

LIST OF AWARD RECIPIENTS
UB2020 RESEARCH AND DEVELOPMENT ACTIVITIES FUND (IRDF)

**Corresponding Investigators
and Co-Investigators
November 2007**

“Defining Cytokine Signaling by Mass Spectrometry”

Corresponding Investigator

Sarah Gaffen
Oral Biology
School of Dental Medicine

Co-Investigator

Troy Wood
Chemistry
College of Arts and Sciences

Project Description

Autoimmune diseases such as rheumatoid arthritis (RA) and Crohn’s Disease are characterized by immune-mediated pathology, which in large part are mediated by pro-inflammatory “hormones” termed cytokines. Indeed, many drugs used to treat autoimmunity act by neutralizing cytokines or their receptors. **Exciting new advances in the field of immunology have identified a new cytokine that appears to play a major role in driving autoimmunity, termed “interleukin-17” (IL-17).** Blocking IL-17 or its receptor (IL-17RA) dramatically reduces symptoms in animal models of autoimmunity including rheumatoid arthritis (RA), and antibodies to IL-17 are currently in clinical trials for treatment of RA. However, little is known about the molecular mechanisms by which IL-17 causes inflammatory pathology. Dr. Gaffen’s lab (Dept of Oral Biology) has recently demonstrated that IL-17 turns on inflammatory genes by activating a cellular transcription factor protein termed “C/EBPbeta.” Dr. Troy Wood’s lab (Dept. of Chemistry) has used sophisticated chemical technique called mass spectrometry to show that IL-17 rapidly triggers a chemical modification of C/EBPbeta in which a phosphate group is added to a specific amino acid residue on the protein. The purpose of this application is to characterize in detail the biochemistry and kinetics of C/EBPbeta phosphorylation and also to identify the cellular enzymes that mediate this modification. Ultimately, understanding precisely how IL-17 controls gene expression through C/EBPbeta may lead to new therapies for treating autoimmunity.

“Determining Best Practices for Treating Ankle Sprains”

Corresponding Investigator

John Leddy
Orthopedics
School of Medicine and Biomedical Sciences

Co-Investigator’s

John Marzo

Orthopedics
School of Medicine and Biomedical Sciences

Dale Fish
Rehabilitation Sciences
School of Public Health and Health Professions

Albert Vexler
Biostatistics
School of Public Health and Health Professions

Program Description

Ankle sprains are among the most common orthopedic injuries to athletes, military personnel, and the general population. Even relatively minor ankle sprains severely limit the physical capacities of athletes and military personnel for days, and more severe sprains can compromise function for weeks or even months. Despite the frequency and impact of ankle sprains, medical practitioners have not determined optimal treatment programs. Sprains are currently treated with variations on a single theme, RICE (rest, ice, compression, elevation), and sometimes with other interventions such as anti-inflammatory drugs, electrical stimulation, or exercises. While symptoms of sprains can be effectively treated with RICE, there is no evidence from controlled clinical trials that this management practice affects rate of recovery of normal function. *Indeed, the efficacy of current management practices for sprains used worldwide, relative to controls (i.e. no specific treatment), is completely unknown, so 'best practices' do not and cannot exist.* We propose to determine whether current management practices for sprained ankles improve recovery to function in a military population.

Broader implications:

Determining whether current management practices for ankle sprains actually work is important because these same practices are applied to all joints (e.g., knees, shoulders, wrists) that sustain sprains and strains. Military personnel, athletes and others who desire or require as rapid a return as possible to physically demanding activities following such injuries will presumably benefit the most from this research, but anyone of any age, gender, or vocation who suffers such an injury could potentially benefit from this research.

“Identification of Novel Antimicrobial Targets in Acinetobacter”

Corresponding Investigator

Thomas Russo
Medicine
School of Medicine and Biomedical Sciences

Co-Investigator's

Timothy Umland
Structural Biology
School of Medicine and Biomedical Sciences

George DeTitta
Structural Biology
School of Medicine and Biomedical Sciences

L. Wayne Schultz
Structural Biology
School of Medicine and Biomedical Sciences

Program Description

Acinetobacter is a bacterium, which until recently was best known for causing a variety of health-care associated infections. Most recently a new series of infections due to Acinetobacter has been reported in U.S. service members injured in Iraq and in Afghanistan. Particularly disconcerting is the degree of antibiotic resistance possessed by these strains of Acinetobacter; with some being resistant to all commonly used antibiotics tested. Needless to say, treatment of infections due to Acinetobacter has become challenging and the need to identify new antibiotics active against Acinetobacter is more pressing than ever. Unfortunately, there are virtually no new antimicrobial agents active against bacteria such as Acinetobacter in the pharmaceutical antibiotic discovery “pipeline”. The goal of this project is to fill that void by using a novel approach to logically identify new, conserved antibiotic targets in Acinetobacter. Subsequently compounds that interact with these targets will be identified and will serve as the basis for developing new antibiotics active against Acinetobacter. This project is possible because the unique skill sets of the collaborating investigators present at the University at Buffalo. Dr. Russo from the Center of Excellence in Bioinformatics and Health Sciences and the Department of Medicine brings his experience with bacterial genetics, molecular biology, and ex vivo and in vivo model systems to the project. Whereas Drs. DeTitta, Umland, and Schultz, from the Department of Structural Biology at the Hauptman-Woodward Medical Research Institute, possess the necessary expertise in bioinformatics and crystallography. Together this team of researchers hopes to solve the important problem of maintaining treatment options for bacteria that are highly resistant to antibiotics.

