School of Medicine Basic Science Departments
Faculty Project Descriptions for the
Undergraduate Honors Program
May 2010

Devendra K. Agrawal, Ph.D. (Biomedical Sciences)

Jason C. Bartz, Ph.D. (Medical Microbiology & Immunology)

Michael Belshan, Ph.D. (Medical Microbiology & Immunology)

Ming Chen, M.D. (Medical Microbiology & Immunology)

Shashank Dravid, DVM, Ph.D. (Pharmacology)

Kristen Drescher, Ph.D. (Medical Microbiology & Immunology)

Richard Hallworth, Ph.D. (Biomedical Sciences)

Laura A. Hansen, Ph.D. (Biomedical Sciences)

David He, Ph.D. (Biomedical Sciences)

Thomas F. Murray, Ph.D. (Pharmacology)

Kristina Simeone, Ph.D. (Pharmacology)

Timothy Simeone, Ph.D. (Pharmacology)

D. David Smith, Ph.D. (Biomedical Sciences)

Garrett A. Soukup, Ph.D. (Biomedical Sciences)

Faculty Project Description

Faculty Name	**Devendra K. Agrawal, Ph.D.**
Department	**Biomedical Sciences**
Office Location	Criss II, Room 510
Telephone Number	280-2938
Email Address	dkagr@creighton.edu
Source of Research Support	NIH; State of Nebraska LB506 and LB692

Overview of Scholarly Research Activities:

1. **Pathophysiological Mechanisms of Allergy and Asthma and Development of Better Therapeutic Approaches**: A widespread inflammation in the lung of patients with bronchial asthma is a common finding. An allergic patient, upon exposure to an allergen such as cockroach and house dust mite, feels difficulty in breathing due to increased mucus secretion and increased susceptibility of the airways to constrict, which restrict the airflow and develops the clinical symptoms of asthma. The research efforts in my laboratory are focused to delineate the underlying pathophysiological basis of allergic asthma at the cellular and molecular level. We are also engaged in examining the underlying mechanisms of the effect of novel mediators to control clinically-relevant allergen-induced immune response. The information obtained from these studies should provide an opportunity to formulate superior therapeutic approaches in bronchial asthma.

2. **Pathogenesis of Occlusive Vascular Diseases:** Occlusive vascular diseases, such as atherosclerosis, intimal hyperplasia and in-stent restenosis, are major health problems all over the world. My research interests in this area are focused on the following three major questions:

   - **Stenosis in Carotid Artery**: Many patients with blockade of their neck artery develop neurological symptoms including transient ischemic attack or stroke. This is primarily due to breaking off the atherosclerotic plaque in the neck artery. Why some patients are symptomatic and others not, even though the degree of blockade due to atherosclerotic plaque is similar in both populations of patients?

   - **Coronary Artery Bypass Graft**: Long term outcome of coronary artery bypass surgeries is compromised by re-closure of the vessels, which predominantly occurs in saphenous vein grafts while the internal mammary artery remains almost resistant to re-closure. Why is the internal mammary artery graft almost immune to restenosis? Why does saphenous vein graft get re-stenosed in almost 20% subjects within the first-year and in about 50% patients in 5-years?

   - **Intravascular Stents in Coronary Artery**: Re-narrowing of coronary arteries in the heart after balloon angioplasty or placement of stents is a serious problem. This is primarily due to uncontrolled growth of smooth muscle cells at the site of injury due to balloon angioplasty or the placement of stent in coronary artery. Coronary arteries following deployment of bare metal stents become re-stenosed in about 30% subjects within the first year. The restenosis rate after deployment of drug-eluting stent is also about 10% within the first year. Thus, drug-eluting stents cause less intimal hyperplasia

and less late luminal loss, but inhibit re-endothelialization of the stented segment making it more susceptible to thrombosis requiring longer periods of anti-platelet therapy. What are the underlying cellular and molecular mechanisms? Could we develop a better therapeutic approach, such as gene therapy?

