2019 ABI Summer Internship Mentor List

Synthesis of novel small molecule heterocycles as potent anticancer and antimicrobial agents

In my group, we synthesize small molecules such as pyrazole, thiazole, and androstane derivatives by using readily available starting material and mild reaction conditions. We have generated a library of more than 1,000 novel small molecules to test their potential to treat different diseases. We have found several lead molecules as potent antibacterial and antimelanoma agents.

Students doing their summer research in my group will get the opportunity to learn to synthesize new molecules by using commercially available substrates and reagents under mild reaction conditions. Based on their interest, students will also get the opportunity to test the compounds against different bacterial strains and several cancer cell lines.

My group's research is in consistent with the ABI mission to improve the health of Arkansans through medical research initiatives.

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Volunteer Firefighter Decision-Making: Using Virtual Reality to Analyze the Process

1.) We will be using high-risk fire scene scenarios in a realistic and mobile virtual reality environment to examine volunteer firefighter decision-making. This research will involve an anticipated 100 volunteer firefighters throughout the State of Arkansas as participants. Thus, an intern could greatly contribute to the research by helping to administer the highly immersive, interactive, virtual reality firefighting scenarios to volunteer firefighters. An intern will be use a system that includes an advanced head-mounted device (HMD) for immersive visualization (HTC VIVE), and the use of a Unity3D simulation game engine for facilitating the firefighting scenarios. This will require travel to several fire departments around northeastern Arkansas, mostly weekday evenings or on weekends. It may also require travel to a firefighter conference in Hot Springs, Arkansas.

2.) Should an intern choose to work with me on this project over the summer, they could anticipate learning about the comparative results of cognitive decision-making readiness between volunteer and career firefighters. They could come away with a better understanding of volunteer firefighters' systematic processes of cue recognition identification, situational awareness, and strategic decision-making methods in high-risk fire situations. Lastly, an intern will familiarize themselves with research methods that may be used to examine the effectiveness of incident command decision making in conjunction with decision process tracking and situational awareness measuring technologies.

3.) This research project adheres to the ABI Mission Statement by helping to improve the health of Arkansans through new and expanded…medical research initiatives. Volunteer firefighting is a dangerous occupation, with several dozen killed and thousands more injured every year. It has been estimated that the cost of addressing firefighter injuries and of efforts to prevent them is between $2.8 to $7.8 billion per year.[a] Notwithstanding, few studies exist of how emergency responders make decisions, and yet poor

decision-making is frequently cited as a major contributing factor to firefighter injuries and fatalities. Virtual Reality can help bring "danger" closer to firefighters without putting them physically at high risk. It is hoped that once decision-making processes by firefighters are better understood, decision-making quality may be improved. Thus, the overall enhancement of emergency responders' decisions will certainly offer tremendous benefit to Arkansas firefighters, their families, and the public, in reduced injuries, deaths, and its corresponding medical costs.

[a] National Institute of Standards and Technology. (2004, August). *The Economic consequences of firefighter injuries and their prevention. Final report.* Arlington, VA: TriData Corporation. https://ws680.nist.gov/publication/get_pdf.cfm?pub_id=101312