“Renal Stem Cells for Regenerative Therapy”

Corresponding Investigator

Mary L. Taub
Biochemistry
School of Medicine and Biomedical Sciences

Co-Investigator

James Springate
Pediatrics
School of Medicine and Biomedical Sciences

Project Description

Regenerative therapy of renal disease may be achieved through the use of adult as well as embryonic stem cells. Despite efforts to identify stem cells in the kidney, adult renal stem cells have not yet been successfully cultured, nor have renal stem cells been used successfully for therapy. The kidney consists of thousands of nephrons which are involved in reabsorbing solutes from the blood. Each nephron is composed of a number of nephron segments. Of particular interest to this proposal is the renal proximal tubule. A number of inherited and acquired renal diseases affect the renal proximal tubule, including cystinosis (an autosomal recessive disorder). In this proposal, we will examine the hypothesis that renal stem cells from the rabbit kidney can be selectively cultured in hormonally defined serum free medium, and used to restore normal function to cystinotic tubules.

The expansion of renal somatic stem cells, will entail enrichment procedures (somatic stem cells are rare in adult tissues), including, 1) their resistance to drugs, including mitoxantrone, based upon the expression of a drug resistant transporter in somatic stem cells, and 2) the ability of stem cells to grow in medium with low a calcium concentration.

Renal stem cells will be employed to alleviate cystinosis in vitro. The disease will be produced in vitro by using small interfering RNA. Renal stem cells will be studied in 3 dimensional cultures with renal tubules that have cystinosis, in addition to in vivo experiments.

“Multilayer Polymer-Clay Nanoassemblies”

Corresponding Investigator

Marina Tsianou
Chemical and Biological Engineering
School of Engineering and Applied Sciences

Co-Investigator

Rossmann F. Giese
Geology
College of Arts and Sciences

Project Description

The design of functional, nanostructured hybrid materials inspired by biology is emerging as a major research focus because of their promising applications in the advanced materials and biomedical fields. In this project, we will capitalize on the Layer-by-Layer assembly (a method of depositing multilayers at the molecular level and in a controlled manner) using non-toxic, biocompatible and/or biodegradable polymers and clays (natural materials) as building blocks to generate new nanostructures. The multilayer assemblies may be stabilized by electrostatic and/or hydrophobic interactions, hydrogen bonding, or covalent bonding, depending on the nature of the building blocks used. The resulting materials can show an exceptionally broad range of structural characteristics and thus unique functional properties, different from those of the individual building blocks of which they are composed. This project will undertake (i) the investigation of interactions between polymers and clays in aqueous solution, (ii) the development and optimization of multilayer assemblies composed of the above, and (iii) the evaluation of the structural characteristics and properties of these nanocomposites, and their sensitivity to external stimuli (especially important in biological applications) The successful completion of this project will enable the fabrication of unique bio-nanomaterials with thicknesses and properties which can be controlled with high precision. These materials can be suitable for biomedical applications (e.g., as scaffolds for protein adhesion, cell growth, and delivery).

“Neurophysiological and Behavioral Characteristics of Heavy Drinkers & Aggressive Drivers”

Corresponding Investigator

Changxu Wu
Industrial and Systems Engineering
School of Engineering and Applied Sciences

Co-Investigator's
Rebecca Houston
Research Scientist
Research Institute on Addictions

Project Description

Aggressive driving and drink/driving are two major factors in traffic accidents. Accordingly, this study considers four groups of drivers: aggressive driver/heavy drinkers, non-aggressive driver/heavy drinkers, aggressive driver/social drinkers, and non-aggressive driver/social drinkers. Although current intervention and treatment programs for problem drivers may address these aspects, it is likely that they focus on these factors as state conditions (i.e., behaviors conducted 'in the moment') as opposed to trait-like aspects of the individual. Studies of individuals with a pattern of heavy drinking (or alcohol dependence) have repeatedly demonstrated deficits in neurocognitive domains, some of which may be relevant for driving behavior.

Individuals with a history of aggressive behavior have shown similar impairments (Houston et al., 2003). Thus, the current study is designed to examine the potentially interactive effects of these two factors on neurophysiological (event-related brain potentials; ERPs) and behavioral measures during a driving simulation task. Moreover, the following quantitative methods will be used to enhance the practical application of the experimental data: 1) computational model of these four groups of drivers will be built and verified by the experimental results; based on these models, driver-adaptive workload management system (Wu et al., 2007) will be designed to optimize the workload of these drivers and improve transportation safety in real time; 2) statistical modeling methods will be used to proactively classify these four groups of drivers based on the relative objective performance and event-related brain potential (ERP) data rather than subjective reports or post-hoc traffic violation tickets.