

2014

**Columbia University
Undergraduate Science & Engineering
Research Showcase Abstracts**



Friday, October 24, 2014

11:00 AM - 12:30 PM

Roone Arledge Auditorium

Lerner Hall

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Sean Ballinger, Applied Physics

Faculty Mentor: Dr. David Humphreys, General Atomics, San Diego, CA

Title: Optimizing Plasma Boundary Control in Superconducting Tokamaks

Plasma shape control is an important aspect of tokamak operations, but is challenging to implement in superconducting machines. A metric to quantify the quality of shape control capability was developed, enabling a comparison of DIII-D to KSTAR and other superconducting machines. Shape control is more complicated in these machines than on DIII-D because of slow power supplies and strong coupling between coils. In addition, the number of free parameters makes hand-tuning PID controller gains impractical. To move toward automated, offline tuning of the feedback loop, a linear closed-loop control simulation was created using Simulink, which allows the use of Matlab's looptune optimizer for control loops. Initial development of the tool is complete, but optimization results indicate that the problem must be simplified further to automatically converge on a solution.

Julia Barasch, Neuroscience and Behavior

Faculty Mentor: Professor Richard Axel, Department of Neuroscience, Columbia University Medical Center

Title: CRTC as a Neuronal Reporter of Environmental Stimuli in Drosophila

The purpose of this research was to determine whether CRTC (short for cAMP-regulated transcriptional co-activators) reports the activation of secondary order neurons of Drosophila. Under basal (non active) conditions, CRTC remains tethered to 14-3-3 protein in the neuronal cytoplasm. Upon neuronal stimulation, however, calcineurin dephosphorylates CRTC, inducing a conformation change and unbinding from the cytoplasm. The dephosphorylated form can then translocate to the nucleus where it binds CREB (a cellular transcription factor). When basal state activity is restored, CRTC is re-phosphorylated and leaves the nucleus. Because of its activity-dependent movement, CRTC has been named a potential neuronal activation marker in Drosophila similar to c-FOS, a highly studied activity marker in mice. I studied stimulus-driven CRTC movement by linking it to GFP (green fluorescent protein) in order to investigate neuronal activation and to identify the exact pathways in the brain that are stimulated by different activities. Pharmacological experiments have been conducted showing complete activation or silencing of CRTC in the Drosophila brain with TTX, the nicotinic antagonist Mecamylamine, and Acetyl Choline, but few natural environmental stimuli have been documented. To characterize and understand the movement of CRTC as a reporter to environmental cues, I did 3 types of experiments, 2 of which are related to olfactory activation under exploration in Dr. Axel's lab. The experiments were: examination of CRTC localization in Drosophila expressing TRPA1 channels as a result of heat treatment induction, examination of CRTC localization in Drosophila after contact and smelling CD8, seminal fluid of Drosophila that activates a specific olfactory

glomerulus (DA1) after mating, and third, examining the comparative levels of CRTC localization in wildtype and dopamine-receptor mutant flies encountering novel scents. As was expected, there was a large difference in CRTC localization in flies that were wildtype versus those that have dopamine receptor mutations. In the mutant flies, the CRTC was consistently concentrated in cellular nuclei or divided between the nucleus and cytoplasm, but in wildtype flies there was more variability in CRTC distribution. The wildtype flies were more strongly affected by environmental stimuli (as was expected). In the case of the mating experiments, hypotheses for the radical results of very highly CRTC concentrated nuclei include the activation of DA1 resulting from the release of seminal fluid. Another hypothesis would invoke a change in internal state after the flies mate. Taken together, my results indicate that CRTC can be used as a neuronal activity marker to gauge the impact of biologically relevant stimuli.

Tess Cersonsky, Biomedical Engineering

Faculty Mentor: Dr. Emre Seli, Department of Obstetrics and Gynecology, Yale University
Title: Embryonic Poly(A) Binding Protein (EPAB) is Required for Meiotic Competence in Mouse Oocytes

Embryonic Poly(A) Binding Protein (EPAB), the predominant Poly(A) Binding Protein expressed in germ cells, regulates the translation of maternal mRNAs and promotes fertility through meiotic regulation. Oocytes enter meiotic arrest following prophase I, during which they synthesize proteins necessary for development; they resume meiosis with germinal vesicle breakdown (GVBD), the breakdown of the nuclear membrane, or germinal vesicle (GV). *Epab*^{-/-} mice are infertile because their oocytes do not undergo GVBD and remain arrested at Prophase I. The goal of this project was to determine if defective Maturation promoting factor (MPF) activation is the reason for *Epab*^{-/-} meiotic arrest. MPF is a protein complex integral to meiotic resumption. Meiotic arrest is maintained by high levels of cyclic-AMP (cAMP), which inhibits MPF. When cAMP is degraded, MPF is activated and the oocyte resumes meiosis.

To determine the mechanism by which *Epab*^{-/-} oocytes are arrested, *Epab*^{-/-} and wild type oocytes were collected and given one of three treatments. Rp-cAMP, a cAMP antagonist that promotes meiotic resumption, induced GVBD in wild type oocytes but not in *Epab*^{-/-} oocytes. Oocytes were treated in Okadaic Acid, a chemical that promotes MPF by inhibiting Ppp2cb, a cAMP independent MPF inhibitor. *Epab*^{-/-} oocytes were also injected with Ppp2cb siRNA, which inhibits Ppp2cb and promotes meiotic resumption. Okadaic acid induced GVBD in wild type and *Epab*^{-/-} oocytes, and significantly more siRNA injected oocytes underwent GVBD than uninjected oocytes. It was also found that some cell cycle proteins were differentially expressed in wild type and *Epab*^{-/-} oocytes. Because Rp-cAMP treatment did not promote GVBD in *Epab*^{-/-} oocytes, but Okadaic Acid treatment and Ppp2cb siRNA injections induced significant GVBD, it can be concluded that there is a defect in *Epab*^{-/-} oocyte cell cycle proteins downstream of cAMP but upstream of Maturation promoting factor. This contributes to

the understanding of the mechanism through which EPAB acts and its importance in fertility.

Kristy Choi, Computer Science-Statistics

Faculty Mentor: Dana Pe'er, Department of Biological Sciences, Columbia University

Title: Benchmarking of Various Alignment Algorithms for Single-Cell RNA-seq

Traditional RNA-seq technology utilizes the transcriptome – the complete set of mRNA transcripts within a cell – to facilitate understanding of the genome with little prior information. By quantifying the dynamic expression levels of each gene during different experimental conditions or stages of development, RNA-seq provides insight into functional genomic elements and has played an integral role in the field's progress. Recent developments in next generation sequencing (NGS) technologies have undertaken the task of minimizing the number of cells needed to extract meaningful information. However, various sources of noise ranging from within-cell heterogeneity to amplification bias in polymerase chain reactions (PCR) have complicated the data analysis process.

This project is a subset of one on a larger scale aimed to interpret single-cell RNA-seq data through the creation of new clustering and normalization techniques. Using Flux Simulator, an in silico pipeline designed to mimic the RNA-seq process, approximately 50 million reads mimicking certain properties of the lab data were generated in order to benchmark the performances of existing alignment algorithms. For example, the reads were probabilistically sampled from a mean distance from the 3'-end of the chromosomes to mirror the prominent 3' bias present in the data. Then, technologies including Bowtie2, Sailfish, STAR, SNAPR, and GSNAP were evaluated according to certain benchmarks such as the identification of known splice sites, genome coverage, and false positive/negative rates. The results from this investigation will then be used to compare the performance of the lab's new alignment algorithm to that of existing technologies, and we hope to discover significant improvements with the progression of this project through the academic year.