4.) Dr. Shawn Bayouth, Department Chair
Disaster Preparedness and Emergency Management
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1. **Research Project:**
   Bioproduction of medicinal compounds from plants. The Medina-Bolivar research team is involved in the discovery and bioproduction of bioactive plant compounds with medicinal applications. Our studies utilize "immortalized" root cultures (known as "hairy roots") as factories for a large diversity of plant natural products. Using a combination of molecular, cellular and biochemical approaches, our research team has developed strategies to increase the levels of selected natural products in hairy roots by more than 1,000 times when compared to the parental plant. Students that participate in the ABI Internship Program will work specifically with hairy root cultures of peanut to produce a class of biologically active natural products known as stilbenoids. These compounds have potential applications in cancer, obesity and Alzheimer's disease. The interns will be involved in different aspects of the research including production, analysis and purification of stilbenoids in hairy roots, and assessing their activity in chemical and cellular assays.
2. ABI Mission compatibility:
   The research focus of this internship is on production and bioactivity of novel plant compounds that have potential applications as preventive and therapeutic agents for cancer and obesity. These are major health concerns in Arkansas. To this end, this research adheres to the ABI mission to improve the health of Arkansans through new and expanded agricultural and medical research initiatives.
3. Contributions to the scholarly or creative community:
   Interns will learn the technical skills associated with a plant tissue culture/analytical/molecular and cellular laboratory. These include aseptic techniques, plant tissue culture, analysis of natural products by high performance liquid chromatography (HPLC) and mammalian cell culture. In addition, the interns will learn how to maintain a research laboratory notebook, how to do research as part of a team and how to present the results of their research in laboratory and scientific meetings. The interns will also learn how to communicate their research to the general public.

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1) Research Project

Research in the Xu lab aims to effectively produce recombinant proteins of potential pharmaceutical or industrial applications (e.g., vaccines, interleukins and enzymes) with plant cell/tissue culture. The ABI intern will make two or three gene constructs encoding an important growth factor that stimulates the proliferation and differentiation of human stem cells. The intern will stably transform the gene constructs into tobacco BY-2 cells and characterize the gene expression. The intern will purify the recombinant growth factors from tobacco cell culture media and test their functions.

2) Experience Gained

The intern will learn standard molecular cloning technique; plant cell culture and genetic transformation; recombinant protein detection such as Western blotting and ELISA, mammalian cell culture, etc.

3) Contributions to the scholarly or creative community

My research exploits plant cell/tissue culture as a safe and cost-effective bioproduction "factory" to produce protein therapeutics, such as antibodies, vaccines, interleukins and enzymes. It supports the ABI Mission Statement to "improve the health of Arkansans through new and expanded agricultural and medical research initiatives". Successful completion of ongoing or upcoming projects will facilitate availability of high-quality low-cost protein therapeutics to the state and to the country. Particularly, ABI at A-State selects "Plant-based production of medicinal molecules" as one of major research growth areas and my research projects dovetails nicely with this effort.

Jianfeng Xu, Associate professor, jxu@astate.edu; 870-680-4812 (Tel)

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1.) Research Project

The overall objective of this research is to confirm and characterize phagocytic B cell activity in squamates (snakes and lizards). Circulating phagocytic B cells in squamates would represent a significant opportunity for examining the role and power of innate immunity. The student will be assisting in validating the following assays: 1a) Confirm and characterize B cell activity in squamates and 2b) Determine if the population of phagocytic B cells change under different contexts. This will be accomplished by 1) utilizing the cell sorter/flow cytometer to separate antibody-tagged B cells that have either phagocytized fluorescent beads or have not, 2) visualizing phagocytosis using confocal microscopy, and 3) demonstrating the antimicrobial capacity by observing phagolysosome formation.

2.) Experience Gained

The student will learn multiple techniques: flow cytometry, antibody validation, and laboratory techniques. Students will also experience developing and testing hypotheses, using experimental design, and working with a team to conduct research.

3.) Contributions to the scholarly or creative community

Bioengineering research that expands genetic knowledge & creates new applications in agriculture/medicine Nutrition and other research that is aimed at preventing and treating cancer, congenital and hereditary conditions, or other related conditions

Dr. Lori Neuman-Lee, Assistant Professor, lneumanlee@astate.edu

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1) **Research Project**:

Similar to animals, plants get sick by a variety of microorganism, including fungi, bacteria, virus, and oomycetes (fungi-like organisms). Plants fight against these infections using immune responses that trigger a

resistance against an invading pathogen. The current research project focuses on studying how soybean plants fight against an oomycete, *Phytophthora sojae*, that causes a Phytophthora stem and root rot (PSR) in soybean. When soybeans are resistant to the pathogen, they utilize a single gene mediated detection mechanism that can detect the invading pathogen. However, *P. sojae* can evolve to overcome the detection mechanism by modifying its genes. This avoidance leads to the death of soybean plants, causing an annual crop loss of $200 million in the US alone. The focus of this research is to find novel soybean genes that can be used to fight against *P. sojae*. We will use a combination of cutting-edge bioinformatics, and molecular biology tools for our research.

