

Summer Research Experience for Undergraduate Students

Hosted by the Center for Protease Research and:
Chemistry and Molecular Biology
Pharmaceutical Sciences
Veterinary and Microbiological Sciences
Biological Sciences

Information and Application Process

Completed applications must be received by March 1, 2009

Women, minorities, and students from other under-represented groups are especially encouraged to apply.

Please send applications and direct inquiries to:

Rose Nichols, Administrative Coordinator
Center for Protease Research
NDSU Dept 2735
PO Box 6050
Fargo ND 58108-6050

Tel 701-231-6114
Fax 701-231-1057
rose.nichols@ndsu.edu

Your submission should include the 3-page application (Word and PDF formats available on the web at www.ndsu.edu/cpr) and a copy of your current college transcripts. Also, arrange to have two letters of recommendation sent directly to the address above (email preferred.)

PROGRAM DESCRIPTION

The Center for Protease Research is pleased to offer qualified undergraduate students an opportunity to carry out state-of-the-art hands-on scientific laboratory research during the summer. Students will receive a stipend of \$4000 for the 10-week program, and on-campus housing will be provided. **The summer of 2009 program will run from May 26 through July 31.**

Students will be paired with a participating faculty mentor and be immersed in an independent research program. Students will participate fully in the daily life of their respective research laboratories. Weekly seminars, informal research meetings, and trips to related industries are planned along with a number of social activities. The summer program will conclude with a symposium where the students will present the results of their efforts in poster sessions and/or oral presentations.

Please review the available summer projects summarized below. For additional information on the Center's goals and facilities: www.ndsu.edu/cpr.

ELIGIBILITY

Requirements for students interested in participating in the CPR Summer Research program at NDSU:

- Completed at least their freshman year (by May 2009) and have, as a minimum, completed college-level general chemistry and biology.
- Required minimum GPA of 3.0 out of 4.0.
- Students must be approved to work in the USA.
- Students who will be graduating in spring 2009 are not eligible.
- A *limited number* of openings are available to NDSU students.

Students are expected to dedicate their time to the research program. Therefore, participants may not enroll for summer courses or accept other employment during the 10 weeks of the program.

APPLICATION: Applications must be received by March 1, 2009.

To apply to the CPR Summer Research Experience for Undergraduates program, send the following:

- completed application form (3 pages), see www.ndsu.edu/cpr
- a copy of your current transcripts
- arrange for two letters of recommendation to be sent directly to the Center

PROJECT DESCRIPTIONS

Please review the project descriptions below to determine which labs you may be interested in. Summary table of the faculty who will be participating in the 2009 program:

Faculty	Discipline
Gregory Cook	Organic Chemistry
Glenn Dorsam	Molecular Biology
Bin Guo	Cancer Biology
Jane Schuh	Immunology
Peggy Biga	Inflammation
Kendra Greenlee	Immunology
Chengwen Sun	Pharmaceutical Science
John McEvoy	Microbial Pathogenesis
Rajesh Murthy	Organic and Analytical Chemistry
Jodie Haring	Immunology and Molecular Biology

Dr. Gregory Cook, Associate Professor Dept of Chemistry and Molecular Biology

The research efforts in our group are directed toward the development of new reactions that will assist us in the synthesis of biologically important molecules. Our synthetic targets include compounds that are found in nature, as well as unnatural compounds, which display potential therapeutic properties. Some of the disease states that we emphasize are cancer, HIV, arthritic, and other autoimmune diseases.

Dr. Glenn Dorsam, Assistant Professor Dept of Chemistry and Molecular Biology

Our research investigates the signaling pathways that regulate mRNA expression of vasoactive intestinal peptide receptor-1 (VPACR-1) in murine, primary CD4 T cells. VPACR-1 is an anti-proliferative, G-protein coupled receptor that is highly expressed on naïve T cells, but is downregulated upon activation. To date, the T cell signaling molecules involved in mediating VPACR-1 downregulation have yet to be identified. Splenic CD4 T cells isolated from C57BL/6 mice by magnetic beads (Miltenyi) were pretreated with several pharmacological inhibitors and activated with plate bound anti-CD3 for 24 hrs. Total RNA was isolated, and VPACR-1 mRNA levels were measured by qPCR. Our results show that the JNK MAPK pathway downstream from src kinases Fyn/Lck is involved in TCR-induced VPACR-1 downregulation. Preliminarily, the adaptor molecule, Zap70, and the JNK upstream G-protein signaling molecule, Rac1, also appear to downregulate VPACR-1. Surprisingly, we did not collect evidence to support other MAPK pathways, such as Ras→PKC→ERK and p38, as having roles in downregulating VPACR-1. Furthermore, two other common T cell signaling molecules, calcineurin and PI3-K, were not statistically involved in VPACR-1 regulation. By studying the signaling pathways that regulate VPACR-1, we can gain greater insight into the role of this receptor in infectious disease, autoimmunity and T cell biology.

