Summer Undergraduate Research Experiences (SURE) 2023 Project Descriptions

Biology

The Center for Genomic Advocacy (Drs. Shaad Ahmad, Kyu Hong Cho, Rusty Gonser, Aaron Gooley, Kris Schwab, and Michael Thompson)

The Center for Genomic Advocacy (TCGA) offers a number of diverse research opportunities. The environment is collaborative with many faculty members working together. Students will first meet with Dr. Gonser, TCGA director (rusty.gonser@indstate.edu), to discuss the TCGA SURE program and their interests and goals in order to match students and faculty mentors. This method has produced a number of collaborative efforts through the years. TCGA usually takes anywhere from 4-12 students, depending on funding availability.

Some of the TCGA projects are listed below:

Dr. Ahmad's lab group is working to understand the roles of Forkhead/Fox transcription factors in heart development and disease. While at least eight Fox domain transcription factors are required for proper cardiac development in mammals, and mutations in four Fox genes have been linked to human congenital heart defects, relatively little is known about the molecular mechanisms or the downstream targets by which these Fox-mediated developmental functions are brought about. The Ahmad Lab previously found and analyzed the *Drosophila* orthologs of Fox genes responsible for proper heart development and has now identified more than 2000 target genes regulated by the *Drosophila* Fox genes. SURE students will attempt to identify the target genes used for heart development by disrupting the individual target genes with mutations. The Ahmad Lab has also identified Zinc finger transcription factor proteins critical for heart development in both humans and *Drosophila.* SURE students will also attempt to pinpoint the specific cardiogenic processes mediated by these Zinc finger transcription factors.

Dr. Cho's laboratory group studies the pathogenic mechanisms of the human bacterial pathogen, Streptococcus pyogenes. The SURE students joining the lab will be involved in investigating how the production of virulence factors such as toxins, capsules, and adhesins are regulated by environmental factors. Second messenger nucleotides play vital roles in the signal transduction pathways that convert external or internal signals into cellular activities. Cyclic di-adenosine monophosphate (c-di-AMP) is a recently discovered one involved in cell growth, survival, and virulence of many bacterial pathogens. Dysregulation of c-di-AMP balance reduces pathogens' survival inside their hosts, indicating that c-di-AMP signaling pathways could be the target for the development of antibacterial agents. A research goal in the Cho lab is to understand the detailed mechanism of c-di-AMP signaling and regulation using *Streptococcus pyogenes* as a model pathogen. *S. pyogenes* is a Gram-positive bacterial pathogen that causes various non-invasive and invasive diseases such as strep throat,

impetigo, rheumatic heart disease, necrotizing fasciitis, and so on. A minimum global burden by *S. pyogenes* infection is estimated over 18 million cases of severe diseases, resulting in over half a million annual deaths. Despite the dire consequences of this pathogen, commercial vaccines are not yet available. Our published studies indicate that c-di-AMP in *S. pyogenes* is required to properly respond to environmental stressors and to exert virulence.

The Gonser lab group investigates genetic and behavioral and evolutionary forces that affect populations. The white-tailed deer project utilized DNA extractions and PCR of microsatellite markers to investigate how annual harvests affect genetic diversity of an putative isolated population in Southern Maryland. The other project involves the polymorphic white-throated sparrow. These ground nesting birds come in two plumage morphs that are determined by their genotype. Furthermore, the different morphs have distinguishable behavior and reproductive strategies. Therefore white-throated sparrows are one of the few species where we can link behavior to genotype. We utilize many research techniques to investigate why the polymorphism is maintained in the species.

The Schwab lab group investigates genetic regulation of mammalian cardiomyocyte differentiation. The development of the mammalian heart requires the step-wise activation of a complex gene regulatory network to specify and differentiate the cardiomyocyte, or heart muscle cell, populations that will generate the contraction force to propel blood through the embryonic, and later, the adult cardiovascular system. Perturbations of this gene regulatory network can cause the developmental malformations in the cardiovascular system that can vary from mild to severe defects. My laboratory is interested in identifying and describing the function of novel cardiac genes that regulate cardiomyocyte differentiation by using 1) high-throughput gene expression data and bioinformatic analyses to investigate cardiac gene expression changes during differentiation, 2) an *in vitro* experimental system that differentiates human pluripotent stem cells (hPSCs) into cardiomyocytes to assess gene function, and/or 3) *Drosophila melanogaster* as model system to study heart development. SURE students will utilize a combination of bioinformatic and molecular biology tools to analyze gene function during cardiogenesis.

