

# **WV-INBRE FUNDED PARTNER INSTITUTIONS MENTORS DIRECTORY**

FOR

**2009-2010 HSTA GRADUATE AND  
2010 SUMMER RESEARCH INTERNSHIP AND  
FELLOWSHIP PROGRAM**

Offered by the

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

to be held at the following Institutions:

**Alderson-Broaddus College  
Bethany College  
Bluefield State College  
Concord University  
Fairmont State University  
University of Charleston  
West Liberty University  
West Virginia State University  
West Virginia Wesleyan College  
Wheeling Jesuit 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 2010 the internship/fellowship period will be from June 14 through August 13, 2010 with the Summer Research Symposium to be held on July 29th at West Virginia University. Listed in this directory are WV-INBRE funded faculty members at our partner institutions who have agreed to participate as mentors in the summer internship/fellowship program. 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 **2009 Summer Program**.

**Applications must be submitted by mail or e-mail; direct electronic submission is not available.**

For general questions about 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 summer research program coordinators.

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

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## **MENTORS AT PARTNER INSTITUTIONS FOR THE 2010 SUMMER INTERNSHIP PROGRAM FOR HIGH SCHOOL SCIENCE EDUCATORS AND FELLOWS**

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### **Molecular Modeling of Cytochrome P450 2C9 and Substrate - Effector Binding.**

The research being conducted in this lab incorporates molecular modeling and kinetic analysis of cytochrome P450. The modeling studies allow us to look at the enzyme that metabolizes various drugs, with and without drugs in the active site. The cytochrome P450 is one of the major enzymes in drug metabolism within the liver. It has been shown that dapsone increases the metabolism of flurbiprofen, this is referred to as atypical kinetics. We are researching the hypothesis that the metabolism of the drug in the enzyme may be controlled by a second drug called an effector within the same active site. Studies using distances and hydrogen bonding of key amino acids as indicators along with correlation with kinetic data will provide us with a clearer picture of the mechanism of action of this enzyme as related to atypical kinetics.

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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 our laboratory is investigating bacterial 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 therefore focuses on the association of stress to chlamydia genital infection. Current research work in my laboratory focuses on examining effect of stress on the pathogenesis of *Chlamydia trachomatis*. Our

laboratory has developed a stress mouse model in which susceptibility to infection, changes in stress hormones and immune responses are major areas of interest to investigate.

Future study is to assess modulation of the immune response over the course of chlamydia genital infection of cold-stressed mice: 1) to assess T helper 1 (Th1) cells and immunoglobulin A (IgA) and IgG responses in the genital tract of stressed mice during chlamydia genital infection; 2) to examine differential gene expression kinetics of proinflammatory cytokines, chemokines and toll-like receptors in the genital tract of stressed mice intravaginally infected with *Chlamydia trachomatis*

### **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. We will identify and characterize the genes and proteins involved in long-term existing ability of *P.aeruginosa* under starvation conditions.

### **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, quantitative PCR, gel electrophoresis), immunoassays (ELISA) development, and maintaining data in computers. Successful establishment of standard tissue culture for Chlamydia inoculation and detection methods has elevated our capacity for educating and training students in biomedical research. After training, the students will be involved in performing experiments. Several students have presented posters in the annual conferences of West Virginia Coober/INBRE, WV Undergraduate Research Technology and Research (STaR), Annual Biomedical Conference for Minority Students (ABRCMS) (Austin, TX, 2007, Orlando, FL, 2008), and in the General meeting of American Society for Microbiology, Philadelphia, PA, June, 2009.

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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.

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### **Bioactive Natural Products from Appalachian Flora**

The focus of the Crick research group is the discovery of novel bioactive compounds from natural sources that can serve as lead compounds for new medicinal agents. Initial studies targeted isolation of compounds from plants with a history of medicinal use while more recent investigations have involved microorganisms, particularly fungi, that are associated with bioactive plants. Species for study are selected using a combination of ethnobotany and genetic relationships to species that have exhibited activity in the NCI anti-leukemia screen. Compounds possessing anti-cancer activity are of most interest but antimicrobial and antioxidant activities are also under investigation.

Three projects are available.

### **Structure elucidation of bioactive compounds from *Euonymus* and *Euphorbia* species**

The project involves purification of milligram quantities of triterpenes from *Euonymus* species and diterpenoid compounds from *Euphorbia* species followed by structure elucidation using multi-dimensional NMR techniques and high-resolution mass spectrometry. Collection of spectroscopic data is completed in collaboration with nearby research institutions.