Basic Skills & Techniques for Undergraduate Students:

Depending on the selected research project, there is an opportunity to learn many techniques, including cell culture under aseptic conditions, Western blotting, quantitative PCR, thin section cutting, histology, Immunohistochemistry, immunofluorescence, flow cytometry, isolation of white blood cells from human blood, measurement of pulmonary function in mouse model of allergic airway inflammation and asthma, collection bronchoalveolar lavage, electrophysiology using whole cell patch clamp in white blood cells, smooth muscle cells, epithelial cells and dendritic cells; an opportunity to do an independent research project under supervision of a postdoctoral fellow and Dr. Agrawal; an opportunity to publish original research findings.

Prerequisites Classes or Other Experience:

Basic knowledge of cell and molecular biology and chemistry; sincere interest and strong motivation to do biomedical research; hepatitis B vaccination.

Time Commitment:

At least 5 hours/week.

Faculty Project Description

Faculty Name	**Jason C. Bartz, Ph.D.**
Department	**Medical Microbiology & Immunology**
Office Location	Criss II, Room 421
Telephone Number	280-1811
Email Address	jbartz@creighton.edu
Source of Research Support	NIH, USDA

Overview of Scholarly Research Activities:

Prions are infectious agents that are comprised entirely of a protein called PrP^{Sc}, which is a misfolded isoform of the non-infectious host encoded protein PrP^{C}. Prions cause disease in humans and in economically important domestic and wild animal species such as bovine spongiform encephalopathy (BSE) in cattle and chronic wasting disease in wild and captive cervids. My laboratory is interested in understanding how prions are persist in the environment, are transmitted from one species to another, and how a protein-only agent can encode strain variation.

Basic Skills & Techniques for Undergraduate Students:

My laboratory relies heavily on Western blot analysis and immunohistochemistry for many of our studies. Additionally, we are one of a handful of labs in the world that successfully performs protein misfolding cyclic amplification (PMCA). PMCA is an *in vitro* technique, analogous to PCR, which can exponentially replicate prions.

Prerequisites Classes or Other Experience:

None.

Time Commitment:

5-10 hours/week.

Faculty Project Description

Faculty Name	**Michael Belshan, Ph.D.**
Department	**Medical Microbiology & Immunology**
Office Location	Criss II, Room 514D
Telephone Number	280-1831
Email Address	michaelbelshan@creighton.edu
Source of Research Support	NIH-NIAID, NSF/Nebraska EPSCoR

Overview of Scholarly Research Activities:

My laboratory studies human Immunodeficiency Virus (HIV), the causative agent of acquired immunodeficiency syndrome (AIDS). HIV infection is incurable and successful treatment requires a combination of anti-retroviral drugs. Despite the efficacy of current therapy regimens, drug resistance to the existing pool of anti-retroviral therapies continues to rise. Continued success in the repression of HIV replication in infected individuals will require the development of new inhibitors that are effective against drug-resistant strains of virus. Drugs that target novel areas of virus replication have the greatest probability to be effective against such viruses. My laboratory uses cutting edge molecular technologies to comprehend poorly understood aspects of HIV replication to identify new candidate targets for anti-viral therapies.

Basic Skills & Techniques for Undergraduate Students:

The student will learn basic molecular and cellular biology research skills as well as experimental design and detailed record-keeping. Techniques that may be used in the laboratory include DNA mutagenesis and cloning, DNA isolation, gel electrophoresis, DNA synthesis by polymerase chain reaction (PCR), real-time quantitative PCR, protein expression, immunoblotting, etc... Note that undergraduate projects do not typically involve the use of “live” HIV.

Prerequisites Classes or Other Experience:

General biology and chemistry courses are required. Advanced courses such as genetics, biochemisty, molecular and cellular biology, biostatistics, and/or microbiology are preferred.

Time Commitment:

6-12 hours/week, with a minimum of 3 hour blocks.

