WV-INBRE FUNDED PARTNER INSTITUTIONS MENTORS DIRECTORY

FOR

High School Science Educators
2024 SUMMER RESEARCH INTERNSHIP PROGRAM

Offered by the

West Virginia IDeA Network of Biomedical Research Excellence (WV-INBRE)

to be held at the following Institutions:

Bluefield State College
Shepherd University
West Liberty University
West Virginia Osteopathic School of Medicine
West Virginia Wesleyan University

Introduction

The WV-INBRE is pleased to offer summer research internships and fellowships to students, high school science educators, and faculty from colleges and universities and high schools participating in the WV-INBRE program. In 2024, the summer internship/fellowship period for high school science educators will be for as long as 9 weeks between May 30 2024 through July 30, 2024 with the Summer Research Symposium to be held on July 30, 2024 at Morgantown Marriott at Waterfront Place in Morgantown WV. Listed in this directory are WV-INBRE funded faculty members at our partner institutions who have agreed to participate as mentors to HS science educators for the summer internship/fellowship program. In some cases, funding is subject to a mentor's submission for additional grants and the mentor may not be available for an internship. Each mentor has submitted a description of the project(s) that is (are) available to interns and fellows in his/her laboratory. Please review these carefully so that you are aware of what is available for summer projects. Some descriptions are more comprehensive than others; therefore, you may want to contact certain mentors for more detail or to ask for clarifications about the opportunities in their labs. In any case, it is a good idea to speak with potential mentors to be sure you understand what will be expected if you work in his/her lab for the summer.

A listing of mentors with a description of their research and the general area of research is presented on page 3. Mentors and project descriptions begin on page 4. Listed for each mentor is an e-mail address, phone number and, where available, a home-page address. The home-page addresses will allow you to learn about the mentors and their research programs.

Separate application forms for high school science educators are available on the WV-INBRE web site (http://www.wv-inbre.net) at a link under **Internship Programs, then, Summer Program**. **Direct electronic submission is now available and is the preferred method of application. Applications may also be submitted by mail or e-mail.**

For general questions about the internships available to HSTA graduates and the summer internship and fellowship program, or if you have difficulty reaching a mentor, please contact one of the following individuals who are serving as research program coordinators.

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Mentors at WV-INBRE-Partner Institutions with INBRE-Funding

MENTORS AT PARTNER INSTITUTIONS FOR THE 2023-2024 ACADEMIC SCHOOL YEAR AND 2024 SUMMER INTERNSHIP PROGRAM FOR HIGH SCHOOL SCIENCE EDUCATORS AND FELLOWS

Dr. Shinichi Asano
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Overview

Research interests in the physiological functions of muscle, which are altered in numerous pathological conditions. Particularly, smooth muscle function is unique and exciting. I have previous experience in the areas of biophysics/toxicology/physiology and I have utilized acute and chronic disease models such as sepsis, metabolic syndrome, aging and depression.

The goal of my lab is to provide students with a unique research experience in biomedical sciences relevant to their clinical applications.

Dr. Tesfaye Belay
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Research projects at Bluefield State College

Overview

West Virginia–IDeA Network of Biomedical Research Excellence (WV-INBRE) has partnership of science research program at Bluefield State College (BSC). Dr. Belay's laboratory research at BSC focuses on stress, immune system and infection. Another research focus in Dr. Belay's laboratory is investigating *Pseudomonas aeruginosa* adaptation to environmental stress.

Research project #1: How cold-induced stress increases susceptibility to chlamydia genital infection.

Sexually transmitted diseases are of major medical and social importance globally. Chlamydia genital infection is the most common bacterial STD that may cause severe irreversible complications particularly in women. The research area of Dr. Belay's lab therefore focuses on the association of stress to chlamydia genital infection. Current research work in the lab is examining the effect of stress on the pathogenesis of *Chlamydia trachomatis*. Data show, exposure of mice to cold water stress resulted in increased stress hormone production and decreased resistance to chlamydia genital infection during primary infection. Moreover, our results demonstrated that exposure of mice to cold water or restraint stress leads to an increase

in the production of proinflammatory cytokines and nitric oxide or interferon gamma by splenic T cells.

Current and future studies are a) to elucidate the mechanisms of lymphocyte recruitment into infected reproductive tract tissues and assess the effect of stress in the recruitment; b) to analyze the histopathology changes in the genital tract during ascending chlamydia genital infection of the stress mouse model. We hypothesize that cold water–induced chronic stress increases the severity of genital chlamydial infection and tissue pathology by modulating the immune response against Chlamydia.