The Thompson lab studies the biochemical regulation of inflammation. These studies use a combination of enzyme kinetic analysis, structure/function analysis, and protein-protein interaction techniques to analyze the interaction and regulation of proteins that are involved in regulating the process and mitigating the effects of innate immune responses on normal body cells and tissues. Students joining the lab would be involved in one or more of the following projects: (1) examining the response of several intracellular and extracellular zinc-containing proteases to reactive oxygen-nitrogen species produced during inflammation, (2) determining the effects of protein tyrosine nitration on the enzymatic activity of leukotriene A_4 hydrolase and its role in regulating neutrophil chemotaxis, (3) examining the zinc and iron ion affinity of lactoferrin in the presence and absence of reactive oxygen-nitrogen species, and (4) establishing protein expression and

mutagenesis systems to study the biochemical properties and activation kinetics of pro-MMP-2 and its interactions with other metal-binding proteins.

Dr. Aaron Gooley (aaron.gooley@indstate.edu)
In the Wildlife Ecology & Ecotoxicology Laboratory we use both field investigations and laboratory work to 1) identify and investigate novel ecological questions, 2) develop and test new methods for the conservation of imperiled species, and 3) investigate the impacts environmental stressors on pollinators and other wildlife. Potential topics for SURE participants include investigating a) the impacts of pesticides on pollinators and other wildlife, b) turtle ecology and research techniques, and c) the biology and ecology of wildlife around Terre Haute.

Chemistry

Dr. Rick Fitch (richard.fitch@indstate.edu)
Project 1: Analysis of Bioactive Alkaloids in Poison Frogs. Certain tropical frogs are brightly colored and contain toxic substances, generally alkaloids. We are interested in what alkaloids are present and in what amounts. We have collaborations with two ecology groups looking at frogs in South America and Madagascar. We use Gas Chromatography-Mass Spectrometry and Liquid Chromatography-Mass Spectrometry to identify and quantify these alkaloids. Participants will learn chromatography-mass spectrometry methods, small and large-scale data analysis and automated identification techniques.

Project 2: Synthesis of Poison Frog Alkaloid Standards. Many poison frog alkaloids are not commercially available and we are synthesizing amines similar to these alkaloids to use for quantitation and identification of natural compounds. This involves conducting microscale to prepare a large number (~100-200) analogs for use in quantitative analysis. Participants will learn organic synthesis, purification and identification techniques including chromatography, mass spectrometry and NMR spectroscopy.

Project 3: Mass Spectrometry Imaging of Chemical Compounds in Biological Tissues. A picture is worth a thousand words. The knowledge of the precise location of biologically relevant molecules is of immense importance in biology and medicine. We are interested in imaging biological small molecules in relevant tissues. These include natural products in plants and animals, particularly chemical defenses; neurotransmitters in tissues such as the brain, and dosed drugs to determine distribution and metabolism. Participants will learn mass spectrometry image production and tissue cryosectioning methods.

Project 4: Ligands for Characterization and Purification of Tyrosinase (collaborative with Dr. Flurkey). Tyrosinase is one of a group of oxidative enzymes responsible for browning reactions in foods as well as melanogenesis in humans. We are interested in purifying this enzyme and isoforms using an affinity column, which we will prepare by chemically bonding an inhibitor of the enzyme to polymeric beads. Participants will learn biochemical

assays for inhibition, synthesis of ligands to conjugate to the affinity column, enzyme purification, gel electrophoresis and MS sequencing of purified proteins.

Dr. Eric Glendening (eric.glendening@indstate.edu)
We use computational chemistry methods to explore the structure (geometry) of molecules and to map reaction pathways as reactants are converted to products. Significant advances in resonance theory over the past three years allow us to understand complex systems using concepts that students learn in freshman and sophomore-level chemistry. I seek one or two students to work full-time on the project. Students should have completed CHEM 106 or higher at ISU.

