

2015

Columbia University Undergraduate Science & Engineering Research Showcase Abstracts



Friday, October 16, 2015

11:00 AM – 12:30 PM

Roone Arledge Auditorium

Lerner Hall

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Olamide Adeniyi, Chemistry

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Faculty Mentor: Professor Maxwell Gottesman, Department of Microbiology and Immunology, Columbia University Medical Center

Title: The Role of NusG in N Antitermination

Abstract: In *E. coli*, NusG is an essential regulator of RNA polymerase. Due to its two domain structure, NusG acts as flexible linker in the anti termination complex, that promotes elongation rates by suppressing transcriptional pausing in vitro. However the specific role of NusG in the process of N antitermination is still unclear as anti-termination has been observed in the absence of NusG, *in vivo*. Several point mutations in the 3D structure of the protein that lie in both NusG-CTD and NusG-NTD have been proven to eliminate Nun exclusion of. All of these alleles can replace NusG in wild type *E. coli*, indicating that they make active NusG protein. Attempts to block N antitermination by isolating a point mutation in NusG has yielded a library of mutants that survive infection by the phage Lambda.

John Avendano, Psychology

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Faculty Mentor: Professor Ann McDermott, Department of Chemistry, Columbia University

Title: Reduction of Radicals as seen by EPR and UV Vis Spectroscopy

Abstract: My research looked at the stability of paramagnetic nitroxides. The McDermott Group uses these compounds to enhance solid-state NMR signals through DNP experiments. However, once added to biological samples of interest, these radicals often have finite lifetimes. To ensure the success of the DNP experiment, it is important to know the rate of nitroxide reduction in biologically relevant samples such as whole cells, protein preparations, and liposomes. Here, we measured the stability of nitroxides by tracking the EPR signal and the UV/Vis absorbance of the nitroxide over time under various experimentally relevant conditions. To rank radical stability, we combined radicals in various concentrations with different reducing agents and also tested them in buffers at varying pHs. We also tracked radical stability in protein and liposome preparations. My results confirmed that ascorbic acid is a stronger reducing agent than cysteine and glutathione, which is encouraging since cysteine is the main biological reducing agent. Preliminary results also show that the DNP-relevant radical AMUPOL reduced more easily than TOTAPOL: a surprising result given prior scientific papers. We also measured the rate of nitroxide reduction in protein and liposome samples and are elucidating the mechanism of nitroxide reduction in these preparations.

Masih Babagoli, Biochemistry

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Faculty Mentor: Professor Perry Sheffield, Mailman School of Public Health, Columbia University Medical Center

Title: Evaluating the Monetary Health Benefit of the Current Citi Bike System and the Impact of Station Location

Abstract: Citi Bike – NYC's bikeshare system – was established in May 2013 and is currently the largest bikeshare program in North America (approximately 24,000 rides/day). However, there is little available literature on the health impacts of not only the current system but also its planned expansion. We had two objectives: 1) to estimate Citi Bike's current annual monetary health benefit and 2) to investigate how station location in areas of different socioeconomic status (SES) would affect the health benefit. A potential concern is that stations in lower SES areas are used less frequently. However, individuals in these areas have higher chronic disease rates that could benefit relatively more from increased physical activity. We used the WHO's Health Economic Assessment Tool (HEAT), which calculates and monetizes reductions in mortality due to increased physical activity. From HEAT, we estimated the health benefit of the current Citi Bike system to be approximately \$46,000,000 per year. Secondly, we found that out of all census tracts containing newly planned stations, the highest and lowest poverty levels were 58.1% and 2.0%, respectively. Using a NYC DOHMH report containing the relationship between census tract poverty levels and mortality rates, we determined that the mortality rate in the lowest SES census tract was 1.7 times that of the wealthiest tract. Again using HEAT, we demonstrated that an equivalent health benefit – from averted deaths - would be obtained from new bike stations in both of these tracts even if rides decreased by much as 1.7 times for the new station in the lowest SES tract. Our findings underscore the immense health benefit from NYC's bikeshare and support establishment and promotion of new bike stations in lower socioeconomic areas.