### **Bioactivity-guided fractionation of organisms with potential medicinal properties**

Extracts will be prepared from selected species of plants and microorganisms and evaluated for anti-cancer, antimicrobial and antioxidant activity. Extracts from active species will be further fractionated using a variety of chromatographic techniques to yield purified compounds for structure elucidation and activity assay against human cancer cell lines.

## **Isolation and culture of microorganisms from plants and other natural sources**

Microorganisms associated with bioactive plants or from other sources with a high potential for bioactivity (i.e. fungicolous fungi) will be isolated and cultured using standard microbiological techniques. Preservation of cells and DNA samples will be conducted to permit culture of large samples and species identification of those microorganisms that are determined to produce novel, useful compounds. Endophytic fungi from bioactive plants are of particularly interest due to their extensive history of bioactive compound production.

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## **Role of USF-1 in Cholesterol and Triglyceride Synthesis**

Familial combined hyperlipidemia (FCHL) is one of the most common genetic lipid disorders in patients diagnosed with coronary artery disease (CAD). Patients with FCHL have elevated levels of both triglycerides and cholesterol. The long-range goal of this investigation is to gain a better understanding of molecular and cellular events that lead to deregulation of cholesterol and lipid concentrations which can lead to atherosclerosis in these individuals. The overarching objective of this study is to define the involvement of the transcriptional regulator Upstream Stimulatory Factor 1 (USF1) in cellular events involved in the development and progression of this disease. The connection between USF1 and FCHL is strong since USF1 is known for its role in regulation of lipid metabolism genes. The central hypothesis of this project is that USF1 is a key regulator of cholesterol and triglyceride synthesis and that defects in its function or expression will result in significant increases in cholesterol and triglyceride levels. This hypothesis will be tested to accomplish the objective of this application by examining the role of USF1 in regulating the expression of lipid metabolism genes by altering USF1 levels in vitro in cultured vascular endothelial and aortic endothelial cells.

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## **Title of Abstract: Steroid Hormone-Responsive Gene Expression in Meningioma**

Abstract will be forthcoming in updated directory.

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## **Mechanotransduction, Intracellular Signaling, and Vascular Cell Biology**

My research group is interested in how cells are able to sense and respond to changes in their environment. We are especially concerned with how smooth muscle cells in blood vessels perform their important functions. Cells of the cardiovascular system are continuously exposed to the effects of mechanical forces such as stretching and fluid shear stress. These forces, which are created by the pulsatile nature of blood flow when the heart contracts and relaxes, have a marked influence on cell structure and function. Our primary concern is in how these cells are able to detect external forces and then to transmit the appropriate signal through chemical pathways inside the cell so that it can respond. We hope to not only work out what signaling pathways are involved but also to see if we can manipulate these signals to perhaps alter how the cell responds. The adaptations of these cells, which include enhanced growth and migration, seem to be important in the pathological conditions that accompany cardiovascular diseases such as atherosclerosis and hypertension.

### **Research Summary**

Cardiovascular disease remains a major cause of morbidity and mortality in the US and the economic and human costs associated with pathologies such as atherosclerosis, hypertension and restenosis are enormous. This has resulted in an intense research interest in the mechanisms which regulate contraction, migration and growth of vascular smooth muscle cell (VSMC). While it is now clear that mechanical forces imposed on VSMC in the vessel wall are important factors in the initiation and progression of these changes, the molecular mechanisms involved in these adaptations are not fully understood. In addition, it is now clear that the basic mechanism of smooth muscle contraction can only be explained in light of extensive remodeling of the cytoskeleton within cells. However, the exact nature of cytoskeletal reorganization and the mechanisms regulating these changes are not well known. The main goal of this project is to elucidate the acute response in cytoskeletal reorganization and intracellular signaling and during mechanical stress of VSMC. Utilizing molecular approaches combined with fluorescence microscopy, my lab evaluates the role that various cytoskeletal structures play in the response of VSMC to stretch. We are attempting to make a systematic determination of effects of various types of mechanical stress on activation of cell signaling molecules. In addition we are working to evaluate the effects of resveratrol, a purported cardioprotective molecule for its potential effects on stretch-induced cell signaling and receptor mediated cellular hypertrophy. The knowledge gained may be useful in the development of therapeutic agents regulating mechanotransduction mechanisms contributing to cardiovascular pathologies.

