2007 UCSD- AMGEN Scholars Program

Research Proposal Titles and Abstract Report

1. Student Name: Beaubrun, Anne
Mentor: Dr. Michael Sailor, Chemistry and Biochemistry Department

Research Project Title: VOLATILE ORGANIC COMPOUND (VOC) SENSOR USING SILICON TECHNOLOGY

Abstract:

VOLATILE ORGANIC COMPOUND (VOC) SENSOR USING SILICON TECHNOLOGY

Anne C. Beaubrun, Chris Giron. Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA.

With recent advances in nanoscale devices, there is an opportunity to create robust, redundant, low power and inexpensive sensors that can effectively monitor and respond to chemical changes in the environment. Here, we investigate the parameters of a VOC sensor that is integrated into a small, low power, electronic device using a light-emitting diode (LED) and a phototransistor. In order to accomplish this, pores are made in the Si chip through an electrochemical process called etching. The porous Si chip is prepared in the form of a photonic crystal. These photonic crystals reflect light of a single color. The top layer of the chip is lifted off and attached to a phototransistor. Absorption of a VOC within the porous nanostructure causes the color of the photonic crystal to shift to the red. The shift in wavelength is an optical signal, indicating that the VOC is in the vicinity of the device. The response of the sensor to three different VOC's (ethanol, acetone, and toluene) is determined. Upon further development, applications for the sensor include the detection of chemical warfare agents and the constant monitoring of toxicity levels in air and water.

2. Student Name: Caro, Eduardo
Mentor: Dr. Kyriacos Nicolaou, Chemistry and Biochemistry Department

Research Project Title: Total Synthesis of Platensimycin Analogs

Abstract: Recently, a compound called platensimycin was discovered and exhibited impressive antibiotic activity. Even more remarkable is that platensimycin exhibits no toxicity and has a new mechanism of action. For this reason the efficient synthesis of this compound and analogs is of great importance to the biomedical field. As many natural products it also represents a great challenge to synthetic chemists. The asymmetric total synthesis of platensimycin has previously been reported by K.C. Nicolaou's group and is the foundation of the method used to prepare these analogs. We report synthetic routes to new platensimycin analogs, specifically in the cage domain.

3. Student Name: Chen, Qing
Mentor: Dr. Partho Ghosh, Chemistry and Biochemistry Department

Research Project Title: THE ROLE OF BORDETELLA REVERSE TRANSCRIPTASE IN DIVERSITY GENERATION

Abstract: Bordetella bacteriophage can generate massive sequence diversity in its retroelement-encoded receptor-binding protein, major tropism determinant (Mtd). The phage is capable of producing ~10(13) possible sequences of Mtd, which enables the phage to adapt to changes as the host Bordetella transits through its infectious cycle. Previous works has shown that this massive diversity is a result of a template-dependent and reverse transcriptase-mediated process. Diversity is caused by a series of nucleotide substitutions at template adenines, and it is unclear whether the reverse transcriptase is sufficient for this adenine-directed mutagenesis. In this project, we examine the function of the Bordetella reverse transcriptase on mediating diversity. The reverse transcriptase was expressed recombinantly in E. coli and purified from inclusion bodies. After refolding, its function was tested in vitro by an RT-PCR assay. Analysis on reverse transcription products is ongoing and will give insight into the role of Bordetella reverse transcriptase in the diversity-generating mechanism.

4. Student Name: Chin, Garwin
Mentor: Dr. Emanuel Todorov, Cognitive Science Department

Research Project Title: NON-PROPRIOCEPTIVE CONDITIONING OF MOTOR PERFORMANCE

Abstract: Inspired by evidence that humans perform reflexive online corrections to perturbed reach targets, we investigate whether motor behavior can be conditioned with non-proprioceptive cues. In the current study we pair an early auditory stimulus with a late target perturbation to probe whether individuals can learn to utilize predictive information to optimize complex reaching movements. Participants executed reaching movements towards a target in a rendered virtual environment while controlling a haptic robot. In one portion of the experiment, the target was visually displaced to a new location to the left or right of the starting position. Displacements occurred with equal probability, and one direction was consistently associated with an auditory cue (randomized across subjects) that occurred immediately after movement onset. Another element of the experiment involved the same type of auditory cue, but the target was stationary. In this case, the auditory cue signified the direction of a viscous force that attempted to knock the cursor off course. We hypothesized that subjects would associate the predictive cue with the unconditioned trajectory correction response and exhibit increased reaching performance relative to baseline trajectories.

