stimuli. However, disruption of chemotaxis can lead to cancer metastasis and cardiovascular diseases, but the disruption process isn't yet fully understood. The mechanistic Target of Rapamycin Complex 2 (mTORC2) comprises network of proteins that have implications in regulating chemotaxis through the organization of cytoskeleton structural proteins. Despite the recognized implications of mTORC2 in chemotaxis, little is currently understood about its precise role and regulation. Recently, we have discovered that Rap1, a small GTPase from the Ras superfamily, has a conserved role in cytoskeleton remodeling and cell adhesion and that it serves as a binding partner of the SIN1 component of mTORC2. We also observed increased mTORC2 activity upon overexpression of constitutively active Rap1 in breast epithelial cells. Although both mTORC2 and Rap1 function as positive regulators of chemotaxis, there is a critical gap in understanding how Rap1 mediates the regulation of mTORC2 to promote chemotaxis. Our research attempts to understand the molecular mechanisms supporting the regulation of chemotaxis by mTORC2 and Rap1 to offer insights into disease processes such as cancer metastasis. The aim of the experiment is to define how Rap1 helps to regulate and localize mTORC2 in MCF10A and HEK293 breast epithelial cells. We hypothesize that membrane-bound Rap1 proteins influence mTORC2 activity by helping it localize to the plasma membrane. Our research so far has indicated that expression of overactive Rap1 upregulates mTORC2 activity as observed by an increase in mTORC2-specific phosphorylation of AKT.

Ika Lin – Biochemistry #64

Research Faculty Advisor: John Jewett, Chemistry & Biochemistry

Exploring Caged Diazonium Ions as Fluorogenic Detection Tools

Tailored chemical probes are essential to targeting and reporting on elements of biological environments. While fluorescent probes can provide key spatial information regarding biomolecules of interest (BOI), they can suffer from low signal to noise ratios and encounter specificity issues due to bioaccumulation. Fluorogenic probes present a compelling alternative in that no fluorescence is emitted until the probe is bound to or activated by the BOI, offering additional functional utility. Previous work in the Jewett Group has established protected triazabutadienes (TBD) as effective intracellular delivery mechanisms for highly reactive aryl diazonium ions (ADI) upon protonation. This project aims to functionalize the TBD scaffold with protection groups sensitive to environmental/enzymatic conditions. Once the TBD is fully deprotected in the presence of said environmental/enzymatic factors, the released ADI will cyclize to form a fluorescent benzocinnoline (CinBen) probe. To this end, an unprotected pro-fluorogenic TBD has been successfully synthesized. The structures of the TBD and resulting CinBen were characterized with 1H NMR and fluorimetry. The maximum excitation wavelength of the CinBen is 395 nm, and the maximum emission wavelength is 490 nm; both consistent with literature values. While the unprotected TBD has shown to be fluorescent, it absorbs and emits at different wavelengths than the CinBen probes. Our next steps involve protecting the TBD at two locations to better control its reactivity. A dual-protected pro-fluorogenic TBD holds promise for exploring multiple intracellular conditions at once. Since each logic-gated outcome from fully protected TBD to released CinBen potentially coincides with a different fluorescence, or lack thereof, this enables quantifiable detection of the probe's real-time state. Further work will yield applications for in vivo imaging and enzymatic assays, offering greater insight into biomolecular functions within complex systems.

Jacob Narr – Molecular & Cellular Biology #53

Research Faculty Advisor: Jeffrey Pyun, Chemistry & Biochemistry

Disulfide Glass: A Novel Commodity Polymer to Plastic Optics

The Pyun Group's use of SC-IV (Sulfenyl Chloride Inverse Vulcanization) has led to the development of a novel highly processable high RI (Refractive Index) optical polymer. SC-IV combines sulfur monochloride (S2Cl2), a chemical derived from elemental sulfur (S8) a waste product of oil refining, with inexpensive allylic monomers. The allylic monomer Triallyl isocyanurate (TIC) is used to make high Abbe number thermosets, but the thermosets cannot be solution-processed. Solution-based polymerization allows for control of the reaction through dilution and careful monitoring via NMR and GPC allows for the development of polymeric ink, making it suitable for thin-film fabrication. Having the ability to be fabricated into thin films allows this polymer to have applications in high refractive index coatings, photolithography, and photonic devices.

Delaney Petruzelli – Biochemistry #46

Research Faculty Advisor: Thomas Gianetti, Chemistry & Biochemistry

Synthesis, Characterization, and Application of Pyrene-Functionalized Carbenium

Stable carbenium ions like AzaDiOxaTriAngulenium (i.e. ADOTA) have a diverse range of applications. This family of organic molecule’s properties can be fine-tuned by varying pendant arm ligands and core functionalization's. This combined with their ability to be easily synthesized adds to their promise in varying fields like catalysis and energy storage. Herein, we report a five-step synthesis of a pyrene-functionalized ADOTA (i.e. pyrene-ADOTA) starting from commercially available pyrene and 1,3-dimethoxybenzene. Moreover, we study the photophysical and electrochemical properties and potential applications of the target molecule.