## **Student/ Teacher Involvement**

There are currently two on-going research projects in my lab:

### Study 1: Determine the effects of static stretch, cyclic unidirectional stretch, cyclic multidirectional stretch, and fluid shear stress on activation of cell signaling molecules.

Cells in the blood vascular system are subjected to a three main types of flow-related forces: fluid shear stress caused by friction between blood and the vessel wall, static stretch created by hydrostatic pressure, and cyclic stretch which is due to the pulsatile nature of blood flow. Perhaps due to the fact that VSMC normally are protected for the effects of shear, very little data is available. However, vascular interventions such as balloon angioplasty and stent implantation denude the endothelium and thus expose underlying SMC to effects of blood shear stress.

To our knowledge, there has been no systematic investigation of the effects of different types of mechanical stress in the same type of cell. Accordingly this study involves a systematic study of four major types of mechanical stress in the same cell line and carefully controlled experiments using the same techniques of sample collection, analysis, and cell passage number.

### Study 2: Determine the effect of different levels of resveratrol on cell signaling associated with stretch induced changes in morphology and chemically induced hypertrophy.

Resveratrol (RV) is a natural compound that is associated with several positive health benefits including protection from cardiovascular disease. RV is found in high concentrations in the skin of red grapes and is a constituent of red wine. The consumption of red wine in France has been suggested to account for the so-called "French paradox", the observation that many French citizens suffer a relatively low incidence of coronary heart disease, despite having a diet relatively high in saturated fats. It is clear that RV has a number of effects on cell biochemistry that is of particular relevance to vascular smooth muscle. Accordingly, this study focuses on the dose-dependent, time-dependent effect of RV on stretch-induced changes in cell morphology and receptor mediated hypertrophy.

## Laboratory Techniques

The research projects in my lab utilize several techniques including basic animal cell culture, mechanical stretching of cells, RNA isolation, cDNA synthesis, microarray analysis of gene expression, and real time PCR. In addition we use immunocytochemistry and fluorescence microscopy to visualize the cytoskeleton and other structural components within individual cells. Participants will be afforded the opportunity to learn these techniques.

## **Recent Undergraduate Projects**

Effect of Unidirectional Stretch on Vascular Smooth Muscle Cell Structure and Function. Brent Pressman. SURE Research Symposium. WVSU. July 2009.

Gene Expression Profiling in Mechanically Stressed Smooth Muscle Cells. Phillip R. Jones. 14<sup>th</sup> Annual WVSU Research Symposium April 2008.

Response of Smooth Muscle Cells to Cyclic Versus Static Stretch. Niki Davis. 14<sup>th</sup> Annual WVSU Research Symposium April 2008.

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**Investigation of Interactions Between Lycopene and Docetaxel in Prostate Cancer.**  
**Michelle L. Herdman, University of Charleston School of Pharmacy.**

Lycopene, a red pigment carotenoid found in foods such as tomatoes, has been investigated as a preventive agent for prostate cancer. In addition to possibly reducing the risk of prostate cancer, in vitro studies have shown that lycopene also causes cell death in prostate cancer cell lines, indicating that lycopene could possibly be used therapeutically. Few studies have investigated how dietary supplements/herbal medicines and conventional chemotherapy agents interact at the cellular level, and we have found no studies specifically using lycopene and docetaxel in prostate cancer. In this study, we propose to investigate if lycopene and docetaxel act synergistically (or additively) to more effectively kill prostate cancer cells, and which cell death pathways these two compounds are activating. By determining these drug interactions, we can begin to establish the underlying mechanisms of a potential new treatment regimen for prostate cancer. Lab techniques include cell culture techniques, cytotoxicity assays, protein gel electrophoresis, and Western blotting. Other techniques will be added as the project warrants. *(Supported by NIH Grant 5P20RR016477 to the West Virginia IDeA Network for Biomedical Research Excellence)*

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**Isolation and characterization of novel antimicrobial and cytotoxic compounds from non-tradition sources.**

In my lab we are looking at non-tradition sources for antibacterial and anti-cancer compounds and trying to develop new ways to figure out how these compounds function. Currently, we are using the common bachelor button (a garden flower) and mangrove seedlings (a tropical tree) as sources for anti-bacterial and anti-cancer compounds. Our goal is to isolate novel compounds that can be used as models for the construction of new antibiotics and cancer therapies. We are also looking at a respiratory pigment from the keyhole limpet (a marine mollusk), keyhole limpet hemocyanin which has previously been shown to kill cancer cells. Unfortunately, the no one knows how this compound kills cancer cells. We are using the round worm, *C. elegans*, as a genetic model to determine the cellular target of keyhole limpet hemocyanin. We are currently focused on the neurotransmitter serotonin signaling pathway as a target.