Faculty Project Description

Faculty Name	**Xian-Ming Chen, M.D.**
Department	**Medical Microbiology & Immunology**
Office Location	Criss I, Room 520
Telephone Number	280-3750
Email Address	xianmingchen@creighton.edu
Source of Research Support	NIH-NIAID, Nebraska LB692

Overview of Scholarly Research Activities:

Small non-coding RNA molecules such as microRNAs are emerging as important regulators of gene expression and represent potential targets for new therapeutic strategies for human diseases. My lab has focused a subset of microRNAs that are responsive to microbial infection in human epithelial cells and our objectives are to test the functional roles for those microRNAs in epithelial anti-microbial immunity. Such studies should provide a rational basis for the design and implementation of new therapeutic strategies for infectious diseases.

Basic Skills & Techniques for Undergraduate Students:

The student will test specific hypotheses on microRNAs in epithelial cell reactions in response to pathogen infection or inflammatory cytokine/chemokine stimulation. The student will learn important basic research laboratory skills such as PCR, Western and Northern blot, siRNA silencing, cell and tissue culture, and immunohistochemistry, etc.

Prerequisites Classes or Other Experience:

General biology and chemistry required. Advanced courses such as biochemistry, molecular biology, or cell biology and associated laboratory courses are highly recommended.

Time Commitment:

5-10 hours per week, preferably in large blocks.

Faculty Project Description

Faculty Name	**Shashank Dravid, DVM, Ph.D.**
Department	**Pharmacology**
Office Location	Criss III, Room 558
Telephone Number	280-1885
Email Address	ShashankDravid@creighton.edu
Source of Research Support	NARSAD, Epilepsy foundation, LB595

Overview of Scholarly Research Activities:

My laboratory studies the role of ionotropic glutamate receptors in the processes of learning and memory and their dysregulation during mental disorders. The overriding goal of these studies is to develop novel targets for intervention in anxiety disorders, schizophrenia, bipolar disorder and other affective disorders. We utilize a range of techniques that include behavioral studies in rat and knockout mouse that mimic anxiety and mood disorders, electrophysiology, molecular biology and kinetic modeling approaches to understand the function of glutamate receptors in central nervous system.

Basic Skills & Techniques for Undergraduate Students:

Molecular biology, cell culture, pipetting, develop experimental design, behavioral analysis in rodents.

Prerequisites Classes or Other Experience:

General biology and chemistry are highly recommended. Advanced courses such as biochemistry, molecular biology, cell biology or drug actions and reactions and associated laboratory courses will enhance the research experience.

Time Commitment:

5-10 hours/week.

Faculty Project Description

Faculty Name	**Kristen Drescher, Ph.D.**
Department	**Medical Microbiology & Immunology**
Office Location	Criss II, Room 424
Telephone Number	280-2725
Email Address	kristendrescher@creighton.edu
Source of Research Support	DOD, NMSS, Nebraska LB595

Overview of Scholarly Research Activities:

My laboratory examines the processes involved in disease development and central nervous system repair in a mouse model of multiple sclerosis. We have identified a protein that appears to be involved in reducing the damage in the CNS in this model, as determined by non-biased functional testing. We are examining the mechanism of action of this protein, and are particularly interested in its role as an immune modulator and/or its role in axonal preservation.

Basic Skills & Techniques for Undergraduate Students:

The student will learn important basic research laboratory skills such as appropriate experimental design and micropipetting. The student is expected to be detail-oriented and keep a well-documented laboratory notebook. Techniques that may be used by the student in the laboratory include RNA and DNA isolation, PCR, quantitative RT-PCR, gel electrophoresis, immunohistochemistry, and cell biology related and may include PCR, in vitro transcription, gel electrophoresis, quantitative RT-PCR, and cell migration assays.

Prerequisites Classes or Other Experience:

General biology and chemistry required. Advanced courses such as molecular biology, immunology, and cell biology are highly recommended.