Bridget Collins, Biochemistry

Faculty Mentor: Tristan Lambert, Department of Chemistry, Columbia University

Title: A Novel Brønsted Acid Catalyst Borne Upon the Cyclopentadienyl Core

Harnessing the stability of Hückel aromatic systems for synthetic and catalytic purposes has proven a useful tool throughout the history of organic chemistry. Here, we present a novel platform of Brønsted acid catalysis which embeds the 6π electron cyclopentadienyl system within a five-point chiral architecture and further establish its

efficacy in the context of biomimetic transfer hydrogenation, nucleophilic diaryl alcohol substitution, and Pictet-Spengler reactions. Following synthesis and derivitization of core molecule 1,2,3,4,5-pentakis (methylcarbonyl) cyclopentadiene via transamidation and transesterification reactions, we construct an understanding of relative catalyst acidity and demonstrate applicability in a variety of synthetically useful reactions. Successful transformations include transesterification of primary and secondary cyclic alcohols, however attempts to install secondary acyclic alcohols have proved unfruitful. Therefore, moving forward we aim to design an alternative method to access such a series of alcohols and study their mechanism of asymmetric induction.

Serena De Stefani, Psychology and Statistics

Faculty Mentor: Prof. E. Tory Higgins, Department of Psychology Department, Columbia University

Title: The Role of Self-Perceived Success in Altruistic Behavior

The latest research on prosocial behavior has investigated how implicit cognition influences the likelihood of helping. We hypothesized that a promotion-oriented person behaves altruistically given a high level of self-perceived personal success, while a prevention-oriented person behaves altruistically given a high level of self-perceived personal failure.

College students (N=129) were asked to remember a personal episode of self-sacrificial altruism, carried out in terms of either promotion- (incurring a loss to help someone achieve a gain) or prevention- (renouncing a gain to help someone satisfy a need) framed action. After completing a task, and being told the study was over, the students were asked to volunteer for future research. We measured the participants' self-perceived success in the task and their likelihood to volunteer. Those in the promotion condition volunteered more hours when receiving perceived success (vs. failure) feedback, whereas those in a prevention condition volunteered more hours when receiving perceived failure (vs. success) feedback (IRR = 1.31, $z = 2.92$, $p = 0.004$). In addition, following the promotion induction the participants perceived volunteering as virtuous, while following the prevention induction they perceived it as dutiful ($t(122) = -2.47$, $p = 0.014$). The results suggest that different ways of motivating altruism may be effective depending on the regulatory orientation of the subjects.

Alexandra DeCandia, Environmental Biology

Faculty Mentor: Dr. George Amato, American Museum of Natural History

Title: Method for the Noninvasive Sex Identification of Order Carnivora

Noninvasive sampling provides an efficient and cost effective means of genetically monitoring species. Rather than directly handling, capturing, or incapacitating organisms for blood or tissue extraction, noninvasive sampling relies on hair traps or scat collections that can be readily obtained without direct contact with the individual. As such, noninvasive sampling is considered an ideal method for monitoring, managing, and ultimately conserving wildlife populations with little organismal disturbance. One application of noninvasive sampling has been molecular sex identification of mammals. Through amplifying regions on the X- and Y-chromosomes, species-specific studies have determined sex ratios of wild populations from noninvasive samples that can provide vital information for studies on behavior, demography, and population viability. To date, these methods have focused primarily on individual species or pairs of closely related species. Few studies bridge taxonomic gaps in search of more universal methods for noninvasive mammalian sex identification. This study presents an effective and reliable method for the genetic sex identification of the eutherian order Carnivora from noninvasive samples. Gene regions analyzed included (1) the sex-determining (SRY) region, (2) zinc-finger homologues (ZFX/ZFY), and (3) amelogenin homologues (AMELX/AMELY). From these analyses, methods were developed for amplification of the SRY gene in numerous species within the order, including felids, canids, and phocids. Carnivores present ideal focal organisms for this study due to their intra-order variability, elusive nature (making noninvasive sampling preferred in population monitoring), and crucial position near the top of most trophic food webs. Establishing a widely applicable and internally confident method for their study enables more efficient and cost effective monitoring, management, and conservation of carnivores through the establishment of more precise sex ratios.

Isabel del Canto, Neuroscience and Behavior

Faculty Mentor: Professor Mina Halpern, Department of Global Public Health, Columbia University Medical Center

Title: Substance Abuse and Condom Use Among the HIV Population at Clínica La Familia La Romana, Dominican Republic

The primary purpose of this cross-sectional investigation was to quantify substance use among the HIV population at Clínica de Familia La Romana, Dominican Republic. The secondary goal was to identify whether there was a relationship between alcohol consumption and condom use. Of 97 participants in the study, approximately half reported using alcohol or tobacco in the last three months. Forty-six percent of those using substances were classified as 'moderate' or 'high risk', requiring an intervention. Additionally, half of the sample reported having sexual intercourse in the last 30 days.

Thirty-three of the 49 participants (or 67%) that are currently sexually active, reported using a condom during their last sexual experience, while 15 (or 31%) reported not using a condom. That is to say, a third of sexually active HIV population was having unprotected sex. The odds risk ratio test found no association between alcohol consumption and unprotected sex.

Shirin Dey, Earth and Environmental Engineering

Faculty Mentor: Professor Robert Farrauto, Earth and Environmental Engineering, Columbia University

Title: Enhancing Oxygen Storage Capacity of Three-Way Catalysts

Three-way catalytic converters found in many transportation vehicles are essential in adhering to EPA regulations requiring the control of carbon monoxide, hydrocarbon, and nitrous oxide emissions. As some materials used to synthesize the converter's catalyst (such as Cerium) or to enhance its performance (precious metals such as Platinum) are rare and/or expensive, alternative materials are currently being researched. We are investigating the ability of different materials to maximize oxygen storage capacity (OSC) of the three-way catalyst (TWC), which directly affects its conversion performance. The larger the OSC, the wider the air-to-fuel ratio and thus the better the ability of a catalytic converter to function in a variety of on-road situations. Primarily using a zirconia-heavy framework (thus cutting down on the use of Cerium, a rare and expensive metal), we are testing incorporation of alternative dopant materials by synthesizing samples of various dopant concentrations and calculating their OSC levels using thermo-gravimetric analysis. We also utilize various characterization methods such as BET (surface area calculation), Raman Spectroscopy, and X-ray diffraction to observe the effects of the dopant material on the TWC and its incorporation into the catalyst structure. We hope to achieve OSC levels similar to those of ceria-heavy solutions, thus optimizing both TWC cost and performance.

Willie Dong, Mathematics

Faculty Mentor: Dr. Joanna Nelson, Department of Mathematics, Barnard College

Title: Reeb Dynamics on Lens Space

We begin by introducing standard definitions, theorems, and examples of symplectic and contact geometry. We then move onto defining the link of the An singularity, its different contact structures, and extend the work of Ustilovsky to find a non-degenerate contact form on it. We then compute the Conley-Zehnder indices of each orbit on the nondegenerate form, with the ultimate goal of defining a contact homology on the link.