Dr. Justin Miller (justin.miller@indstate.edu)
Project 1: Designing a Biocatalyst for Direct C-H Amination.
The ability of the cytochrome P450 enzyme family to selectively activate inert C-H bonds has opened many avenues in biocatalysis. Recent work has demonstrated that these enzymes can be coaxed from their native hydroxylation reactivity into performing direct aminations. Using a rational-design based approach, we will tinker with the active site of the model P450 CYP101A1 to discern the changes necessary to yield a competent C-H amination catalyst. A collaborative team of students will learn a variety of skills related to bioinorganic chemistry—cloning, site-directed mutagenesis, heterologous protein expression, protein purification, anaerobic protein assays, UV-Visible spectroscopy, computer modeling of protein structure, and conducting *in vitro* assays with gas chromatography and liquid chromatography assessment.

Project 2: Computational Design of Inhibitors for Disease-Associated CYP168A1.
The spread of antibiotic resistance among bacteria is a growing international threat to public health. One strategy for stymying the spread of antibiotic resistance is the development of species-specific antibiotics for common infections. Several bacterial P450s have been implicated in disease states from pathogens such as *Mycobacterium tuberculosis* and *Pseudomonas aeruginosa*, presenting them as targets for selective inhibition. This project particularly focuses on CYP168A1 from *P. aeruginosa*. In preparation for the cloning of this P450 and its partner reductases, *in vitro* assays, and inhibitor screening, the student working on this project with me will identify the likely reductase partners of CYP168A1, develop homology models, and use these models to dock and design inhibitors *in silico*. Besides training in these bioinformatics and computational methods, there will be the option of learning wet lab skills by assisting with Project 1 (see above).

Dr. Rob Noll (robert.noll@indstate.edu)
We are interested in electrochemical cells which can convert thermal energy (heat) into electricity, without the need for external recharging. Such cells can produce electricity

using natural variations in temperature, such as heat from the sun during the daytime and the cool of night. In preliminary theoretical work, we have identified 30 promising half-cell combinations based on aqueous systems. This summer, we will build upon work performed by previous research students to find demonstration cells. I seek one or two students to work full time or half-time on this project, although full-time is preferred. Students should have completed CHEM 106/L.

Dr. Fan Zuo (fan.zuo@indstate.edu)
Electrochemistry and photoelectrochemistry. Research in my group is to design efficient catalysts for energy application. We have a complete set of facilities to synthesize electrocatalysts and study their electrocatalytic H_2 and O_2 evolution efficiency, and investigate the reaction mechanism. Integration with the solar simulator and monochromator, we have the capability to study some key characters for photocatalysts, such as the Incident Photo to Charge Carriers Efficiency (IPCE). Students in our group will learn how to use their chemistry knowledge to produce clean energy through electrical and photoelectrical strategy, and have the opportunity to access the state-of-the-art equipment for energy application.

Earth and Environmental Systems

Dr. Jen Latimer (jen.latimer@indstate.edu)
In the Biogeochemistry Lab, we study how metals and nutrients cycle through the environment. We use samples collected locally (water, soil, sediment) as well as samples collected from across the planet from areas such as the Indian and south Pacific Oceans, Antarctica, and Africa. Projects may focus on modern day pollution and environmental change or past climate change across the ice ages or during the Cretaceous greenhouse world. Students should be comfortable handling chemicals and completion of CHEM105 is a plus but not required.

Dr. Jeffery Stone (jeffery.stone@indstate.edu)
Students who engage in summer research in the Paleolimnology lab study modern lake and river systems or microfossil remains from lake sediments. Student projects can include analysis of modern or fossil diatoms, potentially including either paleoecology, paleoclimate, or taxonomy. Research usually involves some combination of field work, laboratory work (particularly on the light microscope), and some time and training using the Scanning Electron Microscope. Student projects can include materials from lakes around the world (US, Africa, South America, the Himalayas, etc.).