Natalie Rawlings – Molecular & Cellular Biology, Biochemistry #66

Research Faculty Advisor: Andrew Capaldi, Molecular & Cellular Biology

The Quantification of TORC1 Activity using Fluorescence Microscopy

The Target of Rapamycin kinase Complex 1 (TORC1) controls the cellular response to nutrient and stress signals in eukaryotes. TORC1, in turn, is regulated by a multimeric complex known as SEAC in Saccharomyces cerevisiae and GATOR in humans. SEAC/GATOR is critical for cell function and is mutated in many serious, chronic diseases, such as diabetes, cancer, and epilepsy. However, it remains unclear how SEAC/GATOR itself is regulated. Previous research in the lab focused on identifying SEAC/GATOR regulators using a phosphospecific antibody and Western Blotting. In this study, we present a more efficient and accurate method to quantify SEAC-related TORC1 activity using fluorescence microscopy. Specifically, we followed the nuclear localization of two transcriptional factors downstream of SEAC and TORC1; Stb3 and Stp1. These proteins were fluorescently tagged, and their nuclear localization ratio was quantified over time in nutrient deprivation conditions such as nitrogen, glucose, amino acid, and leucine starvation. Specific proteins, Ait1 and Npr2, have been identified as critical regulators within the SEAC interactome, but little is known about their precise regulatory mechanisms. This study presents preliminary data involving the deletion of such proteins and the extent of Stb3 and Stp1 nuclear localization following Ait1/Npr2 deletion. Quantifying the movement of fluorescent transcriptional regulators from the cytoplasm (TORC1 active) to the nucleus (TORC1 inactive) in various starvation conditions reveals the potential for high-throughput protein screening, which could provide insight into the complex regulation of eukaryotic metabolism, growth, and response to external stimuli.

Erin Schuette – Biochemistry #68

Research Faculty Advisor: Jared Churko, Cellular & Molecular Medicine

Promoting embryonic stem cell derived cardiomyocyte maturity by gene editing sarcomeric proteins

The research of cardiovascular disease mechanisms involving cardiac muscle cells has always been difficult given that adult cardiomyocytes (CMs) do not proliferate. Thus, adult CMs cannot be harvested from tissue, reproduced in culture, and experimented on in vitro. However, constant development in stem cell research has created new opportunities for discovery in the cardiovascular field. Human embryonic stem cell derived cardiomyocytes (hESC-CMs) provide an abundant and easily attainable source for modeling cardiac muscle cells in healthy and diseased states. Yet, there are many criticisms regarding the accuracy of hESC-CMs in modeling adult cardiomyocyte phenotypes. My project proposes that knockout of three fetal sarcomeric protein encoding genes will induce increased expression of genes that encode for the adult protein isoforms. When differentiated, a more phenotypically mature hESC-CM line will be created with observable differences in various metrics of contraction force, beat rate, and duration.

Jake Shaw – Molecular & Cellular Biology, Biochemistry #62

Research Faculty Advisor: Elisa Tomat, Chemistry & Biochemistry

Chlorophyll-derived iron sensors for photoacoustic imaging

The presence of iron is essential to the survival of all living organisms. Malignant cells require iron in higher concentrations to sustain increased proliferation rates. Investigating the distribution and trafficking of biological iron is of great interest and may lead to better drug design. We are engineering new sensors exhibiting iron-responsive changes of optical absorption to enable the visualization of intracellular iron by photoacoustic imaging. We have chosen methyl pheophorbide-a (PPA), a chlorophyll degradation product, as an ideal scaffold due to its absorption profile in the near-IR region. We have extracted PPA from Spirulina maxima and through synthetic modification we have installed iron-binding motifs to the macrocycle. To test the suitability of the new constructs as photoacoustic agents, we are studying their optical properties in the absence and presence of iron in aqueous media. Future explorations of these systems may include the evaluation of their potential as photosensitizers and theragnostic agents.

Madeleine Tibayan – Chemistry #48

Research Faculty Advisor: Jeanne E. Pemberton, Chemistry & Biochemistry

Arginine-based Glyonic Liquids from Rhamnolipids

Protic Ionic Liquids (PILs) are a category of salts characterized by melting points below 100℃ and synthesized through Brønsted-Lowry acid-base reactions. Despite their advantageous properties, such as low volatility, air and water stability, and electrical conductivity, the synthesis of PILs can be costly and environmentally concerning. The Pemberton laboratory has recently demonstrated PILs from rhamnolipids, a biosurfactant produced by Pseudomonas aeruginosa, as the anionic component along with amine-based cations. Rhamnolipids, which feature a sugar headgroup and a fatty acid tail, are biodegradable and less toxic than other PILs. The combination of various cations with the rhamnolipid's anionic moiety forms a glyonic liquid (GL) which has been shown to be conductive. Promising applications of GLs include their use in electrochemical devices, carbon capture, and energy storage.