Annel Fernandez, Psychology

Faculty Mentor: Professor William Fifer, Department of Pediatrics, Columbia University Medical Center

Title: Autonomic Function Measured Via Heart Rate Variability in One Month Old Late-Preterm and Full Term Infants

This study questions whether, after reaching one month of age, late preterm infants and full term infants still have different autonomic function. We hypothesized that late preterm infants will still have decreased heart variability in comparison to full term infants which displays immaturity. Heart variability was compared between 27 full term infants born 39 to 41 weeks gestational age and 23 late preterm infants born 34-36 weeks gestational. An electrocardiogram was used to record heart rate while infants were asleep, a respiration belt recorded sleep state, and the Gmark program was used to mark baseline as well as extract 3 variables: average heart rate, RRIsd, and RMSsd. Statistical analysis was performed to confirm significance difference between variable averages. The data showed significantly higher heart rates in both quiet and active sleep for one month old late preterm infants in comparison to one month full term infants. One month old LPT infants also had a trend of lower heart rate variability in both active and quiet sleep as well as a significantly lower beat-to-beat variability in quiet sleep. The results lend support to the idea that LPT one month olds still have altered autonomic nervous system function at one month of age. Understanding that late preterm infants still have immature autonomic function and decreased heart variability even at one month may hint at the idea that late preterm infants have a higher risk for developmental disorders such as Sudden Infant Death.

Anna Fuaif, Chemistry

Faculty Mentor: James Turner Vosseller, Department of Orthopaedic Surgery, Columbia University Medical Center

Title: Timing of Open Reduction and Internal Fixation of Ankle Fractures

Ankle fractures are common injuries encountered by orthopaedic surgeons and often require operative treatment. Generally speaking, injuries that are deemed to be unstable are treated surgically in an effort to stabilize the injury, thereby decreasing the risk of post-traumatic arthrosis of the ankle. The most appropriate timing of surgery after injury is currently unclear. Surgery after the time of injury may be delayed due to logistical or clinical factors, which include availability of facilities and complicating factors such as soft tissue swelling. However, more recently, there has been a multifactorial push to do more procedures in an outpatient setting. As a result, these patients are often not admitted to the hospital at the time of an injury, but they will instead be seen as an outpatient, with surgery performed a week to two weeks after injury.

The effect of these small delays has not been overtly studied. From a surgical standpoint the principal concern is that the fracture begins to heal as more time passes, and so the fractured pieces can be harder to mobilize into an anatomic position. As a result, most surgeons have traditionally tried to fix fractures within two weeks of the time of injury. This purpose of this study is to assess the impact of delayed surgical treatment by comparing outcomes for normal vs. delayed groups of patients through an analysis of outcome scores, radiological assessments, and operative complications.

Dominick Fulgieri

Faculty Mentor: Professor Herbert Chase, Department of Biomedical Informatics, CUMC
Title: Machine-Learning and the Development of a Diagnostic Assistant for Multiple Myeloma and Parkinson's Disease

The bone and blood cancer Multiple Myeloma is on average diagnosed years after the first development of cancerous cells, and as such has a very high mortality rate. The neurodegenerative Parkinson's disease is also typically diagnosed years after patients begin to exhibit the first symptoms, and this delay in treatment results in more rapid progression of the disease and earlier loss of neurological function for the patients. This study sets out to find if machine-learning methods can be used to analyze different forms of raw patient data to develop models that can use the predictive probability of the data features to develop a diagnostic assistant for these two diseases. The diagnostic assistant should be able to alert clinicians that patients have a high probability of developing or having either of these two diseases two or three years before a clinician would normally diagnose the disease. The models are constructed using data from patients who have had these diseases in the past. MEDLEE chart codes, ICD-9 billing codes, demographics, and prescription information are all used to develop the model. The model trains on a diagnostic window of +/- 1 year and then tests on the data two or three years prior. After much other analysis of the data and the models, models have been created for both diseases that can discern with high precision and accuracy the difference between patients three years before diagnosis and controls. The next step in this project is to analyze the predictive traits of the models and analyze each one to ensure that they will work with any patient set and any matched control set.

Graham Gobieski, Computer Science and Chemistry

Faculty Mentor: Professor Luis Campos, Department of Chemistry, Columbia University
Title: Synthesis and Study of Novel Polyelectrolytes

Recently there has been much research on the synthesis and characterization of organic polyelectrolytes for applications in ion-conducting membranes, cationic DNA/polymer polyplexes, and materials with microphase segregation. Current organic

polyelectrolytes contain one of three different charged functional groups, including the imidazolium ion, the phosphate ion, or the sulfate ion. We describe the synthesis of a new class of polyelectrolytes based on the cyclopropenium ion, an aromatic, positively-charged cation. Specifically, we developed a post-polymerization functionalization strategy to efficiently functionalize homopolymers and diblock co-polymers, allowing us to easily vary the type of cyclopropenium ion attached. Central to the strategy is the polymerization of a Boc-protected styrene derivative that following polymerization can be deprotected and functionalized. This strategy has been implemented in our synthesis of cationic DNA/polymer polyplexes, which have already been fairly successful as transfection agents of non-transfectable cell lines.

Nathen Huang, Psychology

Faculty Mentor: Valerie Purdie-Vaughns, Department of Psychology, Columbia University

Title: "Graying" Out the Threat: Ageism and Its Effects on Racial Prejudice and Perceptions of Criminality

The research proposed here builds on prior research examining the perceived criminality of Black individuals and mitigated sentencing outcomes of aged criminals. This research comprises four studies, with two separate sets of participants- online participants and students recruited to the study from the Columbia population. The pilot study of the first study gathered ratings on a set of Black and White facial images, measuring each one's perceived racial stereotypicality, attractiveness, familiarity, and age. Utilizing a subset of the faces from the first study, the follow-up study will use an established stimulus association paradigm—gauging the strength of cognitive associations between the various facial images (Black and White; older and younger) and pictures of objects (threat-associated and neutral). While still in development, the last two studies will apply our previous findings. The third study will study the leniency of participants' decision of sentencing decisions based on hypothetical cases of criminals with varying characteristics, and the fourth study seeks to understand how people's perceptions of incremental versus entity attitudes towards criminality will affect their decisions to grant parole to inmates. The research will elucidate how race, age, and the intersection thereof shape social perceptions of threat.

Junghoon Kim, Neuroscience and Behavior

Faculty Mentor: Professor Rafael Yuste, Department of Biological Sciences, Columbia University

Title: Voltage Imaging Characterizes the Penetration of Back-Propagating Action Potentials into Dendritic Spines

In this study, we aim to quantitatively investigate the electrophysiology of the neuron's dendritic spine by utilizing a microbial rhodopsin-based, genetically-encoded voltage indicator known as QuasAr2. Specifically, we use QuasAr2 voltage imaging to examine membrane potential fluctuations in the dendritic spine as compared to those in its adjacent dendritic shaft, for the purpose of shedding light on the function of these supposedly specialized compartments of the dendrite in receiving incoming postsynaptic potentials. Cultured mouse hippocampal neurons were transfected to express QuasAr2, and we subsequently whole-cell patch clamped the neurons and artificially induced back-propagating action potentials in their dendrites via a protocol of systematically controlled current injections. A comparison of fluorescence change relative to baseline for dendritic spines and their parental dendrite shafts shows no statistically significant difference in magnitude, but does suggest a mild dampening in potential from shaft to spine, hinting that the neck of the spine might be involved in some sort of filtering of electrical input to the neuron.