5. Student Name: Daher, Nada
Mentor: Dr. Shane Crotty, School of Medicine, Division of Infectious Diseases

Research Project Title: HUMAN INVARIANT NATURAL KILLER T CELL RECEPTOR

Abstract: Natural killer T cells (NKT cells) are an unique class of T cells in that they express an invariant T cell receptor (TCR) and NK1.1, a marker expressed on natural killer cells. In addition to their unique composition, NKT cells have the ability to impact both the innate and adaptive immune system, contribute to the maintenance of self-tolerance and respond to tumors and microbial infections. A relationship has been found linking the type of lipid ligand presented to the TCR and the immune response it yields. The aim of our project is to produce and study the functional characteristics of the human NKT cell TCR. This will be completed using cloning, expression purification, protein refolding techniques and Biacore studies with various lipid ligands to observe their protein-lipid interactions. Further understanding of these interactions will lend themselves to the future development of immunoregulatory medication.

6. Student Name: Daugherty, Aaron
Mentor: Dr. Emanuel Todorov, Cognitive Science Department

Research Project Title: NON-PROPRIOCEPTIVE CONDITIONING OF MOTOR PERFORMANCE

Abstract: Inspired by evidence that humans perform reflexive online corrections to perturbed reach targets, we investigate whether motor behavior can be conditioned with non-proprioceptive cues. In the current study we pair an early auditory stimulus with a late target perturbation to probe whether individuals can learn to utilize predictive information to optimize complex reaching movements. Participants executed reaching movements towards a target in a rendered virtual environment while controlling a haptic robot. In one portion of the experiment, the target was visually displaced to a new location to the left or right of the starting position. Displacements occurred with equal probability, and one direction was consistently associated with an auditory cue (randomized across subjects) that occurred immediately after movement onset. Another element of the experiment involved the same type of auditory cue, but the target was stationary. In this case, the auditory cue signified the direction of a viscous force that attempted to knock the cursor off course. We hypothesized that subjects would associate the predictive cue with the unconditioned trajectory correction response and exhibit increased reaching performance relative to baseline trajectories.

7. Student Name: Duan, Susan
Mentor: Dr. Hui Dong, Department of Medicine

Research Project Title: EXPRESSION AND FUNCTION OF NCX1 AND NCKX3 IN HUMAN AORTIC SMOOTH MUSCLE CELLS

Abstract: Cytoplasmic free Ca2+ ([Ca2+]cyt) in vascular smooth muscle cells plays an important role in controlling vascular tone and thereby regulating blood pressure and blood flow in the human body. The Na+/Ca2+ exchangers are plasma membrane proteins critical for maintaining [Ca2+]cyt homeostasis in many types of mammalian cells. Two families of Na+/Ca2+ exchanger have been identified in rat aortic smooth muscle: NCX1 (K+-independent) and NCKX3 (K+-dependent). However, nothing is known about the expression and function of Na+/Ca2+ exchangers in human blood vessels. Therefore, this project focuses on the expression and functional identification of Na+/Ca2+ exchangers in human aortic smooth muscle cells

(HASMC) by using RT-PCR, Western blotting analysis and digital Ca2+ imaging. Both mRNA and activities of NCX1 and NCKX3 have been detected in HASMC. The protein expression and their detailed roles are under investigation. This is the first study to demonstrate the expression and functions of NCX1 and NCKX3 in the human blood vessels of the systemic system.

8. Student Name: Dwyer, Ellen
Mentor: Dr. Celsa Spina, Pathology Department

Research Project Title: INHIBITORY EFFECTS OF SHRNA ON HISTONE DEACETYLASE IN HEALTHY PRIMARY CD4 LYMPHOCYTES

Abstract: Resting memory CD4 T cells that are latently infected with HIV are untouchable with available antiretroviral treatments, and therefore, represent a major obstacle to eliminating HIV from infected patients. A novel form of treatment currently being studied to coax HIV out of its latent provirus state is the inhibition of histone deacetylase (HDAC) function. In this project, short-hairpin RNAs (shRNA), targeted to specific HDAC gene transcripts, are being tested for their ability to inhibit HDAC expression in healthy primary CD4 T cells. The shRNAs are delivered into freshly isolated CD4 cells using the nucleofection technique, and HDAC RNA levels are measured using qRT-PCR. The purpose of this study is to determine which shRNA reagents are most effective at inhibiting specific HDAC expression. The selected shRNA will then be introduced into cultures of HIV-infected CD4 cells to gain insight into which HDAC gene products may be involved in the maintenance of HIV latency. The ultimate goal of this work is to identify new targets for drug development to impact HIV latency.