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### **Characterization of Prostate Cancer Cell Lines for DNA Repair Enzyme Genotype.**

Prostate cancer, the leading cancer and second-leading cause of cancer death in men, is often researched in established prostate cell lines. These cells have been characterized for many key molecules, including androgen receptors and DNA repair enzymes. However, the characterization is mostly limited to mRNA and protein expression. Because methods of detecting mRNA or protein may target sites different from those effected by DNA mutations, mRNA or protein detection does not guarantee normal protein function. Therefore, the presence of the protein does not represent the absence of modifying DNA mutations. Publications reporting results of treatment of mutated cells with drugs or supplements that are dependent on functional protein products of the mutated genes, may be erroneous. If the cell line DNA carries a mutation, the effect of the drug observed in the cell line may be very different than the effect that would be observed in a normal cell with DNA that does not carry that mutation. Likewise, the results could not be generalized to humans in the absence of knowledge of their genotype. Therefore, characterization of the genotypes of key proteins in established cell lines is important to the future of pharmacological and pharmacogenomic research using those cells. Much research has examined 3 “classic” prostate cancer cell lines, LNCaP, DU 145 and PC-3, and DNA repair enzymes. The goal of this project is to genotype the classic cell lines for 10 mutations in DNA repair enzyme genes that have been reported to modify prostate cancer risk.

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### **Neuroendocrine Changes During D-Cycloserine Enhanced Treatment for Acrophobia**

D-Cycloserine (DCS) is an NMDA partial agonist with demonstrated enhancing effects of exposure therapy for specific phobias. The current proposal will built on an existing collaborative project between University of Charleston (UC) and WVU-Charleston Division. The UC team will be involved in additional analyses of blood samples collected as part of a trial conducted by Dr. Sirbu and Dr. Kerr at WVU-Charleston Division “D-Cycloserine as Enhancer of One-Session Treatment for Fear of Heights in Adults”.

The main aims of the current proposal are: (1) to study the stability of a new formulation (50 mg) for D-Cycloserine (DCS) capsules and to analyse the *in vitro* dissolution of these capsules; (2) to develop a sensitive and reproducible analytical method for determining the plasmatic DCS

concentration and based on it to investigate the bioavailability of DCS during a three hour exposure treatment and (3) to determine the changes in the plasmatic concentrations of beta endorphins, ACTH, and cortisol during the three hour exposure treatment.

The study will provide important stability and bioavailability information regarding a new formulation (50 mg capsules) for DCS. Blood samples will be collected during the exposure treatment for 80 patients involved in the clinical trial conducted at WVU-Charleston Division. The assessment of changes in concentration for beta endorphins, cortisol and ACTH during treatment will provide important data about neuroendocrine mechanisms of exposure therapy for specific phobias.

The PI and his team will conduct stability and bioavailability studies for DCS and will analyze changes in the plasmatic concentrations of cortisol, adrenocorticotrophic hormone (ACTH) and  $\beta$ -endorphins in blood samples. A lot of emphasis would be given to the analytical method development for the DCS, cortisol, ACTH and  $\beta$ -endorphins. For the analytical assay development, we would be using HPLC (high performance liquid chromatography) and ELISA (enzyme linked immunosorbent assay) as the analytical tools.

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### **The Molecular Actions of Statins**

Ischemic heart disease is the generic designation for a group of closely related syndromes resulting from myocardial ischemia-an imbalance between the supply and demand for oxygenated blood. Up until recently, the disease was believed to be due to reduction in coronary blood flow due to atherosclerotic coronary artery obstruction. Now we know it is much more complicated. The disease of atherosclerosis is now thought to include endothelial cell response to injury and has been compared to chronic inflammation of the vascular wall. It appears that lipid-laden macrophages brought to the vascular wall due to endothelial activation play a role in the stability of the atherosclerotic plaque; rupture of the plaque due to release of matrix metalloproteinases from the macrophages results in exposure of the subintimal space which results in thrombus formation and obstruction (1). Recently, it has been shown that statins, which are used to treat high LDL levels, also lower inflammation of the vascular wall independently of their lipid lowering effects (2). Our long-range goal is to uncover the molecular mechanisms of endothelial cell and macrophage activation by mildly modified LDL (LDL) and to determine whether statins inhibit this activation. One available project is determining which cytokines (involved in cellular recruitment) are stimulated by LDL and subsequently inhibited by statins. Another available project is looking at the interaction of Human Aortic Endothelial Cells and Macrophages.