Johnathan Kuan, Physics and Mathematics

Faculty Mentor: Professor Reshmi Mukherjee, Department of Physics and Astronomy, Barnard College

Title: Observations of the YSO G079.3439+00.3191

It has been suggested that Young Stellar Objects (YSOs), protostars embedded in molecular clouds, may be a potential source of gamma-ray emission. These stars exhibit supersonic, collimated jets that interact with the surrounding molecular cloud. The strong shocks in the termination regions of these jets may be able to accelerate particles to relativistic energies through diffusive shock acceleration. Through relativistic bremsstrahlung and proton-proton collisions, YSOs may be able to produce high gamma-ray fluxes in the high energy and very high energy regimes that may be detectable by current instruments. Observations of gamma-ray emission from YSOs may be able to help answer questions concerning astrophysical jets and star formation. I will describe the results of an analysis of observational data taken by VERITAS, a gamma-ray observatory located in Arizona, of the YSO G079.3439+00.3191. I will also describe the physical principles by which VERITAS operates as well as the scientific questions that the VERITAS experiment addresses.

Nilay Kumar, Mathematics

Faculty Mentor: Professor Robert Friedman, Department of Mathematics, Columbia University

Title: Complex Geometry: An Introduction

Complex geometry is a beautiful branch of modern mathematics that has witnessed years of active and successful research. It has deep connections to various other fields such as differential, algebraic, and arithmetic geometry; more recently it has enjoyed extensive interactions with physics through string theory, mirror symmetry, and conformal field theory. I spent the summer studying the basic ideas and constructions of complex geometry, ranging from the various local properties of complex manifolds to the elegant interactions between their holomorphic vector bundles and intrinsic geometry.

Cameron Lemley, Astrophysics

Faculty Mentor: Michael Castelaz, Department of Astronomy, Pisgah Astronomical Research Institute

Title: Design of a 1420 MHz Receiver for a 12-Meter Telescope

During the summer of 2013, a new 1420 MHz receiver system was designed and constructed for the 12-meter radio telescope at the Pisgah Astronomical Research Institute (PARI). The new radio receiver system consists of a feedhorn (which is a duplicate of the feedhorn that is currently installed on PARI's 4.6-meter radio telescope), a low-noise amplifier, a bandpass filter, a downconverter, a SpectraCyber 1420 MHz Hydrogen Line Spectrometer, CommScope CNT-600 braided coaxial cable, and a power supply. Each component was individually tested on the preexisting 4.6-meter radio telescope receiver system before being installed on the 12-meter telescope. This testing process revealed that the spectrometer that was intended for use in the new 12-meter receiver system would require 12-bit software, which was acquired soon thereafter. The new receiver system was then assembled on a rolling cart for further testing. After the 1420 MHz receiver system was moved outside, it successfully detected its first extraterrestrial radio signal. The next step of this project was the installation of the feedhorn at the focus of the 12-meter parabolic reflector and the mounting of the additional receiver system components inside the radio frequency (RF) room of the 12-meter telescope. Following its installation on the 12-meter telescope, the new receiver system was connected to the PARI network via ethernet using a device called a SitePlayer Telnet. The 12-meter telescope was focused by taking continuum scans of Virgo A during its meridian crossing. The positioning of the feedhorn had to be adjusted several times before the new radio receiver system was precisely focused. After focusing the 12-meter telescope, spectra were taken of both the Orion Nebula and the Crab Nebula to test the abilities of the new 1420 MHz receiver system. As a final test of both the angular resolution and time resolution of the new radio receiver system, the

12-meter telescope was used to observe the pulsar PSR J0332+5434. Fourier analysis resulted in a calculated pulsar period of 0.745 seconds, which is within 0.03 seconds of the accepted value for this pulsar.

Eileen Li, Earth and Environmental Engineering

Faculty Mentor: Professor Robert Farrauto, Department of Earth and Environmental Engineering, Columbia University

Title: Deodor the Motor

The goal of the study was to see whether car rental companies, used car dealerships and detailers would be interested in using a bio-degradable odor eliminator, Odor Crush, and how much money and time it would save them. Overall, it was important to identify where the actual market and need was for such a product that was easy to use, and had a long enough turnover time of about 1 day for the product to effectively eliminate the odor. The objective was to interview as many potential customers as possible within the duration of the internship to collect such information. In order to do so, a customer survey tailored specifically to the type of company was made, asking questions including what percentage and actual number of the cars a customer received that had an odor, what current products they used, where they felt a need had not been met, etc.

Findings indicated that the window of turnover time is a very important factor to whether a customer would adopt Odor Crush or not. Detailers turned out to be the least likely group of customers because they had incredibly small turnover times of only a several hours, while Odor Crush would need sixteen hours to operate at minimum. The same situations applies to rental car companies in that they also have variable turnover times depending on customer needs. From the surveys, it was found that rental car company's fleet services as well as ports that exported vehicles to Asian markets would be most interested in Odor Crush. This is due to the fact that fleet services have long turnover times, and that in Asia, many people are adverse to the new car smell. These findings allowed the project to pivot and target specific markets to do further research.

Kevin Liu, Biology and English

Faculty Mentor: Dr. Megan Sykes, Center for Translational Immunology, Columbia University Medical Center

Title: Measurement of Human Immunoglobulin Levels in Different Humanized Mouse Models to Study Human Immune System Reconstitution

Studies of the human immune system and its related diseases have generally been limited in scope due to the failure of traditional research methods to provide a complete image for scientists. In order to recreate the human immune system and its associated

mechanisms, immunodeficient mice engrafted with human hematopoietic stem cells and other auxiliary organs have been developed as a potential model with revolutionary implications. Through the “humanization” of mouse models, researchers are able to study in vivo the minute details of the human immune system. By quantifying the level of human immunoglobulins and relating them to the levels of lymphocytes, we were able to study the effectiveness of our different humanized mouse models as a tool to study human immune system development as well as autoimmune diseases. Human IgM was found to be present in all humanized mice models, however, the level was lower than in humans. IgG and antigen specific antibodies were not detected, displaying a major limitation in the generation of a full humoral immune response. The development of “humanized mice” is ongoing as these studies continue to reveal to researchers different facets of this new model.

Elora López, Environmental Biology

Faculty Mentor: Professor Mary Blair, American Museum of Natural History

Title: Inferring Molecular Phylogenetic Relationships Among Endangered Slow Lorises (Genus *Nycticebus*) with Mitochondrial DNA Sequences

Slow lorises (genus *Nycticebus*) are strepsirrhine primates native to South and Southeast Asia. The IUCN currently recognizes five species of slow loris, which are designated as either vulnerable or critically endangered with extinction, although more species have been proposed based on analyses of fur coloration. Genetic data for slow lorises are limited, primarily due to the challenges of obtaining samples from these nocturnal, elusive animals. We sequenced the mitochondrial cytochrome c oxidase I, cytochrome b, and NADH dehydrogenase subunit 4 genes from museum specimens (ranging from 42 to 113 years old), samples collected in Vietnam, and specimens confiscated at U.S. airports by the United States Fish and Wildlife Service (USFWS), representing all five currently recognized species of slow loris. We inferred phylogenetic relationships among species using Bayesian inference, maximum likelihood, and parsimony. Consistent with previous studies, we found support for *N. pygmaeus* as a basal taxon to the rest of the group. *N. menagensis* had unexpectedly high diversity, and did not form a reciprocally monophyletic group. *N. bengalensis* and *N. coucang* did not consistently form separate groups, perhaps due to limited representation of *N. coucang* in our sample. Further genetic sampling of *Nycticebus* will better elucidate phylogenetic relationships within the group and determine units of conservation, which will be critical in developing conservation plans that maintain the diversity and integrity of each slow loris species.