9. Student Name: Gamage, Thomas
Mentor: Dr. Jaime Pineda, Cognitive Science Department

Research Project Title: THE POWER OF MU: INVESTIGATING NEUROFEEDBACK TRAINING'S EFFICACY AS A PUTATIVE THERAPY FOR AUTISM SPECTRUM DISORDERS

Abstract: The primary areas that individuals expressing symptoms of autism spectrum disorders (ASD) are deficient in include socially-oriented cognitive and perceptual abilities, such as a theory of mind, empathy, and imitation. Mirror neuron systems (MNS) have been implicated in ASD due to their postulated role in metarepresentation of observed goal-directed action. Electroencephalogram (EEG) measurements of typically developing individuals indicate that the mu wave (an 8-13 Hz oscillation recorded over sensorimotor cortex) is suppressed both when an action is performed and perceived and is therefore believed to indicate the activity of MNS. Individuals expressing symptoms of ASD lack this mu suppression while observing, but not while performing, these actions. Neurofeedback training (NFT) that targets the mu rhythm is thought to ameliorate the deficits in ASD by reinforcing activation of MNS. The present study is aimed at evaluating the efficacy of NFT in adolescents expressing symptoms of ASD. Participants (both male and female, ages 6 to 17 yrs), will undergo a battery of analyses including functional magnetic resonance imaging and measures of related social cognitive and perceptual processes before and after NFT. It is hypothesized that the participants' behavior, electrophysiology, and neuroanatomy will undergo significant changes and that symptoms of

ASD will decrease as measured by tests of theory of mind, empathy, imitation, variables of attention, and mu suppression.

10. Student Name: Garcia, Gary
Mentor: Dr. Richard Gallo, Department of Medicine

Research Project Title: Cathelicidin Related Antimicrobial Peptide and Protein Expression Vector System
Abstract: The skin is the first line of defense from an environment that is thriving with bacteria that cause infections. Antimicrobial peptides such as cathelicidins and defensins contribute to that defense by helping the immune system fight off microbes at the surface of the skin. In humans, nuetrophils process cathelicidin hCAP/LL-37 into a smaller peptide LL-37. In mice, a similar peptide is known as CRAMP. This lab has affirmed CRAMP to be a model for human LL-37 and can protect against infection by Gram-negative and Gram-positive bacteria. To analyze functions of cathelicidin peptides it is necessary to produce the peptides efficiently. This experiment will use a recombinant protein of SUMO combined with cathelicidin antimicrobial peptide domain. With this setup, the peptide can be produced efficiently using in vitro protein expression vector system. The capacity to produce CRAMP in this system will allow us to also make mutated versions of the peptide and permits us to explore the relation between the molecular structure and its biological and biochemical functions.

11. Student Name: Giron, Chris
Mentor: Dr. Michael Sailor, Chemistry and Biochemistry Department

Research Project Title: VOLATILE ORGANIC COMPOUND (VOC) SENSOR USING SILICON TECHNOLOGY

Abstract: With recent advances in nanoscale devices, there is an opportunity to create robust, redundant, low-power and inexpensive sensors that can effectively monitor and respond to chemical changes in the environment. Here, we investigate the parameters of a VOC sensor that is integrated into a small, low-power, electronic device using a light-emitting diode (LED) and a phototransistor. In order to accomplish this, pores are made in the Si chip through an electrochemical process called etching. The porous Si chip is prepared in the form of a photonic crystal. These photonic crystals reflect light of a single color. The top layer of the chip is lifted off and attached to a phototransistor. Absorption of a VOC within the porous nanostructure causes the color of the photonic crystal to shift to the red. The shift in wavelength is an optical signal, indicating that the VOC is in the vicinity of the device. The response of the sensor to three different VOC's (ethanol, acetone, and toluene) is determined. Upon further development, applications for the sensor include the detection of chemical warfare agents and the constant monitoring of toxicity levels in air and water.