Time Commitment:

5-10 hours per week, minimum of 3 hours at a time.

Faculty Project Description

Faculty Name	**Richard Hallworth, Ph.D.**
Department	**Biomedical Sciences**
Office Location	Criss II, Room 407
Telephone Number	280-3057
Email Address	RichardHallworth@creighton.edu
Source of Research Support	Various

Overview of Scholarly Research Activities:

Our work concerns the hair cells of the inner ear, which are the cells that convert the mechanical energy of sound into excitation of the auditory nerve. Our methods include electrophysiology (single cell and whole-animal), advanced imaging techniques, molecular biology, and protein chemistry.

Basic Skills & Techniques for Undergraduate Students:

Microscopy, tissue preparation, Westerns.

Prerequisites Classes or Other Experience:

Some biology required. Some chemistry and/or physics desirable.

Time Commitment:

6-8 hours/week, preferably contiguous.

Faculty Project Description

Faculty Name	**Laura A. Hansen, Ph.D.**
Department	**Biomedical Sciences**
Office Location	Criss II, Room 431
Telephone Number	280-4085
Email Address	laurahansen@creighton.edu
Source of Research Support	NIH-NIEHS, Nebraska DHHS

Overview of Scholarly Research Activities:

My laboratory performs basic research investigating the function of receptor tyrosine kinases in cutaneous development and skin carcinogenesis. We utilize cell culture and mouse genetic models in combination with molecular and cell biology techniques to examine the signaling pathways that control normal development of the skin, and that are disrupted during cancer development. Our primary goals are to understand the basic mechanisms that lead to cancer in order to design strategies for cancer prevention and treatment.

Basic Skills & Techniques for Undergraduate Students:

The student will learn important basic research laboratory skills such as micropipetting, sample handling, laboratory note keeping, and controlled experimental design. Laboratory techniques are generally molecular and cell biology related and may include cell culture, immunoblotting, immunostaining, PCR, gel electrophoresis, quantitative RT-PCR, microscopy and imaging.

Prerequisites Classes or Other Experience:

No prerequisites required.

Time Commitment:

5-10 hours per week, preferably in 2 or 3 blocks.

Faculty Project Description

Faculty Name	**David He, Ph.D.**
Department	**Biomedical Sciences**
Office Location	Criss I, Room 513
Telephone Number	280-1409
Email Address	DavidHe@creighton.edu
Source of Research Support	NIH-NIDCD

Overview of Scholarly Research Activities:

Cochlear hair cells are neuroepithelial cells characterized by hair bundles on their apical surface. Hair cells transduce mechanical stimuli into electrical activity. The research in my laboratory focuses on 1) mechanoelectrical and electromechanical transductions in cochlear hair cells, and 2) regeneration/repair of hair cells. Recordings are made from hair cells *in vitro* and in hemicochlear preparation, in conjunction with molecular, morphological and other novel techniques to investigate properties of these cells and their roles in cochlear functions in mammals.

Basic Skills & Techniques for Undergraduate Students:

The student will learn important basic research laboratory skills such as laboratory note keeping, controlled experimental design, and dissection. Laboratory techniques are generally morphology- and electrophysiology-related and may include immunohisto-chemistry, microdissection, microscopy and imaging, tissue culturing, and electrophysiological (voltage-clamping) recordings.

Prerequisites Classes or Other Experience:

General biology, chemistry, and physics are highly recommended. Advanced courses such as biochemistry, molecular biology, cell biology, or developmental biology, biomechanical (or optical or electrical) engineering, and associated laboratory courses will enhance the research experience.

Time Commitment:

5-10 hours per week, preferably in large blocks.