Tatini Mal-Sarkar, Biology

Faculty Mentor: Dr. Adam Ratner, Department of Pediatrics, Columbia University Medical Center

Title: Programmed Necrosis in Erythrocytes

Though it was originally thought that there was only one form of programmed cell death, recent evidence demonstrates the presence of at least one other type, necroptosis. Characterized by its inflammatory response and specific to RIP1 phosphorylation, necroptosis has been studied in many nucleated cell types. However, it has also been observed in red blood cells (RBCs), which were the cells we chose to study. Necroptosis is employed as a mode of cell regulation, but can also be caused by certain toxins which lead to sepsis and other infections. Pore-forming toxins are toxins that create pores of various size in cells, generally leading to cell lysis. We questioned which specific PFT-forming pathogens caused necroptosis, specifically of the cholesterol-dependent cytolysins. We studied Group B Strep., Group A Strep., and *L. monocytogenes*, and noted that though they were PFTs, they did not induce necroptosis. However, previous research had indicated that any PFT cross-linked with CD59 would lead to necroptosis, so we cross-linked GBS, PLO, and LLO with CD59. The results demonstrated that not just any PFT would suffice – the mode of necroptosis seems to require a certain pore size as well. It also illustrated precisely how critical CD59 is. In conclusion, programmed necrosis appears to necessitate both CD59 and relatively pore size in its function of cell regulation and death.

Kyle Misquitta, Chemical Engineering

Faculty Mentor: Prof. Robert Farrauto, Department of Earth and Environmental Engineering, Columbia University

Title: Investigating Catalyst Performance in the Three-Way Catalytic Converter

The three-way catalytic converter is a device found in automobiles and is designed to facilitate the reduction of NO_x as well as the oxidation of CO and hydrocarbon emissions from the exhaust of cars. The conversion of these various emissions is made possible when the air-to-fuel ratio of the exhaust is maintained at what is referred to as the stoichiometric point. As precious metals (such as Pt, which is very expensive) are used in catalytic converters, research into more cost-effective transition metal catalysts that can perform well under testing conditions without sacrificing performance is continuing to grow in importance. Palladium on some support such as ceria-zirconia (CZO) or alumina (Al₂O₃), for instance, is such an alternative. In order to mimic the conditions in the three-way catalyst (TWC) found in cars, we made use of a furnace to carry out both the steam reforming (SR) process of hydrocarbons and the oxidation of the metal catalyst (which is reduced during SR). We repeated cycles of SR and performed several characterization tests to investigate both the conditions under which the various catalysts achieved heightened performance and the reasons why the catalyst

performance may have decreased over time. These tests included Brunauer–Emmett–Teller theory (BET), Temperature-programmed reduction (TPR), and X-ray diffraction (XRD). By studying these runs, we were able to narrow down the reasons for catalyst deactivation and better understand the conditions under which oxidation and reduction of the catalyst was best performed. Our research has led to increased interest in Pd/CZO and alumina catalysts and has given us reason to believe that rhodium reacting with the alumina support is the clear reason for deactivation over time.

Daniel Multerdam, Chemical Physics

Faculty Mentor: Professor Kjersti Sterri, Institut für Anorganische Chemie, RWTH Aachen University

Title: Synthesis of Metal Carbodiimides

Zinc carbodiimide (ZnNCN), a precursor in the synthesis of many other metal carbodiimides, was synthesized from the reaction of cyanamide (H_2NCN) with zinc chloride (ZnCl_2) and was analyzed with X-ray powder diffraction (XRPD); the diffraction pattern and lattice parameters agree well with the literature on ZnNCN (7). The synthesis of cobalt (II) carbodiimide (CoNCN) from $[\text{Co}(\text{NH}_3)_6]\text{Cl}_3$ and H_2NCN was performed, and the products were analyzed with XRPD. After an initial synthesis attempt yielded elemental Co, milder reaction conditions led to the production of CoNCN in addition to an unknown compound. The diffraction pattern of the unknown compound did not match that of any of the reagents, expected products, or molecules that the reactants decompose into.

Samuel Nicoll, Mathematics and Physics

Faculty Mentor: Paul Siegel, Department of Mathematics, Columbia University

Title: Spectral Graph Theory and Bipartiteness

It turns out a graph is disconnected if and only if the smallest eigenvalue of the Laplacian is zero. One might then assume that a small eigenvalue somehow indicates a nearly disconnected graph. It again turns out that yes, this eigenvalue does give some measure of how connected the graph is, as dictated by the Cheeger inequality. We realized that a graph is bipartite if and only if the largest eigenvalue of the Laplacian is 2. We then pursued the same line of thinking as in the disconnected case and obtained analogous results, including a Cheeger inequality relating bipartiteness to the largest eigenvalue. We were also able to adapt some of the methods used to calculate connectedness to calculate bipartiteness.

Kevin Pawlak, Biochemistry and Economics

Faculty Mentor: Professor Lars Dietrich, Department of Biological Sciences, Columbia University

Title: Determining Effect of Phenazines on Pseudomonas Aeruginosa Biofilm Strength

Biofilms are colonies of bacteria that aggregate and develop a protective phenotype; this phenotype greatly reduces the efficiency of antibacterial compounds, which allows bacteria to more persistently infect hosts. Quorum sensing (QS), a form of bacterial cell-cell communication, is known to upregulate biofilm production and virulence through the expression of specific genes downstream of the QS system. While QS inhibitors are successful in inhibiting these genes, their distance upstream creates a need for inhibitory compounds that act further downstream in bacteria. Phenazines are redox-active, QS-mediated molecules that not only assist in host infection but also mediate their own smaller set of genes, which makes them an effective target for inhibition. This study investigated whether bacterial biofilm viability was decreased when the gram-negative opportunistic pathogen *Pseudomonas aeruginosa* PA14 was not able to produce specific phenazines or express phenazine-regulated genes. Our results indicate that the phenazine-null mutant Δ phz produces ~ 30% less biofilm (**p < 0.001) compared to wild type in the crystal violet assay. In addition, mutants missing phenazine-regulated genes (PA2274 and PA3718) had the same phenotype as Δ phz. This suggests that inhibitors of phenazine biosynthesis could be utilized as drugs to interfere with biofilm formation in *P. aeruginosa*.

Anusha Ponduriap, Biology and Economics

Faculty Mentor: Professor Lars Dietrich, Department of Biological Sciences, Columbia University

Title: Characterization of Circadian Rhythms in Pseudomonas Aeruginosa Communities

The Gram-negative opportunistic bacterium *Pseudomonas aeruginosa* is a leading cause of hospital-acquired infections and mortality in immunocompromised and cystic fibrosis patients. We have found evidence for metabolic regulation in *P. aeruginosa* that follows a circadian rhythm. When this bacteria is grown as a colony on agar under a 12-hour light/ 12-hour dark cycle, it forms morphologically distinct rings that indicate different metabolic states, visualized by the red coloration of reduced triphenyltetrazolium chloride. To explore the molecular mechanisms behind this phenomenon we screened a transposon mutant library for putative regulators of *P. aeruginosa* circadian rhythm. We identified two distinct candidates that exhibited phenotypes of altered circadian rhythmicity with shorter or longer periodicity. A transposon mutant of PA14_21120 showed an advanced phenotype with more and narrower rings than in a wild-type colony. PA14_00470::Tn showed a delayed phenotype with distinctly concentrated and less rings than the normal phenotype of a *P. aeruginosa* colony. In the future, we will check the transposon insertion sites by

arbitrary PCR and make nonpolar, markerless deletions of the target genes. These deletion strains will be used for further characterization of circadian rhythm regulation, which will include changing the time intervals of light/dark cycles, light intensity and wavelength. A better understanding of *P. aeruginosa*'s physiology may lead to the development of novel antibiotics.