12. Student Name: Hinds, Richard
Mentor: Dr. Susan Hopkins, Physiology Department, School of Medicine

Research Project Title: EFFECT OF PULMONARY INTERSTITIAL EDEMA INDUCED BY RAPID SALINE INFUSION ON PULMONARY GAS EXCHANGE

Abstract: Extensive pulmonary edema is potentially fatal and often occurs in end stage cardiac disease. Pulmonary interstitial edema is the early stage of extensive pulmonary edema. We are studying the effect of mild pulmonary interstitial edema induced via rapid saline infusion on pulmonary gas exchange. By infusing human test subjects with saline and monitoring pulmonary gas exchange changes using the Multiple Inert Gas Elimination Technique (MIGET), we hope to better understand the mechanism by which pulmonary gas exchange efficiency is reduced. MIGET provides the ability to detect ventilation and perfusion efficiency changes which correspond to a change in pulmonary gas exchange. Preliminary data will be reported.

13. Student Name: Jones, Ryan
Mentor: Dr. Hui Dong, Department of Medicine

Research Project Title: EXPRESSION AND FUNCTION OF NCX1 AND NCKX3 IN HUMAN AORTIC SMOOTH MUSCLE CELLS

Abstract: Cytoplasmic free Ca2+ ([Ca2+]cyt) in vascular smooth muscle cells plays an important role in controlling vascular tone and thereby regulating blood pressure and blood flow in the human body. The Na+/Ca2+ exchangers are plasma membrane proteins critical for maintaining [Ca2+]cyt homeostasis in many types of mammalian cells. Two families of Na+/Ca2+ exchanger have been identified in rat aortic smooth muscle: NCX1 (K+-independent) and NCKX3 (K+-dependent). However, nothing is known about the expression and function of Na+/Ca2+ exchangers in human blood vessels. Therefore, this project focuses on the expression and functional identification of Na+/Ca2+ exchangers
in human aortic smooth muscle cells (HASMC) by using RT-PCR, Western blotting analysis and digital Ca2+ imaging. Both mRNA and activities of NCX1 and NCKX3 have been detected in HASMC. The protein expression and their detailed roles are under investigation. This is the first study to demonstrate the expression and functions of NCX1 and NCKX3 in the human blood vessels of the systemic system.

14. Student Name: Krow-Lucal, Elisabeth
Mentor: Dr. Shane Crotty, School of Medicine, Division of Infectious Diseases

Research Project Title: Exploring the Interplay of CD4 T Cells and B Cells in SAP Deficient Mice Using a Lymphocytic Choriomeningitis Virus Fusion Peptide

Abstract: Germinal centers are of critical importance in the generation of long-term immunity due to their role in the creation of long-lived plasma cells and memory B cells which are necessary for protection against infection. SAP (SLAM associated protein) plays a key role in the development of humoral immunity. Mutations in SAP (SH2D1A) results in XLP, X-linked lymphoproliferative disease a severe form of immunodeficiency. We intend to study the role of SAP in long-term immunity, especially the CD4+ T cell help to the B cells in the germinal center reaction. To effectively study the B and CD4+ T cell relationship in SAP-/- mice, we have fused the LCMV gp61 minimal epitope (amino acids 66-77) which is recognized by the CD4+ T cells with the gp2 epitope which is recognized by B cells. This would allow a better quantification of the changes in germinal center formation and cell migration to the germinal centers. It could

also be used in the LCMV system as a plausible alternative to ovalbumin and the OTII system for protein immunization experiments.

15. Student Name: Kyubwa, Espoir
Mentor: Dr. Robert Sah, Bioengineering Department

Research Project Title: IN VITRO CALCIFICATION OF ARTICULAR CARTILAGE EXPLANTS

Abstract: Articular cartilage has a zonal structure with variations in cell and matrix content with depth from the articular surface. At the cartilage-bone interface, a zone of calcified cartilage facilitates load transfer and attachment. The objective of this study was to induce calcification in vitro in articular cartilage explants and determine whether the calcification depends on cell potential or tissue zonal cues. Osteochondral blocks were harvested from the patellofemoral groove of bovine calf, and cartilage was sliced either en face to separate the cartilage zones or longitudinally to preserve the full-thickness tissue. Discs (3-mm diameter) from the en face slices and strips (1-mm width) from the longitudinal slices were cultured for up to four weeks2 in a calcification culture medium including fetal bovine serum. Media was changed every 3 days and tissue collected every 4 days to obtain a time-course. Biochemical analysis included calcium-45 uptake, DNA content, and glycosaminoglycan content. Structural analysis will include scanning electron microscopy, elemental analysis, and histology. Controlling the calcification of articular cartilage may be useful for integrating the cartilage-bone interface in osteochondral graft treatments for damaged cartilage or osteoarthritis.