2) ABI Mission compatibility:
Our research aims to address the ABI Mandated Research Areas 2: Bioengineering research that expands genetic knowledge & creates new applications in agriculture/medicine. Our long-term goal is to utilize cutting-edge computational and molecular biological techniques to strategically decipher the components of signal transduction pathways during biotic stress in soybean. This research will help us to learn the fundamentals of the gene regulations and use this information to create new transgenic plants to maximize yield potential while managing diseases caused by plant pests and pathogens.

3) Contributions to the scholarly or creative community:
Interns will have the opportunity to get exposed to a wide variety of techniques in computational biology, construct development, gene editing, plant transformation techniques, plant pathology, and plant phenotyping. These techniques are high in demand by academia and industry and will prepare interns well for their next career move. In addition, interns will learn how to maintain a laboratory notebook, communicate with other researchers and work collaboratively, and present their research work in various meetings.
Asela Wijeratne– Assistant Professor, Bioinformatics
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Rice Bran Polysaccharides as Dietary Modulators in Innate Immune Responses

My research program investigates nutritional components isolated from rice bran fiber to determine their dietary contribution in healthy colon functioning. This addresses a primary mission of the Arkansas Biosciences Institute at A-State: interfacing AR agriculture and human health. The ABI summer intern will have the opportunity to learn and apply bioanalytical (e.g., chromatography), biochemical (e.g., western blotting), and cell culture bioassay (e.g., TEER) techniques used in my Laboratory. The intern will learn to culture human epithelial cells and test rice bran oligosaccharides with them to determine anti-inflammatory and immunomodulatory responses. The goal for the summer internship will be to gain an understanding of my rice bran nutrition project, acquire hands-on skills in a multidisciplinary research laboratory, and obtain practice with preparing a scientific presentation – all invaluable experience in preparing for future graduate and professional studies. Training from the internship will also enable continuing undergraduate research participation in my Laboratory.
Dr. Brett J. Savary
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Human Computer Interaction interfaces to accelerate drug discovery

Project Lay Abstract:

One of the major goals of my laboratory is to use emerging technologies to enable access to functionally relevant structures of biological systems and provide structural clues towards complex biomolecular interactions. . Recent advancements in 3D printing and the availability of open source computer vision (openCV) tools and microcontroller-based kits for building digital devices and interactive objects that can sense and control objects in the physical world (microcontrollers) has enabled us to generate gaming tools to enhance scientific problems. The purpose of our project is to expose students to the exciting world of protein chemistry using a combination of 3D printed peptide and protein models.

Scientific Abstract:

Structure-based drug discovery of target specific drugs greatly rely on the existence of high resolution X-ray crystal structure of the target proteins. Flexible and dynamic regions including hinges and loops which constitute major protein-protein interaction sites as well as allosteric sites are often beyond the scope of current tools and techniques available for protein folding and modeling. Human ability in recognizing patterns and to solve complex puzzles are far superior to any existing computer program at folding these atypical regions of proteins. We have utilized an unconventional combination of using dynamic three-dimensional protein models as physical human computer interface (HCI) devices and integrated proteomics data to predict flexible and dynamic protein-protein interfaces and allosteric pockets of key regulatory proteins to accelerate compound discovery. To this end, we have successfully utilized 1) Flexible HCI devices to generate an ensemble of dynamic three dimensional structures which includes a subset of biologically active conformations among others (thereby exploring the viable chemical space) and 2) Structure refinement and efficient filtering of biologically active conformations can be accomplished by integrating protein-protein interface and fold proteomics data. Streamlining of HCIguided tools to enable access to dynamic druggable pockets in protein targets will accelerate drug discovery.