Research project #2: *Survival of Pseudomonas aeruginosa* in starved conditions

Pseudomonas aeruginosa is well adapted for growth in low nutrient environments, however its ability to survive in these environments is not well investigated. During space flight the immune system is affected and organisms such as *P.aeruginosa* poise a health risk. We recently initiated investigating the viability of *P. aeruginosa* growing in water without nutrients and have observed distinct changes in the morphology or visual appearance of the organisms. Our hypothesis is: Starvation adaptation of *P. aeruginosa* in water results in expression of stress proteins that may enhance long-term existence of the pathogen under nutrition-limited conditions.

Variation in frequencies & intensities of protein bands was observed in response to starvation in water and further characterization of the total profiles in starved and non-starved cells of *Pseudomonas aeruginosa* is underway by Protea Biosciences Inc (Morgantown) using iTARAQ labeling, mass spectometry and Protein Pilot 3.0 software. The identification of proteins will allow further experiments and develop new hypotheses.

Involvement of undergraduate students in research

Student training includes biosafety, keeping records of laboratory supplies and inventory, animal handling and usage for research, basic microbiological methods, tissue culture, basic molecular biology methods (RNA/DNA isolation, regular/quantitative PCR, gel electrophoresis), immunoassays (ELISA) development, and maintaining data in computers. Successful establishment of standard tissue culture for *Chlamydia* inoculation and detection methods in the lab has elevated our capacity for educating and training students in biomedical research. After training, the students are involved in performing experiments by developing hypotheses of their own. Several students have presented posters in several Annual Summer Research Symposiums of West Virginia INBRE, Research Day at the Capitol, in the Annual Biomedical Conference for Minority Students (ABRCMS) (Austin, TX, 2007, Orlando, FL, 2008), and in the American Society for Microbiology General Meetings, Philadelphia, PA, June, 2009 and San Diego, CA, May 23-27, 2010.

Dr. Stuart Cantlay
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Title: Investigating the Morphological Differentiation of *Francisella tularensis*

Francisella tularensis is an intracellular pathogen that causes the rare but potentially lethal infection, tularemia. Exposure to *F. tularensis* can occur when populations are in close proximity to natural hosts such as rodents and arthropod vectors and this highly infectious organism is also considered a risk as an agent of bioterror. *F. tularensis* invades a range of host cells although infection typically involves replication within host macrophages. Pathogenicity involves modulation and suppression of host cell immune responses which is believed to be mediated by components of the bacterial outer membrane. *F. tularensis* is known to enter a viable but non-culturable (VBNC) state but very little is known about this process or the conditions that promote resuscitation. We have generated preliminary data showing that these VBNC cells are able to invade host cells and stimulate pro-inflammatory immune responses in macrophages using *in vitro* assays. Coincident with entry into the VBNC state, we have also shown that *F. tularensis* undergoes a morphological change. This proposal aims to use TEM and live-imaging to fully characterize this morphological differentiation. Cytokine assays and cell invasion assays will be used to analyze the effect this has on the ability of *F. tularensis* to interact with and invade host cells. Finally, proteomic analysis will investigate differences in membrane proteins that may mediate these interactions. This proposal will generate data that will directly enhance our understanding of how cell morphology is modulated in *F. tularensis* and identify potential host cells and molecular determinants of infection of this potential bioterror agent when it has entered a persistent VBNC state.

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Ovarian cancer is the leading cause of death in women diagnosed with gynecological cancers. Despite the improvements of treatment of ovarian cancer, the prognosis and overall survival rates remain dismal. Cisplatin-based combination chemotherapy is the first line treatment for ovarian cancer patients. Although, cisplatin produces good therapeutic response in patients, a majority of the patients relapse and this relapsed tumor is not responsive to chemotherapy. Such sobering statistics define the arena where novel molecular targets and therapies are urgently required to treat this lethal malignancy disease. Several convergent studies show that phytochemicals display robust anti-cancer activity (as single agents or in combination with chemotherapy) in a diverse array of human cancers. Therefore, the identification of novel anti-neoplastic dietary compounds may be a plausible strategy to combat ovarian cancer.