16. Student Name: Lee, Jonathan
Mentor: Dr. Hui Dong, Department of Medicine

Research Project Title: ROLE OF CA2+ IN THE REGULATION OF ACID STIMULATED DUODENAL BICARBONATE SECRETION

Abstract: It is well-documented that duodenal mucosal bicarbonate secretion (DMBS) can protect against the gastric acid-induced injury in the duodenum. The mechanism and regulation of this process, however, remain ambiguous. Cytoplasmic free Ca2+ ([Ca2+]cyt) is an important signaling messenger in the cell, but its role in the acid-induced DMBS is poorly understood. Our laboratory sought to investigate this through an isolated portion of the duodenum from C-57 mice and measuring duodenal DMBS with a CO2-sensitive electrode. When duodenum was perfused with 10 mM HCl, obvious DMBS could be detected, however, after duodenum was pretreated with 0.1 mM BAPTA-AM, a cytoplasmic-specific Ca2+ chelator, acid-stimulated DMBS was abolished, suggesting the importance of [Ca2+]cyt in this process. The detailed mechanisms of Ca2+ regulation DMBS is under investigation.

17. Student Name: Lin, Jonathan
Mentor: Dr. Robert Sah, Bioengineering Department

Research Project Title: UTILIZING CELLS DERIVED FROM THE CARTILAGE OF TOTAL KNEE ARTHROPLASTY SURGERIES TO ENGINEER FUNCTIONAL

CARTILAGINOUS CONSTRUCTS

Abstract: Current treatments for osteoarthritis and cartilage injuries include the implantation of biological grafts from tissue donors. However, this requires a supply of healthy tissues that is not readily available. A potential alternative is to use tissue engineered constructs to treat damaged cartilage. Despite that, cell sources from healthy tissues are limited, and their removal involves morbidity at the harvest site. A possible solution is to utilize cells derived from osteoarthritic joints after cell expansion. Our study seeks to evaluate the feasibility of this solution by using cells derived from surgical remnant tissue from total knee arthroplasty (joint replacement) surgeries to build cartilage constructs. This project focuses on isolating cells from the tissue with high yield, screening conditions to maximize cell expansion, and screening conditions facilitating redifferentiation and extracellular matrix production after expansion. Preliminary studies suggest that the use of certain growth factor combinations as well as human and bovine serum can help redifferentiate cells to the chondrogenic phenotype. This study expands on these results by further screening for conditions for cell redifferentiation and also evaluating conditions towards the goal of creating a functional cartilage construct with chemical and mechanical properties similar to healthy cartilage.

18. Student Name: Liszczak, Glen
Mentor: Dr. Michael Sailor, Chemistry and Biochemistry Department

Research Project Title: CONJUGATION OF LyP-1 HOMING PEPTIDE TO POROUS SILICON AS A METHOD OF IDENTIFICATION AND TREATMENT OF OVARIAN CANCER

Abstract: Porous silicon is a micron-sized device that can be equipped with nano-sized features. The silicon can act as a ‘mother ship’ that deliver payloads to cancerous tumors and perform various tasks when properly equipped. LyP-1 is a peptide that has been found to bind specifically to ovarian cancer tumor cells. It is believed that when LyP-1 is conjugated with the porous silicon, it can lead the mother ships directly and specifically to the ovarian cancer tumor site. The goal of the project is to find a way to attach the LyP-1 to porous silicon while maintaining the homing properties of the peptide. The homing properties of the silicon-peptide product will be evaluated via a cell binding assay involving cells from the 2008 ovarian cancer tumor cell line.

19. Student Name: Lou, May
Mentor: Dr. David W. Rose, Department of Medicine

Research Project Title: Regulation in Adipocytes of VCAM-1 Expression by Oct-1

Abstract: In vascular endothelial cells, IL-6 causes activation of the POU domain transcription factor Oct-1. This factor inhibits the expression of vascular cell adhesion molecule (VCAM-1), a cytokine-inducible adhesion molecule that mediates leukocyte recruitment during an inflammatory response. The objective of this research is to determine whether a similar mechanism occurs in adipocytes. Obese adipose tissue is characterized by inflammation, which contributes to insulin resistance and the eventual development of type 2 diabetes. Since VCAM-1

is activated by proinflammatory cytokines, it is also being recognized as a potential mediator for insulin resistance. This system will be studied in 3T3-L1 cells by using immunoprecipitation and western blotting analysis. It is expected that when treated with IL-6, the 3T3-L1 adipocytes will express Oct-1. The results of this research are important because obesity and insulin resistance are leading causes of type II diabetes.