Dr. Bin Guo, Assistant Professor Department of Pharmaceutical Sciences

Matrix metalloproteinases (MMPs) are promising targets for cancer therapy. Research in Dr. Bin Guo's lab studies how MMP-9 regulates prostate cancer apoptosis by regulating TGF-beta. The objective of this project is to define the role of MMP-9 in prostate cancer apoptosis and how the effects of MMP-9 change along with prostate cancer progression. We will use molecular and cell biology techniques to determine how MMP-9 regulates apoptosis in prostate cancer cells and investigate the effects of MMP-9 in different stages of prostate cancer. At the completion of this project, we expect to clarify the role of MMP-9 in apoptosis regulation in prostate cancer and how this role may change in relation with the changes of TGF-beta signaling. This will help optimize the future design of clinical trials with MMP-9 inhibitors.

Dr. Jane Schuh, Assistant Professor Veterinary and Microbiological Sciences

Research Interests: Immunology; biomedical significance of the initiation and maintenance of allergic asthma; the immune response to mold in health and disease; murine models of human asthma.

Asthma is a chronic lung syndrome that affects over 20 million Americans and costs nearly \$18 billion annually. Allergens commonly trigger asthma in sensitized individuals, and airborne fungal spores are of distinct concern. Mold allergens are ubiquitous in the environment, but can be a particular problem in chronically damp indoor environments or in post-flood clean-up. Our laboratory focuses on the assessment of innate, acute, and chronic lung responses that occur during the evolution of fungus-induced airway inflammation. Our laboratory uses experimental animal models (mice) to assess the role of various cells and mediators during the initiation, maintenance, and resolution of the pulmonary immune response. We are predominantly interested in chronic lung remodeling, a common and irreversible outcome of allergic asthma.

Dr. Peggy Biga, Assistant Professor Department of Biological Sciences

Obesity and type II diabetes exhibit very complex pathophysiology, which include increased gluco- and lipotoxicity, excessive fat storage in muscle tissue, and increased systemic inflammatory responses. It is unclear what role inflammation plays on muscle tissue locally, and

if there is a direct inflammatory cell infiltration into the skeletal musculature following high-fat dietary intake. Also, a negative muscle growth regulating gene, myostatin, has recently been implicated in regulating dietary-induced diabetes and it is possible that there is a link between myostatin and inflammation. This summer we will be evaluating the presence of inflammatory cells in skeletal muscle tissue in response to high-fat dietary intake and stress. We will utilize molecular and hormonal approaches to evaluate the localization of myostatin and inflammation markers in muscle tissue. This work will lead to a better understanding of how muscle tissue can resist increased lipid load without becoming glucotoxic.

Dr. Kendra Greenlee, Assistant Professor Department of Biological Sciences

Insects are the most numerous and diverse animals on our planet, yet we know little about their basic functions. Insects are remarkably tolerant of exposure to low oxygen, yet the mechanisms by which they accomplish this are not well understood. In our lab, we study the respiratory physiology of insects at the molecular, cellular and whole organism levels. One class of proteins commonly expressed in respiratory systems is the matrix metalloproteinases (MMPs). MMPs are a large family of enzymes known to degrade most cellular components. In addition, MMPs are important modulators of leukocyte functions such as cell migration and adhesion. As such, MMPs are critical for proper immune responses in animals, and their dysregulation can contribute to pathology observed in several human diseases. MMPs have been discovered in numerous invertebrate taxa, including insects, and there is strong evidence for their role in the responses to hypoxia and immunity and their importance during molting. We are characterizing the function of these proteins and others in response to hypoxia, infection and throughout development in the tobacco hornworm caterpillar, *Manduca sexta*, using flow cytometry, histology, zymography and western blotting. We use real-time PCR to investigate gene expression patterns. We also use respirometry and synchrotron x-ray imaging to quantify gas exchange in developing caterpillars.