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**Title of Abstract: Expression and Functional Studies of *Burkholderia cenocepacia* LlpE**

Abstract will be forthcoming in updated directory.

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### **Kaempferol Induces Apoptosis in Ovarian Cancer Cells**

Ovarian cancer is one of the most significant malignancies in women. Prevention and early-diagnosis of ovarian cancer has been difficult due to unknown risk factors and a lack of specific biomarkers. To prevent continuous growth of early-stage and symptom-free ovarian tumors, an effective, non-toxic, convenient, and affordable agent is desired for chemoprevention. Kaempferol is a natural flavonoid that is widely distributed in fruits and vegetables including tea, strawberry, and broccoli. Our early studies have indicated that kaempferol inhibits angiogenesis and is a good candidate for chemoprevention of ovarian cancers. Our recent data also suggested that in addition to angio-prevention, kaempferol executes direct effect on ovarian cancer cells and induces apoptosis. In this research project, we propose to further investigate kaempferol's direct effects in inducing apoptosis in ovarian cancer cells, and the underlying mechanisms / pathways for kaempferol's effects. Both intrinsic and extrinsic pathways for apoptosis will be investigated for kaempferol treatment, and p53 gene will be knocked down with siRNA to learn whether kaempferol-induced apoptosis is p53-dependent. Signaling molecules including Akt and ERK will also be studied and manipulated by plasmid transfections. By acquiring more information on kaempferol's direct effect on apoptosis, together with its known effect on angio-prevention, this proposed study will have a dietary flavonoid better characterized and pave the way to potential chemoprevention of ovarian cancers with kaempferol in animal models or human trials in the future.

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**Synthesis and Characterization of C8-Guanine Modified DNA lignonucleotides  
To Study B form to Z form Transitions in DNA Secondary Structure**

The synthesis of modified DNA to study the effect of the change for anticancer and antiviral uses is an area of high interest. In particular modified nucleosides are used in oligonucleotides to serve as models for the changes that occur in DNA during carcinogenesis. Aryl hydrazines, known carcinogens, cause production of C8-aryl substituted purines. Specifically, research on C8-substituted guanines has been done as a model for the effect of chemical carcinogens like N-acetylaminofluorene to study conformational changes in DNA secondary structure caused by the base modification. These changes are similar to the effect of mutations on DNA from cancer.

The secondary structure of DNA is B form under normal physiological conditions. The A form can occur under higher salt concentrations or lower hydration. The Z form is rarer and is a left handed double helix, unlike the B or A forms. The Z form happens in regions of high occurrence in GC base pairs and under higher salt concentrations of the solution. The interest in Z form comes from studies that have shown Z DNA may play a role in regulation of gene expression and cell transformation. Specifically, during replication the DNA changes from B to Z form and then back to B when done. A cancer cell which is always replicating, may be one stuck in Z form. The conditions and modifications that favor Z form are therefore important. The synthesis of C8-arylguanine nucleosides is the focus of this project. They are incorporated into a DNA oligomer and then the conditions studied by NMR and CD for the transition from B form to Z form.

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**Title of Abstract: Inhibition of metastasis via stomatostain signaling in breast cancer lines**

Abstract will be forthcoming in updated directory.