20. Student Name: Martinez, Freddyson
Mentor: Dr. Enrique Cometto-Muñniz, Department of Surgery

Research Project Title: ODOR DETECTION OF HOMOLOGOUS ACETATES BY HUMANS

Abstract: Odor detection thresholds reported in the literature for any given compound show staggering variability across studies and across subjects within a study. The variability lies in differences in methodology but also, quite commonly, on poor control and quantification of the chemical stimulus. As a result, reported thresholds are of little practical value and obscure the development of structure-activity relationships in olfaction. In this study we have used a strategy that optimizes factors related to the odorant stimulus as well as those related to the subjects's smell performance. With these tools, we measure concentration-detection functions for the odor of ethyl, butyl, hexyl, and octyl acetate. These functions fully describe the detectability of the stimulus from chance to perfect detection as a function of vapor concentration. The results will begin to provide a reliable odor threshold database to explore the physicochemical basis for the odor potency of volatile organic compounds.

21. Student Name: Meguro, Melanie
Mentor: Dr. Toshiaki Kawakami, Department of Medicine, Division of Cell Biology

Research Project Title: MAPPING THE STAT5 INTERACTION SITES OF A NOVEL TUMOR SUPPRESSOR

Abstract: Activation of signal transducer and activator of transcription-5 (STAT5) has been observed in many human cancers, especially leukemia. Suppression of STAT5 leads to apoptosis in leukemic cells, making this protein a prime target for leukemic therapy. In this research project we identified a new tumor suppressor that negatively regulates STAT5 activity. Deficiency of this molecule causes myeloproliferative disease and lymphoma in mice, in a STAT5-dependent manner. It has also been observed that the expression of this gene is extremely downregulated in certain types of human leukemia. We demonstrated that this molecule is able to interact with STAT5. Currently we are mapping the STAT5 interaction sites of this molecule. Findings from this study may not only contribute to our knowledge of STAT5 and its role in cancer, but may also add to the development of a new cancer treatment.

22. Student Name: Miller, Darren
Mentor: Dr. Mark H. Tuszynsky, Neurosciences Department

Research Project Title: NEUROTROPHIN TREATMENT IN A PRIMATE MODEL OF SPINAL CORD INJURY: CHARACTERIZATION OF RAPHESPINAL TRACT SPROUTING

Abstract: Spinal cord injury (SCI) causes deficits that range from chronic pain to paralysis or loss of life. Some recovery occurs in the weeks and months following SCI, and it has been postulated that this recovery is at least partially due to sprouting of axons spared by the lesion. Sprouting of the raphespinal tract, for example, could improve function after SCI. Neurotrophic factors such as BDNF and NT-3 have shown efficacy in preclinical animal models and may be beneficial in enhancing sprouting after SCI. This study investigated lesion-induced sprouting and the effects of neurotrophic factors on the raphespinal tract in the primate spinal cord. Sixteen adult male rhesus monkeys underwent a right hemisection of the cervical spinal cord (C-5 to C-7); lesioned subjects were assigned to one of three groups: short-term (anatomical analysis 12 days post-lesion, n = 4), long-term (6 months post-lesion, n = 5), or long-term with BDNF treatment (6 months post-lesion, n = 7). Three intact subjects were also studied as controls. Light level immunohistochemistry for serotonin is being used to identify and quantify raphespinal tract fibers in the cervical and lumbar regions of the spinal cord. We predict that lesion-induced sprouting will occur in the raphespinal tract by 6 months post injury, and that BDNF treatment will enhance the sprouting response. Thus, enhancement of lesion-induced plasticity may represent a method to improve recovery after SCI.