Aishwarya Rajaar, Biomedical Engineering

Faculty Mentor: Dr. Jeffrey Smith, Cellular and Systems Neurobiology Section, National Institutes of Health

Title: Respiratory Motor Pattern Generation: Role of Transient Receptor Potential (TRP) Channels

Breathing movements in mammals are driven by a neural rhythm generator located in the brainstem. The inspiratory rhythm is generated in the brainstem pre-Bötzinger complex (pre-BötC) (Smith et al., 1991), involving sodium- and calcium-based ionic mechanisms operating in key populations of excitatory neurons (Del Negro et al., 2001). Recently, calcium-activated non-selective cationic currents (ICAN) mediated by a subset of calcium-activated transient receptor potential (TRP) channels have been proposed to contribute to rhythm generation in the pre-BötC inspiratory neural network. TRP channels mediate the transmembrane flux of cations, depolarizing neurons by raising intracellular Ca^{2+} and/or Na^{+} concentrations. Members of the TRPM (M4/5) channel family have been hypothesized to be the molecular correlates of ICAN. We have now identified TRPM4 channels in pre-BötC excitatory neurons by molecular assay (Chia et al., unpublished data). We have also shown by electrophysiological experiments that the application of TRPM4 channel blockers in rhythmically-active neonatal rat brainstem slice preparations containing the pre-BötC in vitro does not perturb the inspiratory motor rhythm but strongly disturbs the amplitude of the inspiratory motor pattern. This project further investigated the function of these channels in a more intact neuraxis by combining electrophysiological and pharmacological methods in a unique in situ arterially perfused preparation of the juvenile rat brainstem-spinal cord. Using TRPM4 channel blockers, we found a profound decrease in the amplitude of the recorded respiratory motor pattern along with changes in the rate and duration of the inspiratory neural activity. Hence, we provide experimental evidence for the first time that endogenously activated TRPM4 channels play a major functional role in modulating the amplitude and frequency of the respiratory motor pattern in the more intact rodent nervous system.

Jeremy Sacks, Biology

Faculty Mentor: Professor Frank Costantini, Genetics and Development, Columbia University Medical Center

Title: Analysis of Ret-Dependent Gene Expression in the Developing Murine Ureteric Bud Using In Situ Hybridization

Congenital Anomalies of the Kidney and Urinary Tract affect a striking number of newborns and comprise a high percentage of prenatal anomalies. It is also known that low numbers of glomeruli play a role in causing hypertension, with glomeruli counts decreasing as people age. As many complexities of renal development remain to be elucidated, we investigated the gene pathway involved in the developing kidney. Kidney development takes place at the caudal end of the Wolffian Duct with the swelling of the ureteric bud (UB). The UB invades the surrounding metanephric mesenchyme (MM), forming trunks and newly developed tips as a result of repeated bifurcations. Research has characterized the tyrosine kinase receptor Ret, highly expressed in the UB tips, as essential to proper renal development. Microarray assay was previously used to determine genes differentially expressed in the caudal versus rostral Wolffian Ducts as well as WT versus the transgenic Ret^{-/-} caudal Wolffian Ducts in mice. In situ hybridization was implemented here to confirm genes as UB specific and Ret-dependent. Expression in the UB was tracked through embryonic development by looking at progressively developing caudal halves, urogenital ridges, and kidneys. Tissues were also embedded and cross-sectioned to further qualitatively determine gene expression localization. This research has shown that the genes Ptpn3, Plet1, Krt23, Cthrc1, and S100a6 are expressed in the UB among a greater number of genes that were tested here. This study finds Ptpn3 and Krt23 as genes expressed specifically in the UB tips. Research here also suggests that Plet1 is expressed in both the UB tips and trunks. This study finds proposed Ret-dependent regulation of Plet1, Ptpn3, and Krt23 to be inconclusive.

Emma Sarachan, Physics

Faculty Mentor: Brian Humensky, Department of Physics, Columbia University

Title: Cherenkov Telescope Array Mirror Panel Edge Sensors

The Cherenkov Telescope Array (CTA) is the next-generation ground-based observatory for very high energy ($E > 100$ GeV) gamma-ray astronomy. It will integrate several tens of imaging atmospheric Cherenkov telescopes (IACTs) with different apertures into a single astronomical instrument. The US part of the CTA Consortium has proposed and is developing a novel IACT design with a Schwarzschild-Couder (SC) aplanatic two-mirror optical system. A full-scale prototype telescope of this design is being built at the Fred Lawrence Whipple Observatory in southern Arizona. Each telescope will consist of two mirrors made of 48 and 24 separate mirror panels, respectively. To ensure that these panels remain in alignment, the mirror panels will be equipped with edge sensors

(MPES) to measure displacement between adjacent panels, and actuators to finely adjust the panels' positions. At Columbia, we are working on the MPES. Each MPES consists of a laser and pinhole attached to one mirror panel, and on an adjacent panel, a diffuser and webcam to detect the relative position of the laser. This summer, we worked on building, testing, and writing software for the MPES.

Shannon Shipley, Neuroscience and Behavior

Faculty Mentor: Dr. Tae-Kyung Kim, Department of Neuroscience, University of Texas Southwestern Medical School

Title: Efforts towards Characterization of the Antisense Long Non-Coding RNA at GAD1 Gene

Long non-coding RNAs (lncRNAs) have been increasingly appreciated as integral components of gene regulation at various levels. Antisense lncRNAs, those transcribed from the complementary DNA strand of a protein-coding gene in overlapping fashion, are especially well-suited to regulate transcription of their corresponding sense transcript. However, specific functions and regulatory mechanisms of most lncRNAs are only just beginning to unravel and still remain largely unknown. Here, we identify and begin to investigate the function of a long non-coding antisense RNA transcript for GAD1, a crucial gene in GABA synthesis and thus in distinguishing inhibitory neuronal functions. To first understand more about the general nature of this transcript and to discern the best investigative approach, we measured GAD1 coding RNA expression levels after knocking-down the predicted GAD1 non-coding RNA transcript through lentiviral-mediated shRNA infection. These data were largely inclusive and may suggest that our GAD1 non-coding RNA primers target unspecific sites. GAD1 antisense lncRNA is unannotated, which could account for this primer unspecificity; in order to accurately target the GAD1 antisense lncRNA transcript, we began efforts to map its sequence. To sequence the transcript, we circularized purified RNA transcripts harvested from DIV7 cortical neurons and performed nested PCR, which amplifies the transcripts' 5' and 3' ends. Sequence data indicated that the amplicon was unspecific to our desired target sites. We performed and analyzed data from four independent trials, and we predict that this unspecificity may again be attributed to an ineffective primer set. We are now using the Rapid Amplification of cDNA Ends (RACE) procedure to sequence the GAD1 antisense lncRNA, but have yet to gather enough data to perform conclusive analysis. These challenges suggest that, in order to successfully sequence the transcript, we must further investigate the transcript's molecular nature, such as potential start, end, and exonic sites, as well as the transcript's expression pattern throughout development, both of which are being investigated now. Elucidating the characteristics and function of the GAD1 antisense lncRNA may have vast implications not only in GAD1 regulatory mechanisms and thus the mechanism that distinguishes a neuron as inhibitory, but also in the pathophysiologies that result from the dysregulation of these aforementioned mechanisms, ranging from neurodegeneration to Autism-spectrum disorders.