Faculty Project Description

Faculty Name	**Thomas F. Murray, Ph.D.**
Department	**Pharmacology**
Office Location	Criss III, Rm 551
Telephone Number	280-2983
Email Address	tfmurray@creighton.edu
Source of Research Support	NIH

Overview of Scholarly Research Activities:

Natural products, especially neurotoxins, play prominent roles as tools in pharmacology and cell biology due to their potent and selective targeting of specific biochemical pathways and receptors. Such compounds are highly useful as probes and, in some cases, also have therapeutic value. Marine cyanobacteria and algae are rich in structurally-diverse and biologically-active natural products. We are engaged in an ongoing collaborative program with a natural products chemist (Dr. Bill Gerwick at the Scripps Institute of Oceanography) to characterize biologically-insightful neurotoxins. The long-range goals of this project are the identification of new probes for pharmacology and cell biology, and the development of marine neuroactive substances as potential lead compounds for **drug discovery**. This latter goal is currently the focus of the project inasmuch as we have recently described the ability of sodium channel activators to enhance **neuronal growth** and **synaptogenesis**. This finding has potential implications for novel therapeutic approaches in the treatment of stroke, traumatic brain injury and neurodegenerative disease.

These studies involve the assessment of natural product influence on neuronal calcium ion dynamics, membrane potential and cell signaling pathways. An additional dimension of the ongoing work involves determination of drug influence on neuronal growth and synaptogenesis.

Projects include further characterization of sodium channel activators on neurite outgrowth and synaptogenesis in primary cultures of mouse cerebrocortical neurons. The role of a glutamate receptor signaling in this action will also be assessed.

Prerequisites Classes or Other Experience:

General biology/chemistry. Other beneficial coursework include biochemistry, physiology, neurobiology, and pharmacology.

Time Commitment:

5-10 hours/week.

Faculty Project Description

Faculty Name	**Kristina Simeone, Ph.D.**
Department	**Pharmacology**
Office Location	Criss III, Room 566
Telephone Number	280-2734
Email Address	KristinaSimeone@Creighton.edu
Source of Research Support	HFF

Overview of Scholarly Research Activities:

My laboratory conducts neuropharmacology research focused on epilepsy. Epilepsy is a common neurological disorder affecting more than 60 million people worldwide and a detrimental co-morbidity associated with epilepsy is sleep disorders. Sleep dysfunction can negatively influence cognition, stress, productivity, etc; thus, it is critical to understand how seizures disrupt normal circadian neurobiology and how biological rhythms influence seizure occurrence in order to elucidate novel therapeutic targets. We are interested in discerning how seizures influence pathology and function of regions involved in regulating sleep such as the hypothalamus.

Basic Skills and Techniques for Undergraduate Students:

Students will learn neuroanatomy during the rotation. Laboratory experiences and skills may include immunohistochemistry, confocal microscopy, electrophysiology, mitochondrial bioenergetic assays, and/or behavior analyses of seizures and circadian rhythms.

Prerequisites or Other Experience:

Basic laboratory pipetting skills.

Time Commitment:

20 hrs/week.

Faculty Project Description

Faculty Name	**Timothy A. Simeone, Ph.D.**
Department	**Pharmacology**
Office Location	Criss III, Rm 558b
Telephone Number	280-3242
Email Address	timothysimeone@creighton.edu
Source of Research Support	HFF

Overview of Scholarly Research Activities:

The hippocampus is a brain structure involved in learning and memory. Our laboratory examines hippocampal function during normal and pathologic conditions in young and adult mice. We use a mouse model of epilepsy to study two related but distinct areas of interest:

1) Discerning the role of natural neuronal population rhythms in the development and expression of epileptiform activity.
2) Investigating the role of ion channels of the mitochondrial inner membrane in pathological processes and in potential neuroprotective strategies.

The techniques used in the laboratory include *in vitro* electrophysiology (multi-electrode array, whole-cell patch clamp, single channel patch-clamp), immunohistochemisty, behavioral studies, and *in vivo* eeg recordings.

Basic Skills & Techniques for Undergraduate Students:

Along with learning basic research laboratory skills, the student will learn neuroanatomy, neurophysiology and neuropharmacology. Techniques that the student may learn include DNA isolation, PCR, western blot, immunohistochemisrty, microscopy, electrophysiology, animal handling and behavior. The student is also expected to participate in weekly lab meetings to deepen their understanding of ongoing projects and expose them to scientific thinking.