23. Student Name: Raleigh, Joseph
Mentor: Dr. Andrew McCulloch**,** Bioengineering Department

Research Project Title: THE EFFECTS OF ENVIRONMENTAL ELASTICITY ON CALCIUM INFLUX IN NEONATAL RAT VENTRICULAR MYOCYTES

Abstract: Heart disease can result in a change in elasticity of the extracellular environment. Previous studies have found that neonatal rat ventricular myocytes cultured on a substrate with an elastic modulus near that of the native myocardium exhibit maximal contractile force. Furthermore, cells cultured on softer and stiffer substrates have decreased contractile force. Contractile force directly depends on the concentration of intracellular calcium and studies have verified that cells cultured on substrates that lead to maximal contractile force also have maximal calcium transient peaks. However, the mechanistic cause of this difference in calcium peaks and the major source of intracellular calcium, whether from sarcoplasmic stores or through membrane channels from the extracellular space, is unknown. We hypothesize that neonatal rat ventricular myocytes cultured on substrates of different elasticity will have altered calcium transients via calcium influx. We examined the effects of varying the substrate elastic modulus of polyacrylamide gels on calcium influx in cardiac myocytes by varying concentrations of extracellular calcium in the gels. We used fluo-4 to dye and measure the calcium transients and platinum electrodes to stimulate the myocytes. The results of this experiment will help us better understand the influence of stiffness on cardiac myocyte function.

24. Student Name: Rodriguez, Maria
Mentor: Dr. Andrew McCulloch**,** Bioengineering Department

Research Project Title: The Effects of Environmental Elasticity on Calcium Influx in Neonatal Rat Ventricular Myocytes

Abstract: Heart disease can result in a change in elasticity of the extracellular environment. Previous studies have found that neonatal rat ventricular myocytes cultured on a substrate with an elastic modulus near that of the native myocardium exhibit maximal contractile force. Furthermore, cells cultured on softer and stiffer substrates have decreased contractile force. Contractile force directly depends on the concentration of intracellular calcium and studies have verified that cells cultured on substrates that lead to maximal contractile force also have maximal calcium transient peaks. However, the mechanistic cause of this difference in calcium peaks and the major source of intracellular calcium, whether from sarcoplasmic stores or through membrane channels from the extracellular space, is unknown. We hypothesize that neonatal rat ventricular myocytes cultured on substrates of different elasticity will have altered calcium transients via calcium influx. We examined the effects of varying the substrate elastic modulus of polyacrylamide gels on calcium influx in cardiac myocytes by varying concentrations of extracellular calcium in the gels. We used fluo-4 to dye and measure the calcium transients and platinum electrodes to stimulate the myocytes. The results of this experiment will help us better understand the influence of stiffness on cardiac myocyte function.

25. Student Name: Schandera, Verena
Mentor: Dr. Doris Trauner, Neurosciences Department

Research Project Title: Hippocampal volume and memory function in children with early--onset focal brain lesions

Abstract: Studies of adults with acquired brain damage indicate that damage to the hippocampus results in memory impairment. Children who suffer brain damage early in life may have a different outcome, since the developing brain has greater capacity for reorganization (known as “plasticity”). This study was conducted to determine whether children with early damage to the hippocampus would demonstrate deficits in memory functions.
Methods: MRI scans were performed on 28 children with unilateral brain damage acquired before or at birth and 25 typically developing children.
The volume of the hippocampus was determined using a voxel-based analysis, after manually drawing the hippocampus on sagittal and coronal T1-weighted MRI images. The hippocampal volumes were correlated with performance scores of memory tasks and compared between FL children and controls.
Results: Data analysis is not as yet completed. Based on studies of language function in children with unilateral brain damage that show intact language skills despite large cortical lesions, we hypothesize that children with hippocampal damage will show little or no impairment in memory processes. Results and interpretation will be presented at the conference.

26. Student Name: Singer, Zakary
Mentor: Dr. Henry D. Abarbanel, Department of Physics, Institute of Nonlinear Sciences

Research Project Title: A METHODOLOGY FOR PARAMETER ESTIMATION IN NONLINEAR NEURONAL MODELS

Abstract: In neuronal modeling, there exist a number of mathematical systems that capture the active and passive behavior of the excitable membrane. Given a set of nonlinear equations that

describe a physical or biological system and a small amount of time dependent data from experiments on that system, it should be possible to extrapolate its defining parameters. For systems with complex nonlinear behavior, parameter estimation methods developed for linear systems fail and more sophisticated methods must be developed. Therefore, starting with the Hodgkin-Huxley model for a neuron's action potential, a method for predicting the parameters of the system will be developed using an optimization package called SNOPT7. Once this has been accomplished with known data, more complex systems will be modeled. Ultimately we hope to design a model for a network of coupled Hodgkin-Huxley neurons, determine the parameters of the network, including the connectivity among the neurons, and then predict how it will develop with time.