The long term objective of my laboratory is to investigate the anti-tumor activity of bioactive natural compounds including capsaicin (the spicy pungent component of chili peppers) in human cancers. Published data reveal that capsaicin potently decreased the viability of human ovarian cancer cells in cell culture systems. In addition, capsaicin sensitized human ovarian cancer cells towards the growth inhibitory activity of cisplatin. Such findings imply that capsaicin may have potential applications in the treatment of ovarian cancer.

The clinical application of capsaicin as a viable anti-cancer drug remains problematic due to its adverse side effect profile. The administration of capsaicin causes stomach cramps, pain in the gastrointestinal system and a burning sensation in the gut. Such unbearable side effects

have resulted in patients opting out of capsaicin-therapy. Such drawbacks may be circumvented by the identification of non-pungent capsaicin analogs, which retain the anti-tumor activity of capsaicin but lack its ability to produce a “heat-sensation”. Structure-activity relationship (SAR) studies have revealed that the addition of long chain unsaturated fatty acyl groups to the C-terminus of capsaicin yields non-pungent analogs with potent analgesic activity. These capsaicin analogs are referred to as N-acetyl vanillylamide capsaicin analogs (hereby referred to as N-AVAMs). Although the pain-relieving activity of N-AVAMs is well studied, only a few reports have explored the anti-cancer activity of N-AVAMs. The N-AVAM compounds olvanil, arvanil and dohevanil display robust growth-suppressive activity in numerous breast, lung and brain cancer cell lines. The growth-suppressive activity of N-AVAMs have not been studied in ovarian cancer. The present grant aims to fill this void of knowledge.

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Proposed project: The mechanism of erythrocyte invasion by *Francisella tularensis.*

Francisella tularensis is one of the most infectious organisms as inhalation of a single bacterium can lead to a fatal disease referred to as tularemia. It has therefore been categorized by the Centers for Disease Control and Prevention as a Category A biodefense agent. Many seminal studies have shown that the ability of *F. tularensis* to replicate within macrophages is a feature of this organism during infection. Only recently we have appreciated that interactions with non-macrophages are also extremely important during infection as these cells provide a niche for immune protection, proliferation, and other unexplored roles. Although much of the work in the field of F. tularensis has focused on the intra-macrophage biology of this organism, interactions with other cell types have not been thoroughly investigated. We recently showed that *F. tularensis* invades and persists in erythrocytes. This invasion enhances resistance to antibiotics and is involved in the pathogenesis of *F. tualrensis*. In-frame deletion of *yfgL* or *mglA* leads to a significant decrease in erythrocyte invasion. Importantly, both of these genes are essential for the pathogenesis of *F. tularensis* - a finding consistent with data suggesting that erythrocyte invasion is involved in pathogenesis. In the work proposed here, we will compare strains having mutations in these genes with wild-type bacteria to further elucidate the bacterial mechanism of erythrocyte invasion. Invasion of erythorcytes is dependent upon both heat-labile and heat-stable components of serum. Here, we will investigate the role of specific components of serum in erythrocyte invasion by *F. tularensis*.

Students and teachers may participate in the investigation of serum components that contribute to erythrocyte invasion.

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Dr. Holly Racine
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Craniosynostosis (CS) is the premature fusion of one or more cranial (or calvarial) sutures and is a condition of complex etiology. However, the CDC has reported that augmented thyroid hormone, or thyrotoxicosis, during fetal development increases the risk for CS. The pathogenesis of thyroid-related craniofacial anomalies is obscure. It is therefore important that new research efforts aim to fill the gap in knowledge of the molecular and morphological abnormalities with suture development accompanying thyroxine exposure during embryonic development.

The Racine lab working towards the delineation of the molecular details of the thyroid-related mechanisms involved in the pathogenesis of CS. Our lab aims to identify suture specific molecular pathways that are important in enhanced suture closure following thyroxine exposure. We work with animal models as a means for studying the physiological response to *in utero* thyroxine exposure. Both morphology and molecular mechanisms must be taken into account in this project, students working in this lab will therefore be gathering morphological data through histological analyses of the crania, as well as performing western blot analysis and qRT-PCR experiments. These results will be analyzed to determine if the cranial morphology has been altered by our treatment, as well as if the cranial tissues have specific protein or gene expression changes.