Dr. Jim Speer (jim.speer@indstate.edu)
In the Biogeography and Dendrochronology Laboratory, we work on a variety of projects related to the use of tree rings to date environmental variables and also look at soil microorganisms as a measure of soil health. We have many tree-ring research projects that a student could choose from. We also have an ongoing project to examine soils in the Otter

Creek Watershed related to our IDEM 319 grant to improve agricultural best management practices. This work involves students collecting soils from the field, extracting microorganisms (mites and spring tails) under dissecting microscopes, and imaging them on the Scanning Electron Microscope.

Physics

Dr. Sean Bartz (sean.bartz@indstate.edu)
I am looking for 1-2 students to work on projects in computational physics. Prior programming experience is beneficial, but not necessary. Students will gain experience with python, Mathematica, and parallel processing.

Project 1: Holographic model of deconfinement in quark matter. This is a project in theoretical/computational nuclear physics. We are examining the phase transition between ordinary nuclear matter and the quark-gluon plasma produced in heavy ion collisions, where the protons and neutrons melt at temperatures of a trillion degrees. Only open to full-time students.

Project 2: Computational modeling of collisions of spherical magnets. When spherical neodymium magnets collide, they can stick together and rotate at a surprisingly high frequency. Possible projects may include determining which initial conditions allow the magnets to stick vs bouncing off of each other or determining the frequency where the magnets suddenly stop spinning when in contact with a surface. Open to full- or half-time students.

Dr. Guoping Zhang (guoping.zhang@indstate.edu)
Project 1: Computer simulation of the interaction between amyloid beta plaques in Alzheimer diseases and olecanthal. The student is expected to use the computer program, Gromacs to carry out a massive simulation to understand the interaction between amyloid beta plaques in Alzheimer diseases and olecanthal (from olive oil).

Project 2: All-optical spin switching. This project targets a growing frontier for the magnetic storage devices.

Project 3: High harmonic generation in solids. High harmonic generation in solids becomes a focus of new light source for the future. Students will use some exotic materials to generate strong harmonic radiation.

IU School of Medicine—Terre Haute

Dr. Scott Canfield (sccanfie@iu.edu)
Dr. Canfield's lab focuses on modeling the blood-brain barrier (BBB) utilizing human induced pluripotent stem cells (iPSCs). We have recently obtained Alzheimer's disease

(AD)-derived iPSCs to model the AD BBB. Specifically, we are interested in investigating the effects of anesthetics on the AD-derived BBB. AD patients have been shown to be at an elevated risk of post-operative delirium following anesthesia treatment. Our working hypothesis is that anesthetic exposure is detrimental to critical barrier properties contributing to post-operative delirium in AD patients. A SURE student will be responsible in measuring barrier properties in AD-derived BBB models following exposure to varying anesthetic treatments.

Dr. Américo López-Yglesias (alopezyg@iu.edu)
The López-Yglesias Lab's research is focused on identifying mechanisms of the host innate immune system that are specifically targeted to the protozoan parasite and the causative agent of toxoplasmosis, Toxoplasma gondii. It is currently estimated that a third of human population has been infected with T. gondii. Parasite infection results in persistent cysts that develop in the skeletal muscle, cardiac tissue, and the brain. Regrettably, T. gondii can lead to serious complications including retinochoroiditis, cardiovascular disease, congenital toxoplasmosis of the fetus, and death among immunocompromised individuals. Additionally, recent studies have shown evidence between patients with latent T. gondii infections and increased deterioration of cognitive function. Unfortunately, current treatment regimens are not specific for T. gondii and are unable to eliminate the latent stage of the parasite. A long-term goal of the lab is to Identify unique anti-parasitic functions of the host immune system that are precisely geared toward T. gondii that can facilitate the development of new medicines with enhanced efficacy.
https://lopezyglesiaslab.wixsite.com/2020

Dr. Steven Templeton (sptemple@iupui.edu)
Dr. Templeton's lab focuses on learning about infection with and immune responses to the opportunistic fungal pathogen *Aspergillus fumigatus*. We have recently begun a collaboration with a laboratory at IUSM-Indy, investigating the effects of an antimicrobial electroceutical wound dressing on the growth and survival of filamentous fungi. This project will help to further determine the ability of this experimental material to prevent wound infections with fungal pathogens. A SURE student will work with members of my lab to grow different strains of fungi in the presence or absence of the appropriate dressing, using different techniques to assess the effect on growth and survival.