Maxim Sigalov, Mathematics and Computer Science

Faculty Mentor: Professor Raimondo Betti, Department of Civil Engineering, Columbia University

Title: Structural Damage Detection Using a Random Forest Algorithm

Random Forest, a machine learning algorithm, is applied to the problem of damage location and severity measurement in several situations, both modeled and real. This algorithm, which unlike the popular Bayesian classifier requires no pre-processing of data (that is, time histories can be used directly from sensors), is shown to be fast and accurate, as well as robust under different signal types, structure types, and various other parameters. The algorithm is shown, with proper training, to be effective at handling both combined and intermediate damage cases. As Random Forest is a supervised learning algorithm, several methods are proposed to apply it more generally to real data by mimicking unsupervised learning.

Varadarajan Srinivasan, Astrophysics

Faculty Mentor: Professor Prasenjit Saha, Institute for Theoretical Physics, University of Zurich

Title: Computing the Influence of a Gravitational Wave on an Electromagnetic Field

General Relativity applied to electromagnetism: what happens to an electromagnetic field when the spacetime it is embedded in is oscillating? I present a numerical model that answers this question for any arbitrary boundary conditions. This is particularly useful as this problem cannot be solved analytically for complicated boundary conditions. This model could in principle be applied to gravitational wave observation without being restricted to simple boundary conditions such as LIGO's simple interferometers.

Tyler St. Denis, Chemistry

Faculty Mentor: Professor James Leighton, Department of Chemistry, Columbia University

Title: Synthesis of Novel Ligands for Potentiation of Asymmetric Allylsilylation and Crotylsilylation Reactions

One of the greatest challenges in synthetic organic chemistry is the selective, controlled, and high-yielding generation of stereocenters from prochiral starting materials. Our group has developed a series of chiral silane Lewis acid (CSLA) reagents for the allylation and crotylation of carbonyls. Recently, our group has developed a stoichiometric diaminophenol CSLA using a diaminophenol activator ligand which

allowed the development of an experimentally sustainable, efficient, and scalable one-pot procedure, allowing for recovery of the ligand and is different from its predecessors in that it is not dependent on the presence of a scandium(III) triflate catalyst. Theoretical calculations have determined that this system's performance is due to conformation restraints of the phenol, and that this may be drastically potentiated by further restricting the conformational freedom of the phenol by creating the diaminoindanol activator ligand. This project describes recent efforts and challenges towards the production of a system for the enhancement of allylsilations and crotylsilations.

Eric Tong, Biomedical Engineering

Faculty Mentor: Professor Clark Hung, Department of Biomedical Engineering, Columbia University

Title: Effect of Concentration of Articular Cartilage Wear Particles on Articular Chondrocytes

Osteoarthritis (OA) is a joint disorder characterized by pain and swelling caused by wear of the hyaline cartilage on articular surfaces of bones. Due to the lack of vascularization, cartilage tissue has a very low propensity of self-repair, making OA a chronic disease. In the United States alone, OA affects 27 million people and costs more than \$60 billion per year. Studies have shown that in elevating grades of OA, higher concentrations of cartilage wear particles were present in the synovial fluid of the joint capsule. Additionally, cartilage wear particles injected into lapine knee joints led to marked cartilage degradation and synovitis. Due to these findings, in this study, articular cartilage wear particles were applied to chondrocytes to better understand OA. Cartilage particles were first generated from cartilage tissue using a custom wear particle generation device. The size of these wear particles were characterized and these wear particles were coulter counted to determine concentration of particles. The particles were subsequently applied at increasing concentrations to chondrocytes in order to study chondrocyte viability at various concentrations. Finally, chondrocytes were imaged to show phagocytosis of particles. Through this process, chondrocytes were shown to have a lower viability at higher concentrations of wear particles. This work suggests that sub-10 μ m cartilage particles above a specific threshold may be pathological and involved in OA onset and progression. Phagocytosis of wear particles may be a potential mechanism for the role of wear particles in OA development. Future work will continue to elucidate the mechanism by which cartilage wear particles interact with cells of the synovial joint, including synovium derived stem cells and chondrocytes. Studies will also characterize the biochemical and metabolic cellular changes and expression of OA biomarkers in relation to application of wear particles.

Bert Vancura, Biochemistry

Faculty Mentor: Professor Jonathan Owen, Department of Chemistry, Columbia University

Title: The Synthesis, Structure, and Reactivity of Novel Platinum Complexes with an N-Heterocyclic Carbon Donor Ligand

In recent years, the development of N-heterocyclic carbon donor ligands has been of great theoretical and practical interest to chemists. Theoretical interest rests in the electronic structure of transition metal complexes of these ligands, as the extent to which the ligand participates in backbonding with the transition metal center has not been conclusively determined. Practically, such transition metal complexes have had great success in catalyzing certain organic reactions, such as olefin metathesis and aryl halide cross couplings. In this work, we synthesized a novel Pt (II) complex with a N-heterocyclic carbon donor ligand from the methylation of 1,10-dichloro-5,6-dimethyl-4,7-phenanthroline and subsequent oxidative addition to Pt(PPh₃)₄. The resulting complex was characterized by ¹H NMR spectroscopy, ³¹P NMR spectroscopy, and X-ray crystallography. Future work will focus on the reactivity of this Pt (II) complex, specifically on its propensity to undergo oxidative addition to the untouched C-Cl bond.

Srikar Varadaraj, Mathematics

Faculty Mentor: Professor Jennifer Hom, Department of Mathematics, Columbia University

Title: Left-Orderable Groups and Knot Surgery

Boyer-Gordon-Watson have conjectured a correspondence between two very different invariants of 3-manifolds: the fundamental group and Heegaard Floer homology. The goal is to verify this conjecture in certain special cases arising from surgery on knots.

Amy Xia, Biology

Faculty Mentor: Professor Donna Farber, Columbia Center for Translational Immunology, Columbia University Medical Center

Title: The Role of Type I Interferon Signaling in Lung Resident Memory T Cell Populations

Influenza is a common respiratory tract infection that affects up to 20% of people and causes around 36,000 deaths per year. As a preventative measure, influenza vaccines present weakened or inactive forms of the virus to the human body's immune system, which helps the body develop protective antibodies against the virus. Studies show that influenza's viral activity is localized to the lung epithelium; after the infection occurs,

the body generates memory T cells that are only resident at the site of infection—the lungs. Therefore, resident memory T cells generate local immunity and protection in the specific tissues affected by infection and inflammation. This project aims to study how lung resident T cell populations are maintained in mouse models, specifically the role of Type 1 Interferon signaling. In lung resident memory T cells, Type 1 Interferon signaling is known to promote anti-viral responses when a ligand binds to the interferon receptor. Therefore, this project determined whether blocking a Type 1 Interferon alpha receptor in mouse lymphocytes caused a decrease in lung resident memory T cells.

Mice were infected with influenza and allowed to recover, thereby generating resident memory T lymphocytes in their lungs. Confocal microscopy was used to image the lung samples and determine that the resident cells largely reside along the lung airways. Then, mice with protective immunity were treated in vitro and in vivo with a control antibody or an antibody that blocks type 1 interferon alpha receptor (IFN- α R1). To determine the effect of the blocking antibody, lymphocytes extracted from the lung tissue were stained and analyzed using flow cytometry, which processes each cell in the sample and differentiates it depending on its staining.