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"The habenula (Hb) is a region of the dorsal forebrain comprised of multiple subpopulations of neurons and has a prominent bilateral efferent projection towards the midbrain. This makes the Hb a valuable model for exploring how diverse neural types are generated from a single progenitor population, and how axons are oriented towards their targets. Additionally, the Hb has been implicated in mental health disorders, including drug abuse, addiction, schizophrenia, bipolar disorder, and major depressive disorder. Despite the importance of this brain region, we have only a preliminary understanding of how the Hb is formed and how its axons are directed to connect with their major target. The zebrafish embryo is an excellent model to study habenular development as the dorsal habenulae (dHb) are easily visualized in both live and fixed whole organisms due to their large size, superficial position, and distinct axonal tracts. A single population of dHb progenitors, as identified by their expression of developing brain homeobox protein 1b (dbx1b), have been found to generate all dHb neurons. Shortly after losing dbx1b expression, newly born neurons express a chemokine receptor Cxcr4b, which has been implicated in orienting nascent axons. Our objectives are to determine how this progenitor pool gives rise to the multiple types of dHb neurons and how chemokine signaling influences axon outgrowth. We propose the following aims: Aim 1: Determine how dHb neural diversity is generated from a seemingly homogeneous population of progenitors. In this aim we will investigate if the dbx1b progenitors are a self-maintaining population, or if these cells mature to become neurons. Additionally, we will test if individual progenitors produce neurons of a single subpopulation or multiple subpopulations in the dHb. Aim 2: Investigate the role of chemokine signaling in habenular axon outgrowth. We will explore the respective functions of chemokine signaling ligands Cxcl12a and Cxcl12b in orienting the outgrowth of axons from the dHb. These experiments will use lineage tracing techniques, genetic and transgenic tools, and molecular techniques such as RNA in situ hybridization."

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TITLE: Investigation of genes associated with resazomycin susceptibility

The development of new antibiotics is essential to combat the escalating global health crisis of antibiotic-resistant bacterial infections. The focus of this proposal is on characterizing the mechanism of action of resazomycins, a novel family of antibiotics based on the compound resazurin (Rz). Rz exhibits potent antimicrobial activity against a relatively narrow spectrum of Gram-negative pathogens including bioweapon threat *Francisella tularensis* and multi-drug resistant *Neisseria gonorrhoaeae*. We have identified one resazomycin, resorufin pentyl ether (RPE), that significantly reduces vaginal colonization by *N. gonorrhoeae* in a mouse model of infection. In order to

proceed with further *in vivo* testing of these compounds, the observed mechanism of inhibition by resazomycins must be clearly defined. Through a screen for Rz-resistant isolates of *F. tularensis*, we identified two genes – FTL_1306 (*dipA*) and FTL_0959 (*pilD*) - that were mutated in approximately 50% of the isolates sequenced. Therefore, in this proposal, we aim to determine the role of *dipA* and *pilD* in *F. tularensis* susceptibility to resazomycins. Secondly, we seek to investigate whether genes induced in *F. tularensis* and *N. gonorrhoeae* in the presence of Rz are involved in inhibition of bacterial growth by resazomycins. Understanding the mechanism of action of resazomycins would facilitate further development of these compounds as potential treatments for numerous infectious diseases.

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Project Title: Modeling and Stability Analysis of Mixed Immuno-chemotherapy of Tumors by Impulsive Control

A good mathematical model helps aid cancer research in providing insight into and making good prediction of tumor growth. It may also lead to the development of optimal treatment strategies in a cost effective manner. In this project, a differential equation model describing the effect of tumor cells on the immune response in conjunction with chemotherapies will be formulated. The optimal therapeutic dosage and timing using combination of immunotherapy and chemotherapy in cancer treatment will be identified. The long-term goal of this research is to identify treatments for cancer that combine chemotherapies and immunotherapies more maximum clinical benefit using in silico screening and to expose undergraduate students to contemporary research questions at the interface between mathematics and biology. The objective of this proposal is to investigate in silico the effectiveness of combining anti-CTLA4 (Cytotoxic T-Lymphocyte Antigen 4) therapy (such as ipilimumab) with temozolomide, a chemotherapy drug that alkylates DNA, to reduce tumor growth. The results of this work are anticipated to improve the timing and dosage of combination immunotherapy/chemotherapy regimens for optimal clinical response.

Examples of specific projects for summer researchers: 1). Calibrating model parameters using experimental data. 2). Screening potential treatment strategies in silico. The projects provide opportunity to learn about state-of-the-art techniques (including using computing software in computation and graphing and programming skills) in the use of simulation using examples drawn from every-day society.