

WV-INBRE FUNDED PARTNER INSTITUTIONS MENTORS DIRECTORY

FOR

High School Science Educators 2022 SUMMER RESEARCH INTERNSHIP PROGRAM

Offered by the

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

to be held at the following Institutions:

**Alderson-Broaddus College
Bluefield State College
Shepherd University
University of Charleston
West Liberty 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 2020, the summer internship/fellowship period for high school science educators will be for as long as 9 weeks between May 28 2019 through July 31, 2019 with the Summer Research Symposium to be held on July 30, 2019 at Marshall University in Huntington 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.

Dr. Werner Geldenhuys
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Mentors at WV-INBRE-Partner Institutions with INBRE-Funding

<u>Mentor</u>	<u>Institution</u>	<u>Description of Research</u>	<u>Page #</u>
Dr. Tesfaye Belay	Bluefield State College	Role of stress & susceptibility to infection	4
Dr. Yi Charlie Chen	Alderson-Broaddus College	Effect of plant compounds on Angiogenesis	5
Dr. Tamer Fandy	University of Charleston	Molecular epigenetics and treatment	6
Dr. Joseph Horzempa	West Liberty University	Erythrocyte invasion by <i>Francisella tularensis</i> .	6
Dr. Deanna Schmitt	West Liberty University	Genes associated with resazomycin	7
Dr. James Walters	Bluefield State College	Regulation of lipid absorption	8
Dr. Qing Wang	Shepherd University	Modeling & Stability Analysis of Mixed Immuno-Chemotherapy of Tumors	9

MENTORS AT PARTNER INSTITUTIONS FOR THE 2017-2018 ACADEMIC SCHOOL YEAR AND 2018 SUMMER INTERNSHIP PROGRAM FOR HIGH SCHOOL SCIENCE EDUCATORS AND FELLOWS

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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* pose 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 spectrometry 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. Yi Charlie Chen
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Title: Molecular and biochemical mechanisms of the effect of plant derived compounds on cancer angiogenesis and growth

The main focus of our group is to understand the effect of chemicals and antioxidants found in plants on the growth of the blood vessels (termed as angiogenesis) and tumor in cancers that affect humans. Participants in the INBRE program will work along with faculty and other students to contribute to this INBRE and NIH funded research. Projects range from studying the signal transduction and role of genes, gene knockdown and activation to see their effects on angiogenesis and tumor growth. Our studies are of importance in understanding the role of these genes in signal transduction and in developing novel therapeutic drugs in treating cancers.

Participants will join with an active team of researchers to work with a variety of flavonoids, cancer cells and animal models that mimic the diseases. They will also perform techniques depending on skill levels and interest. On-the-site training will be provided. Techniques include cell growth, cytotoxicity, apoptosis assays, gene transfection and expression, electrophoresis,

immunofluorescence microscopy, luciferase reporter assay, RT-qPCR, ELISA, Western Blotting, tube formation assays and CAM assays.

Dr. Tamer Fandy
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My laboratory focuses on both basic and translational research in the field of molecular epigenetics and experimental therapeutics. I am interested in dissecting the molecular changes associated with drugs that target the epigenome (epigenetic modifiers) and how these changes contribute to their antitumor effect. Current projects in the lab include: Genome wide DNA methylation and histone modifications profiling in hematologic malignancies.

Development of DNA methylation inhibitors.

Development of rational combinations of epigenetic modifiers as antitumor agents.

Investigating the potential of dietary agents that target the epigenome in cancer chemoprevention and therapy.

Dr. Joseph Horzempa
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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. tularensis*. 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 erythrocytes 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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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 gonorrhoeae*. 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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Title: Determining regulation of lipid absorption in vertebrate intestine

Lipid processing within the vertebrate intestine profoundly impacts whole animal metabolism. Dietary lipids are initially absorbed by intestinal enterocytes where they are sorted and packaged en route to the blood. Various subcellular compartments such as lipid droplets (LDs) and cholesterol transport proteins like NPC1L1 have been implicated in this process, but central questions remain unanswered. For instance, how cholesterol is taken into enterocytes and packaged in LDs is unknown. The Walters lab has developed a zebrafish model to track key lipid processing proteins and dietary lipids during intestinal absorption. The larval zebrafish is an ideal model of vertebrate intestinal physiology because the optical clarity of the intestine enables live imaging of lipid absorption in vivo and the availability of genetic tools. Our studies show that cholesterol transport activity into enterocytes increases in response specific dietary fatty acids (FAs) such as oleic acid and palmitic acid that are preferential substrates for the enzyme ACAT which esterifies dietary cholesterol. This response suggests potential signaling mechanism to regulate cholesterol and fatty acid homeostasis within the enterocyte. Our objective is to study the subcellular dynamics of dietary cholesterol uptake and incorporation into lipid droplets as it relates to specific dietary FAs. We propose the following aims. AIM 1: Determine the mechanism whereby fatty acids mediate cholesterol uptake activity into enterocytes. AIM 2: To compare changes in mitochondrial gene expression patterns during different dietary challenges. AIM 3: To compare changes in enterocyte transcriptomics before and during a high fat challenge. This study will increase our understanding of clinically relevant therapeutic targets of lipid uptake and metabolism which impact cardiovascular, diabetic, and hyperlipidemia outcomes.

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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.