What the student would do? (will the flexible and is depending on the students background)

Initial phase will involve students will solve key protein-protein interaction puzzles and identify protein dimer interfaces without prior knowledge about the interactions. Phase-2 will involve picking a protein or peptide and 3D printing them. Phase-3 will involve simulation of protein interactions and learning about the chemistry behind key protein interactions.

Prior Skills and Pre-requisites: NONE (Walk with a curious mind and willingness to collaborate with people)

Alignment with ABI Mission: This multidisciplinary project will enhance the current understanding of protein interactions from multiple dimensions. Expected to increase natural collaborations among ABI students and scientists. Further, this will add structural informatics and biomedical engineering niche to existing and new ABI projects.

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Therapeutic Protein Production using Plants as "Bio-factories"

Undergraduate research scholars joining our lab will be a part of a dynamic research team that includes undergraduate and graduate researchers focused on using plants as "factories" and recombinant DNA techniques to produce animal therapeutic proteins. An important issue in human and environmental health is development of antibiotic resistance that is contributed through the use of antibiotics in livestock production. Our lab team is exploring the utility of plants for producing more targeted protein-based therapeutics as alternatives to antibiotics in controlling disease outbreaks in farmed raised fish (aquaculture) and poultry. Student researchers will have opportunity for hands-on experience using some of the skills and techniques

seen/learned in your lab courses including buffer preparation, pipetting, molecular cloning, PCR, DNA and protein extraction, electrophoresis and animal cell culture. Student scholars are paired with senior researchers in the lab to train in the techniques they will use to carry out their research project. This project aims to contribute innovations to the fastest growing sector of the pharmaceutical market, protein biologics, and thus aligns with several ABI Research Mandate Areas addressing agricultural bioengineering for improved animal health implications and enabling technology that serves an important the aquaculture industry regarded as an important agriculture sector in Arkansas.

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Reports indicate that the No. 1 cause of death in Arkansas, United States and also worldwide is cardiovascular diseases. Dr. V. Raj's laboratory investigates mechanisms of cardiovascular disorders and strategies to improve cardiovascular health. To this end, one of the areas of focus in Dr. Raj's lab is related to role of novel RNA molecules in cardiovascular disorders associated with hormonal abnormalities using advanced biomedical technologies. Drug development studies in collaboration with A-State plant biology is also emerging. Student interns will have opportunities to work in one or more of these projects.

Interns in the laboratory can get exposure to work with cutting edge biological/medical technologies in molecular biology, genetics, biochemistry, physiology, pharmacology, histology, etc. Successful candidates will also learn how to present research findings in professional settings and to general public.

The projects in the laboratory contribute to improving the health of Arkansas through biological, medical and plant-based research initiatives.

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Description of research
After sufficient training, the intern will assist in collecting and analyzing data from Actigraph wGT3x-BT triaxial accelerometers using ActiLife software. All data will be collected from children age 3 – 5 years old attending the programs at the ASU Child Development center. The analysis will consist of validating wear time of the accelerometers and cleaning data files based on exclusion criteria specified by previous investigations. Variables retrieved from this process include the amount of moderate physical activity, vigorous physical activity, sedentary time, as well as estimates of energy expenditure. Additionally, the student will assist with data management strategies and assist in the process of writing scientific research.
What the intern will learn and experience

The intern will learn how to implement valid accelerometer protocols and to manage the large sets of physical activity data that accelerometers provide. Once learned, this skill can be used in nearly any population and is one of the most common methods of quantifying physical activity in the literature.

Relation to ABI Mission Statement

In close relation with the mission of ABI, this project will be used to assess physical activity levels of participants and to search for relationships with other variables such as the child's confidence in performing physical activity. This research ultimately will help provide objective physical activity level targets for preschool age children in northeast Arkansas – a top 5 state for obesity and other comorbidity's. Additionally, these skills could be used in research extending beyond the timeline of this internship.