Dr. Chengwen Sun, Assistant Professor Department of Pharmaceutical Sciences

The research in our laboratory is focused on central blood pressure regulation and pathogenesis of hypertension to identify new targets for the treatment of hypertension and other cardiovascular diseases. Then, based on the molecular structure of these target proteins, we are going to develop novel therapeutic agents for the treatment of those deadly diseases.

The project that summer students will be involved in is to identify a new target for the treatment of hypertension: Angiotensin-converting enzyme 2 (ACE2). ACE2 is a novel zinc metalloprotease that cleave Angiotensin II to form Ang (1-7). Our previous studies have demonstrated that ACE2 expression in a brain cardiovascular regulatory region is decreased in SHR, a hypertensive animal model and that over-expression of ACE2 in this brain region with viral vector-mediated gene-transfer technique decreased the blood pressure in SHR. Based on these evidence, we hypothesized that decreased expression of ACE2 in the RVLM contributes to the development of hypertension. The aim of current investigation is to determine the role of ACE2 in the brain in blood pressure control and in pathogenesis of hypertension by answering the following questions: 1) whether ACE2 expression is decreased in brain cardiovascular regulatory regions in hypertensive animal models. 2) whether selective silencing ACE2 gene expression in brain cardiovascular regions could induce hypertension, 3) what is the consequence of ACE2 over-expression in BP regulation; 4) what is the neuronal mechanisms underlying the actions of ACE2.

To answer those questions, multiple levels of techniques will be used in our laboratory: 1) In vivo animal surgery: radiotelemetry (to monitor blood pressure in conscious rat), physiological recording system (to record ECG, blood pressure, blood flow, sympathetic nerve activity, and cardiac function), brain microinjection system (to central drug-delivery). 2) In vitro: cell culture and patch clamp technique to study the molecular and intracellular mechanisms; 3) Molecular levels: to detect the gene-expression (real-time PCR, Western Blots, Immunohistochemistry) and to construct gene-transfer tools for silencing ACE2 or over-expression of ACE2 (gene therapy).

Dr. John McEvoy, Assistant Professor Veterinary and Microbiological Sciences

Cryptosporidium is an obligate intracellular parasite that causes cryptosporidiosis, an infectious disease affecting humans and animals for which there is no effective chemotherapeutic

treatment. Cryptosporidiosis is especially severe in immunocompromised persons, such as those with AIDS, where diarrhea can become chronic and life threatening. As an obligate intracellular parasite, invasion of host cells is critical to the success of *Cryptosporidium*; yet, current knowledge of invasion mechanisms is limited. Using data from sequenced *Cryptosporidium* genomes, and knowledge gained from related parasites, *Toxoplasma* and *Plasmodium*, our lab is focused on characterizing mechanisms of attachment, motility and invasion. Students this summer will gain experience in a number of research techniques including, bioinformatics, cell culture, extracting and purifying RNA, and quantifying gene expression by quantitative real-time reverse transcription PCR.

Dr. Rajesh Murthy, Research Scientist Core Synthesis Facility

The Core Synthesis Facility was established to act as a strong in-house support system, so as to facilitate principal investigators in accomplishing their research targets. The research in this facility is primarily focused on organic synthesis of small molecules for biomedical applications and analytical characterization of substrates of interest. The chemistry involves fluorescent tagging of peptides/amino acids, developing a library of HDAC inhibitors and building an anti-cancer drug delivery model system. The analytical part includes analysis of samples by HPLC and LC-MS. On the whole, the core synthesis facility's research is dedicated towards the treatment of autoimmune diseases.

Dr. Jodie Haring, Research Assistant Professor Core Biology Facility

Students working with Dr. Haring will gain considerable knowledge of molecular biology techniques while studying gene expression in yeast, tissue culture cells, and primary mouse lymphocytes. Target genes of interest are involved in cancer, and adaptive immune responses to bacterial infections. Techniques that will be used in these research projects include tissue culture, nucleic acid isolation, reverse transcription, PCR, quantitative PCR, and multi-parameter flow cytometry.

For more information on the Center and these researchers, please visit our web site at: www.ndsu.edu/cpr.

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