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**Title of Abstract: Allelic Exchange Mutagenesis of Motility Genes in *Borrelia burgdorferi***

Lyme disease is the most prevalent vector borne disease in the United States today affecting more than 27,000 people in 2007. *Borrelia burgdorferi*, the causative agent of Lyme disease, is a member of a unique group of bacteria called spirochetes. Due to their unusual morphology in which flagella are located in the periplasm rather than externally, spirochetes have a specialized motility that allows them to traverse highly viscous gel-like media, such as that found in the extracellular matrix of host connective tissue. Furthermore, it has been demonstrated that spirochete motility, provided by rotation of periplasmic flagella, is necessary for virulence. To better elucidate the role of spirochete motility in virulence, basic research is required to understand the structures and regulation of gene products involved in motility and chemotaxis. Thus far, the overall structure and function of periplasmic flagella were determined to be similar to flagella of other bacteria. However, mounting evidence suggests that the regulation of periplasmic flagella synthesis differs markedly from the regulation of flagella synthesis in other bacteria. It is our goal to continue examining the structure and regulation of periplasmic flagella in *B. burgdorferi*. As a genetic system is currently in place to inactivate motility and chemotaxis genes, construction of knock-out mutants in this organism will allow for detailed examination of the role for specific gene products in spirochete motility. Research students are encouraged to participate in these studies by engaging in projects involving vector design, DNA manipulation, bacterial cell culture, and various methods for evaluating mutant phenotypes including microscopy and immunoassays. Again, because spirochete motility contributes to virulence, a thorough understanding of basic spirochete biology may provide valuable insight for treatment or prevention strategies for Lyme disease.

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**Title of Abstract: In Vitro Evaluation of Antisense NF- $\kappa$ B microspheres during Inflammation**

Abstract will be forthcoming in updated directory.

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**Area of research: Cancer**

**Title: Homer2 as a suppressor of filopodia formation and cell invasion.**

Filopodia and lamellipodia are extensions of the plasma membrane that are associated with cell motility, and are implicated in invasion by cancer cells. Their formation involves rearrangement of actin filaments through the interaction of a host of actin-binding proteins. Included in this group is the actin filament associate protein AFAP1, an adaptor protein that links the protein kinase C-alpha and src signaling systems. Although it is generally accepted that AFAP1 is a src activator, the mechanism by which src activation leads to filopodia formation is not fully understood. The regulation of AFAP1's ability to activate src may be a key event in filopodia formation. A yeast two hybrid study to identify binding partners of AFAP1 indicated that Homer2 as a strong binding partner.

Homer2 is an adaptor protein that is widely expressed in organs and tissues. Originally called cupidin because of its binding affinity with a numerous proteins, it is known to interact with actin filaments and has been demonstrated to inhibit filopodia formation in HeLa cells expressing active Cdc42. The goals of my research are to investigate the nature of AFAP1/Homer2 interactions with regard to src activation and filopodia formation.

There are four projects that are currently available in my lab. The student or faculty member who chooses any of these projects will learn cell culture, cell transfection, western blot analysis and fluorescence microscopy techniques.

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**Finding New Medicines for Bacterial Infections and Cancer Through the Isolation of Novel Biologically Active Natural Products from Plants.**

We seek to discover new medicines through the discovery of novel structural templates. One such technique is to search for new biologically active compounds from plants. Plants have long been known to be a rich source of important medicines. Compounds such as Taxol from the bark of the yew tree, digitalis from foxglove, and Aspirin from the bark of the willow tree are just three prominent examples. We have begun the process of isolating anti-bacterial and cytotoxic compounds from the propagules of the red mangrove tree and also from the common

flower *Centaurea cyanus* (bachelor button). We were led to the potential for activity in the red mangrove through a partnership with the University of Belize and based on its use in folk medicine in that region. Other species from the genus *Centaurea*, that are endemic to Greece, have recently been reported to contain some anti-bacterial and cytotoxic compounds. Gratifyingly, we have antibacterial and cytotoxic activity in the crude ethanol extract from the red mangrove propagules. Anti-bacterial and cytotoxic activity has also been found in the ethanol extract of the flowering parts of *Centaurea nigra*, a locally growing invasive flower. Cytotoxic activity only has been found in the ethanol extract of *Centaurea cyanus*.

We have begun fractionation of these different sources by silica gel flash column chromatography. Our next step is to further separate each of the fractions using preparative high pressure column chromatography (HPLC). We have obtained a brand new, state of the art, preparative HPLC instrument for this purpose. The instrument is controlled by a computer. The operator need only inject a solution of the initial fractions and utilize the correct method on the computer. The operator will collect fractions by watching the increase or decrease in UV absorbance on the detector, which utilize UV spectrophotometry. The fractions will then need to be condensed using a rotary evaporator before being submitted for additional biological testing. Active fractions will be once again separated on the preparatory HPLC, although the method on the computer will be modified to accomplish further separation. This project can be accomplished by someone with no previous chemistry experience. Familiarity with computers is a plus.