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The effects of physical literacy, physical activity, and adverse childhood experiences on health-related lifestyles: The PLACES study

Adverse childhood experiences (ACEs) have been recognized as highly damaging to the early developing brain and affect a range of important functions such as learning, adaptation to stress, and adaptation to future adversity. According to a recent Child Trends report, 56% of children in Arkansas experience some form of ACE, much higher than the national average of 45%. However, physical activity (PA), observed as a way to combat the effects of toxic stress on the body, has not been explored to consider long-term beneficial health effects on populations with a high number of ACEs. In fact, physical inactivity during childhood has been shown to predispose children for detrimental health outcomes in both childhood and adulthood. A report funded by the Trust for America's Health and the Robert Wood Johnson Foundation suggested a need for interventions at the early childhood level due to 60% of children from the ages of three to five are cared for in an early childhood education (ECE) facility. The ages of 2-5 are a critical period for establishing healthy habits for PA, since childhood obesity is related with poor academic performance and risk for bullying and depression. By providing physical education to local preschool students, we hope to explore if exercise, recognized as medicine, can improve future health, academic, and social outcomes of youth who have had a difficult start to their lives.

1. <u>ABI Mission compatibility:</u>

By participating in this study, students will gain a better understanding of how the body and brain interact. Students with an interest in exercise science and physical education will experience the implementation of a PA intervention and collect data on how that intervention impacts the cognitive abilities of students. The team will follow the students into later grades and be able to see how the intervention may impact participant behaviors far into the future. Participation in the study will help students explore the booming field of research in PA, and spark expanded curiosity in how such research could affect the undergraduate student's surrounding community.

2. <u>Contributions to the scholarly or creative community:</u>

To date, research in the area of PA has found relationships between PA and health outcomes in adults and youth. However, PA has only been used as a covariate (a variable to be removed to avoid confounding results) when examining ecological impacts on health. Arkansas ranks first in the nation for adult physical inactivity and top ten in the nation for both percentage of adults who are obese and percentage of children who are obese or overweight. Cunningham, Kramer, and Venkat Narayan (2014) found that children who were obese entering kindergarten were four times more likely to be obese in eighth grade. Obesity has a

compounding effect in children and adults as fundamental motor skills are built through the process of PA. Due to having more difficulty with coordination tasks and moving a body through space, obese youth very likely find weight to be a barrier to PA (Malina, 2014).

Inactivity during childhood has been shown to predispose children for detrimental health outcomes in both childhood and adulthood (Clark & Blair, 1988; Durrant, Linder, & Mahoney, 1983). In recent years, research has shown PA to be imperative for, not only curbing the progression of the obesity epidemic, but also improvement of cardio-respiratory health (Donnelly et al., 2016; Martin et al., 2012), cognitive function in children and adults (Loprinzi & Kane, 2015), and improved academic achievement (Blom, Alvarez, Lei, & Kolbo, 2011; Donnely et al., 2016; Fedewa & Ahn, 2011).

The current study is intended to be a continuation of research that is examining the relationship between ACEs and PA. The research group will fill the need for longitudinal research investigating the effect of PA interventions on preschool populations by providing physical education to local preschool students and following the effects of physical education through time. Our findings will dramatically advance our understanding of the relationship between PA and ACEs and possibly provide an intervention to positively impact the health and academic achievement of almost 50% of America's future adults.

3. UG Summer Research Intern:

UG Summer Research Interns will contribute by doing the following:

- Deliver physical education and summer enrichment to students attending summer programming at the Child Development Center
- Assess student motor skill competence and perceived motor skill competence at the beginning and end of summer programming
- Revise and document physical education curriculum that was delivered based on success of delivery and reflection of how content was received.

Experiences of the summer research intern are intended to support future physical educators in gaining knowledge and skills that will be immediately transferrable to the field.

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