During the IFN- α R1 blockade, the influenza specific resident memory T cells were reduced, as the proportion of circulating cells increased while resident cells decreased; in addition, the proportion of memory cells decreased. Therefore, this project confirmed the hypothesis that Type 1 Interferon signaling plays a pivotal role in the retention of memory T cells in tissues. This research increases our understanding of resident memory T cells, which could change the role that influenza and other diseases are treated. Instead of focusing on vaccination, a new alternative treatment method could focus on generating specific memory populations. In a broader sense, understanding the mechanism of resident memory T cells can allow for the therapeutic reduction of harmful cell populations that cause auto-immune disease like asthma.

George Yu, Math-Computer Science

Faculty Mentor: Professor Tim Leung, Department of Industrial Engineering and Operational Research, Columbia University

Title: Analysis of Discrepancies in Theoretical Black-Scholes and Option Metrics Greeks

The S&P 500 options contracts are among the most traded in the world, and hence accurate financial info is of high importance. The Black-Scholes partial differential equation (PDE) is an important tool used in the financial industry to accurately price European-style options—that is, options with a fixed exercise date. From the Black-Scholes equation the so-called “Greeks”—price sensitivities—are derived, and of these, we focus on Delta, the derivative of option value with respect to price. The monotonicity of the Black-Scholes equation also implies the existence of a unique inverse function, from which the implied volatility can be calculated from the market option price. We seek to determine if there is potential for discrepancy between the

values provided by some databases and the calculated Black-Scholes values on these S&P 500 contracts. Using OptionMetrics data for the date of August 1st, 2013, we examine both European- and American-style options written to expire on August 17th, 2013. We look at the implied volatility from a new angle, calculating it analytically from the option's delta and using standard numerical approximation techniques, and compare these with OptionMetrics' implied volatility data. We also examine a new method of calculating the delta for each option using the corresponding implied volatility data from OptionMetrics as opposed to setting a constant volatility across all options, and compare with the database's delta values.

Frank Zhong, Biochemistry

Faculty Mentor: Professor Michael Sheetz, Department of Biological Sciences, Columbia University

Title: Study of Mouse Embryonic Fibroblast Lateral Wave Spreading

Cell motility and migration is a key aspect of understanding how cells in the body move about to perform their functions. Motility and migration have been shown to be an important factor in a wide variety of different diseases and ailments ranging from tumor formation to infectious diseases. Here, we performed a study that looks at cell motility through the spreading of Mouse Embryonic Fibroblasts (MEFs) using submicrometer pillars of lengths 0.9 and 1.3 μm . We observed that the spreading phase of these cells is critically different between the 0.9 μm and the 1.3 μm pillars by measuring the amount of focal adhesions that were formed during the spreading phase. In addition, we examined lateral wave formation of MEF's under the strain of 2 different drugs, Calyculin A and Blebbistatin due to the inhibition of protein phosphatases and myosin II respectively.

Helen Zhou, Neuroscience and Behavior

Faculty Mentor: Professor Charles Zuker, Department of Neuroscience, Columbia University Medical Center

Title: Characterizing Cell Populations in the Gastrointestinal Tract

The gastrointestinal (GI) tract is a major sensory organ responsible for mediating food intake, digestion, and fluid homeostasis. It is home to over 60 taste receptor genes that detecting nutrients on the lingual epithelium, playing a role in nutrient sensation, satiety, and GI disorders. However, the intestinal taste pathway remains poorly understood, and the behavioral effects of its sensory capabilities have yet to be fully delineated. Enteroendocrine cells are specialized epithelial cells that express various taste receptors, and comprise the largest endocrine organ. EECs secrete over 20 hormones responsible for regulating digestion, metabolic response, and intestinal

motility. We have sought to identify and characterize intestinal cells expressing a number of receptors, hormones, and other proteins implicated in taste sensation and transduction pathways. Ultimately, these studies will help us assess the role of these candidate molecules in metabolic response, fluid homeostasis, intestinal inflammation, and microbiome maintenance. In order to characterize EEC populations in the GI tract, we screened for the presence of candidate molecules previously determined by RT-PCR of TrpM5 animals by performing double-fluorescence in situ hybridization. Whether and where different molecules—such as Chromogranin A, Glucagon, Neurogenin 3 (all thought to mark enteroendocrine cells), PYY, GLP-1, and others—are expressed and whether the stainings colocalize with one another can provide valuable insight into the different types of cell populations within the GI tract. We attempted two different methods of FISH to optimize results. In the first method, wild-type mice were sacrificed and gastrointestinal tissue dissected out, embedded fresh-frozen in OCT, and sectioned at 12 μ m. All RNA probes and FISH reagents were made from scratch, and we used a four-day ISH protocol. This method involves hybridization of digoxigenin- or fluorescein-labeled RNA probes to the mRNA sequences of interest within the cell, then visualization of signal using anti-DIG or anti-fluorescein antibodies to labeled probe and then tagging the antibodies with fluorescent markers using an alkaline phosphatase substrate system. In the second method, wild-type mice were again sacrificed and gastrointestinal tissue dissected out, but were embedded in paraffin and sectioned. We then used the Affymetrix Panomics QuantiGene 2-Plex Assay as well as commercial probes and carried out a 2-day protocol. The Affymetrix system labels individual mRNA through construction of a branched DNA structures which bind to each RNA probe hybridized to the target mRNA, and subsequent binding of AP-conjugated label probes to each branch on the tree-like amplification structure, providing up to a 3,000-fold amplification per target mRNA. Wild-type mouse tongue tissue is often used as a positive control for taste receptors such as T1R1, T1R2, T1R3, and T2R19. Wild-type mouse pancreas tissue is used as a positive control for other molecules such as glucagon, PYY, and GLP-1. The second method, using paraffin wax microbeads to embed tissue, has the advantage of preserving the morphology of tissue and prolonging the life of stained sections for long periods of time. The amplification technology also allows for more specific staining of cells and higher sensitivity to molecules of low expression, whereas the first method detects cells that are highly expressed but appears to be insensitive to many targets that are less highly expressed. The characterization of different cell populations in the GI tract. Peptide YY, implicated in appetite and satiety, colocalized completely with glucagon, which raises blood glucose concentration, suggesting both may be markers for a single population of cells. Chromogranin A, a neuroendocrine secretory protein, and glucagon were both originally thought to be markers of Although many results have been inconclusive, we have made some progress in nearly all EECs. However, ISH results demonstrated that ChgA- and Gcg-positive proteins did not completely colocalize in the GI tract, suggesting existence of two distinct subpopulations of EECs and raising questions about how they may differ in function and molecular makeup. Based on these observations, we plan to investigate the expression of ChgA and Gcg in EECs using conditional knock-outs as well as cell stimulation and ablation to characterize cell subpopulations as well as study the functions carried out by these cell types. At present, we are still working towards

optimizing the FISH protocol to detect low expression of target molecules and minimize background staining. Characterization of EEC populations in the GI tract will continue using the second method as described above, and the functional significance of other candidate molecules will be investigated by conditional knock-out, and cell stimulation and ablation. The project's results could lend themselves to behavioral studies based on the function of certain GI tract cell types, potentially aiding development of new strategies for the prevention, management, and treatment of GI disorders, such as inflammatory bowel disease, irritable bowel syndrome, and metabolic disorders.