Prerequisites Classes or Other Experience:

General biology and chemistry required. Advanced courses in neuroanatomy, neurobiology biochemistry, molecular biology, cell biology or pharmacology are highly recommended.

Time Commitment:

10 hours/week in large blocks.

Faculty Project Description

Faculty Name	**D. David Smith, Ph.D.**
Department	**Biomedical Sciences**
Office Location	Criss I, Room 314
Telephone Number	280-1898
Email Address	dsmith@creighton.edu
Source of Research Support	Nebraska LB 595

Overview of Scholarly Research Activities:

Calcitonin gene-related peptide (CGRP), a ubiquitous neuropeptide of the central and peripheral nervous systems that causes potent vasodilation of blood vessels, is implicated in causing discomfort and headache associated with migraine attacks. My research has focused on the design and synthesis of potent antagonists of CGRP and recent data shows that a novel benzylation of a histidyl residue in position 10 of the CGRP antagonist CGRP(8-37) leads to an increase in binding affinity and antagonistic potency. Ongoing studies to develop an unambiguous synthesis of this benzyl-histidine derivative will lead to a facile synthesis of our highly potent, human selective antagonist N-α-benzoyl-[4-benzyl-His^{10}]-CGRP(8-37). This antagonist will be useful as a pharmacological tool to elucidate the physiological role of CGRP in normal and disease states and may serve as the basis for the design of a new class of therapeutic agents for the treatment of migraine attacks.

Basic Skills & Techniques for Undergraduate Students:

The student will develop new methods for the stereoselective synthesis of 4-benzylhistidine containing appropriate protecting groups for solid phase peptide synthesis. The student will learn basic synthetic skills including thin layer chromatography, flash silica chromatography, vacuum distillation and crystallization techniques, reversed-phase high performance liquid chromatography, nuclear magnetic resonance spectroscopy and mass spectrometry.

Prerequisites Classes or Other Experience:

General chemistry and two semesters of organic chemistry are required. Advanced courses in biochemistry, molecular biology or synthesis would be helpful.

Time Commitment:

5-10 hours/week preferably in large blocks.

Faculty Project Description

Faculty Name	**Garrett A. Soukup, Ph.D.**
Department	**Biomedical Sciences**
Office Location	Criss II, Room 425
Telephone Number	280-5754
Email Address	gasoukup@creighton.edu
Source of Research Support	NIH-NIDCD, Nebraska DHHS

Overview of Scholarly Research Activities:

My laboratory performs basic research investigating the function of microRNA genes in the development of neurosensory cells and epithelia in the inner ear. We largely utilize mouse genetic models and cell culture models in combination with molecular and cell biology techniques to examine the genetic regulatory effects of microRNAs. Our primary goals are to characterize how microRNAs effect the development and maintenance of mechanosensory hair cells in the inner ear, and to determine whether hair cell microRNAs and transcription factors can be utilized to effect hair cell differentiation. Our long-term objective is to understand and manipulate microRNA-regulated genetic pathways to protect hair cells and maintain hearing, or to regenerate hair cells and restore hearing.

Basic Skills & Techniques for Undergraduate Students:

The student will learn important basic research laboratory skills such as micropipetting, sample handling, laboratory note keeping, and controlled experimental design. Laboratory techniques are generally molecular and cell biology related and may include PCR, in vitro transcription, gel electrophoresis, quantitative RT-PCR, dual luciferase assays, in situ hybridization, immunohistochemistry, microdissection, microscopy and imaging.

Prerequisites Classes or Other Experience:

General biology and chemistry are highly recommended. Advanced courses such as biochemistry, molecular biology, cell biology, or developmental biology and associated laboratory courses will enhance the research experience.

Time Commitment:

5-10 hours per week, preferably in large blocks.