27. Student Name: Suarez, Paul
Mentor: Dr. Michael Berns, Bioengineering Department

Research Project Title: DESIGN OF A ROBOTIC SYSTEM FOR MECHANOTRANSDUCTION AND REMODELLING STUDY IN MECHANICALLY LOADED ENDOTHELIAL CELLS

Abstract: Stress fibers in endothelial cells (EC) subjected to uniaxial stretch have been shown to orient themselves in a direction orthogonal to the axis of stretch. It is thought that this orthogonal orientation subjects the fibers to less tension, thus lowering the internal mechanical energy of the cell. As of yet, the mechanisms, as well as the overall consequences, of this cell remodeling are unknown. In this project a systems-integrated testing apparatus incorporating an EC stretching machine and a confocal microscope will be built and software developed to facilitate computerized control locally, as well as over the internet. This computer automated testing system will allow an increased throughput in the investigation of the cell signaling pathways responsible for the reorientation of the EC stress fibers as well as the consequences of this reorientation.

28. Student Name: Tangsombatvisit, Stephanie
Mentor: Dr. Michael Sailor, Chemistry and Biochemistry Department

Research Project Title: Development of a Nano-Diagnostic Tool to Identify Tumors in-vivo: Fluorescence Resonant Energy Transfer in Iron Oxide Nanoparticles-NeutrAvidin Aggregates

Abstract: The effective treatment of cancer hinges on early detection and diagnosis. The subject of this study is an MR contrast agent in the form of superparamagnetic iron oxide nanoparticles (IONPs) that can both specifically and nonspecifically accumulate in tumor tissues and enhance tumor imaging. The ease and versatility with which its surface characteristics can be manipulated via conjugation makes it an ideal platform. In this study, the interactions between NeutrAvidin and iron oxide nanoparticles conjugated to both biotin and monofunctional cyanine dyes (CyDye) will be monitored for the occurrence of fluorescence resonant energy transfer (FRET). Two conditions will be tested to isolate the minimum conditions required for FRET to occur: NeutrAvidin concentration and the ratio of biotin to CyDye attached to the IONP. Dynamic light scattering and fluorescence measurements will be employed to quantify aggregation and

fluorescence, respectively, of the IONP self-assemblies. The results of this preliminary study could lead to further exploration of FRET between IONPs containing fluorescent probes as an effective means of targeting and identifying tumor tissues.

29. Student Name: Tran, Chau
Mentor: Dr. Paul Price, Division of Biological Sciences

Research Project Title: THE ROLE OF MATRIX GLA PROTEIN IN PREVENTING SYSTEMIC CALCIFICATION OF SOFT TISSUES

Abstract: Cardiovascular disease (CD) is the leading cause of death in the United States. While there are multiple subdivisions of CD, many are correlated with the level of calcification (hardening) of arterial walls. Serving as the main line of defense against artery calcification, the vitamin-K dependent Matrix Gla Protein (MGP) plays a role in the prevention of CD. Although MGP has been extensively studied as an artery calcification inhibitor, we hypothesize that MGP acts to inhibit mineralization not only in the cardiovascular system, but also in other soft tissues known to be vulnerable to calcification in pathological conditions such as uremia. Our experiment utilizes rats that are treated with Warfarin, a vitamin-K antagonist, to inactivate the inhibitory function of MGP to determine the role of MGP in soft tissues such as the kidneys and the stomachs. We predict that these soft tissues, which typically contain a high level of MGP, are more vulnerable to calcification and will calcify in the absence of functional MGP.

30. Student Name: Wittenberg, Rebecca
Mentor: Dr. James Posakony, Division of Biological Sciences

Research Project Title: UNDERSTANDING PERIPHERAL NERVOUS SYSTEM DEVELOPMENT USING MISEXPRESSION IN DROSOPHILA MELANOGASTER

Abstract: How cell fates are specified in development has been a major topic of research; however many aspects of it remain poorly understood. A good way to study this topic of cell fate specification is by assaying phenotypes in the mechanosensory bristle lineage of Drosophila melanogaster, or fruit flies. In fruit flies, the technique of gain of function has been long established as a method for deducing gene function; thus, in order to understand the normal function of the genes that play a role in cell specification, this “gain of function” approach was utilized. In particular, an approach of misexpression was taken in which genes and their protein products were expressed in cell types wherein they were not normally expressed. Genes that are known to take part in determination of cell fates were analyzed using particular drivers and responders of interest in a GAL4-UAS system for misexpression in fruit flies. Data and interpretations of the phenotypes of the fruit flies will be presented and will help to shed light on the normal functions of the genes involved in cell fate determination.