To further assess the properties of glyonic liquids and their future utilization, the densities of five different GLs using monorhamnolipids with cations formed from amines, including ammonia, t-butylamine, n-butylamine, octylamine, and oleylamine, were determined. All densities determined fall within the range of 1.1 - 1.2 g/mL. In addition, a new glyonic liquid was synthesized by employing arginine as a cation, and its properties were

subsequently evaluated. Validation of GL formation with arginine was confirmed through 13C and 1H NMR spectral analysis showing changes in chemical shifts for atoms on both the arginine and rhamnolipids in the GL relative to the native species. Rheology measurements provide quantitative insight into the dynamic viscosity of this GL and reveal a decrease in viscosity with increasing temperature. Furthermore, the addition of very small amounts of water to this GL significantly augments its conductivity and drastically decreases viscosity. These results are consistent with the mechanical properties measured for other glyonic liquids, including those combined with amines. In total, these results indicate that the utilization of arginine offers a fully renewable alternative to previously synthesized glyonic liquids.

Jaden Todd-Nelson – Biochemistry, Molecular & Cellular Biology #69

Research Faculty Advisor: Anita Koshy, Neurology

Investigating the role of a putative copper transporter in the differentiation of Toxoplasma gondii

The Koshy Lab studies the protozoan intracellular parasite Toxoplasma gondii, which is estimated to persistently infect up to a third of the world's population. While these infections are generally asymptomatic, they can have significant pathological consequences for the immunocompromised, such as fetuses or patients with Acquired Immunodeficiency Syndrome. Specifically, our lab studies the mechanisms by which the parasite establishes a latent, often lifelong, infection through encystment in the central nervous system. Some strains of T. gondii are particularly efficient at differentiating within the central nervous system and establishing this latent infection. My project focuses on a gene that is upregulated in one of these efficient strains, when the strain is encysting. This gene has been identified as a putative copper transporter. Using CRISPR/Cas9, the lab generated a strain that lacks this gene (IIΔpCuT) and an ectopically expressed, HA tagged complement strain (IIΔpCuT::CuTHA). Using these two strains as well as the parental strain, my project aims to characterize the specific role this putative copper transporter plays in parasite virulence and encystment in the central nervous system both in vitro and in a murine model.

Matthew Urbanski – Biochemistry #49

Research Faculty Advisor: Robin Polt, Chemistry & Biochemistry

Synthesis of Glycosides for CNS Glycopeptide Drug Development

Goal of the lab, my work in the lab, and future directions. Summary of what I have learned this year along with presenting key findings in lab.

Karen Valencia – Pharmaceutical Sciences #54

Research Faculty Advisor: Jeffrey Pyun, Chemistry & Biochemistry

Synthesis of Solution Processable High Sulfur Content Polymers for Coatings and Photolithography

The Pyun Group is developing new methods for the utilization of sulfur polymers for the fabrication of innovative optoelectronic polymeric devices, specifically for integrated photonics applications. Elemental sulfur possesses many intriguing properties such as high electrochemical capacities and high refractive indices. These properties are highly desirable for applications such as integrated photonics due to sulfur polymer material being inexpensive to synthesize and for having a refractive index (RI or n) ranging between 1.75-2.0 across the visible and IR spectrum. However, sulfur polymers often have limited solubility in the majority of organic solvents, making them difficult to fully solution process into thin film. In this research project, using inverse vulcanized poly(S-r-DIB) material, the procedure was optimized for higher solubility through optimization of polymerization conditions and sulfur copolymer molar mass, followed by multiple rounds of filtration (to remove) residual sulfur. Dichloromethane (DCM) and chlorobenzene were the solvents used for the purification and processing for the ink fabrication. The efficiency of the material can be visually determined by its viscosity, pigmentation, and the spin coating process optimization.

Jamison White – Biochemistry #59

Research Faculty Advisor: Michael Taylor, Chemistry & Biochemistry

New methods for photochemical protein modification

Using organic photocatalysts has been shown to enable the labeling of biomolecules and particular protein amino acids. Here we display new approaches in photochemical modification of biomolecules by engineering a new quinoline-based photocatalyst and thalidomide-ligand-based compound.

English – The End
Afrikaans – Die Einde
Albanian – Fundi
Armenian – Վերջը
Azerbaijani – Son
Basque – Amaiera
Belarusian – Канец
Bulgarian – Краят
Chinese – 结束
Chinese – Jie Su
Croatian – Kraj
Czech – Konec
Dutch – Het Einde
Filipino – Ang Pagtatapos
Finnish – Loppu
French – la fin
Georgian - დასასრული
German – Das Ende
Greek – Το τέλος
Haitian Creole – Nan Fen
Hindi – अंत
Hungarian – A vége
Icelandic – Endir
Indonesian – Akhir
Irish – An Deireadh
Italian – alla fine
Japanese – Owari
Korean –끝
Latvian – Beigas
Lithuanian – Pabaigos
Macedonian – Крајот
Malay – Akhir
Persian - پایان
Polish – koniec
Portuguese – O Fim
Russian – Конец
Serbian – Крај
Slovak – Koniec
Spanish – El Fin
Swahili – Mwisho
Swedish – Slutet
Tagalog - sa katapusan
Thai – สิ้น
Turkish – Sonunda
Ukrainian – Кінець
Vietnamese - Cuối
Welsh - Y Diwed

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