Julia Barasch, Neuroscience and Behavior

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

Title: Continued Study of the Drosophila CRTC Molecule as a Potential Activity Marker in Response to Physiological Stimuli

Abstract: Activity markers allow us to study how a brain encodes valence by indicating the pathways active in response to a variety of stimuli. Knowledge of an activity marker in an organism of study allows us to learn about how brain structure informs behavior (or how behavior alters brain structure) through artificial and physiological experimentation. Martin et al. describe the rodent CRTC molecule (CREB-regulated transcriptional co-activator) which they report is capable of conveying recent neural activity. Specifically, they found that CRTC is dephosphorylated and moves from a neuron's cytoplasm to nucleus upon calcium influx. Dephosphorylation frees CRTC from the 14-3-3 protein tethering it in the cytoplasm and allows it to enter the nucleus; upon re-phosphorylation, the molecule returns to the cytoplasm where it sits until calcium levels spike again. They note that since its movement does not

require transcriptional or translational changes in the neuron, it serves as an ideal activity marker. A homolog of this rodent activity marker is also found in *drosophila*. We tested whether CRTC in flies also exhibits activity-dependent translocation (and can thus be called an activity marker) by driving CRTC-GFP expression in a set of cells and using external stimulation to test its movement. Specifically, Melissa drove expression of a temperature sensitive cation channel, TRPA1, in a small subset of projection neurons (PNs) and compared nuclear CRTC levels between flies exposed to heat and those kept in basal (25-degree) conditions. This artificial stimulation caused CRTC-GFP to flood the nucleus of cells expressing TRPA1. Melissa tested this in 2 sets of cells, MZ19 PNs and $\alpha'3$ mushroom body output neurons (MBONs), and found that in both cases the flies in the activating condition (those with TRPA1 exposed to heat) had significantly higher levels of nuclear CRTC than those that were not artificially activated or that did not have UAS-TRPA1. Through these experiments, *drosophila* CRTC has been shown to undergo activity-dependent translocation in response to artificial activation but we have yet to test this with physiological stimuli.

The olfactory system of *drosophila* is good for such physiological experimentation because of its size and clean circuitry. In it, each different odor activates a specific PN pattern allowing for controlled experiments in which we study activation of just a small subset of neurons. If we expose flies to odors and examine CRTC-GFP movement in the specific PNs for these odors, we can answer the question of whether CRTC can detect physiological stimuli and act as an activity marker in response to them. Also, by altering conditions of odor exposure, we can determine the sensitivity of CRTC's movement in this physiological system. With knowledge of the conditions of odor exposure that cause the most robust movement of CRTC, we can use the olfactory system to ask biological questions. Questions such as: Does a fly's mating status affect activity in its PNs that respond to mating-related scents (like cVa)? Is there a difference in dopamine neuron (DAN) activity for innately important or synthetic (neutral) odors?

These are the questions I set out to answer this summer, in my third year of investigating the CRTC molecule's movement. To do this, with the help of the postdoc whom I worked with (Daisuke Hattori) and his technician, I designed, built, and coded the program of an olfactometer machine from scratch using MATLAB. We then conducted a variety of experiments on this olfactometer and the 2-photon microscope to test CRTC movement in the MZ19 line, known to respond to the scents of farnesol and cVa. We saw positive results when exposing flies to farnesol in the olfactometer and comparing their nuclear: cytoplasmic CRTC levels in the cells of the MZ19 known to be responsive to this odor with flies that had only been exposed to oil, but need much repetition of this experiment in order to prove that CRTC moves after exposure to this scent as there is much basal level variability between organisms!

William Carson, Neuroscience and Behavior

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Faculty Mentor: Professor Martin Chalfie

Department of Biological Sciences, Columbia University

Title: Identification of a Mutation that Causes Defective Anterior Touch Receptor Neuron Touch Polarity in *C. elegans*

Abstract: Mutations of genes in the Wnt pathway have a prominent role in determining the polarity of the gentle touch neurons in *C. elegans*. For instance, deficiency of lin-44, a Wnt ligand, results in reversal of the posterior PLM. It is indicated that lin-44 is the primary Wnt needed to establish PLM polarity (Prasard and Clark, 2006). Reversal in polarity of the anterior touch receptor neurons ALM AP to occur, mutations in 3 different Wnt genes are needed, cwn-1 and egl-20 and lin-44 (Prasard and Clark, 2006). We have observed a single mutation that causes reversal of polarity in the ALM touch receptor neurons. The strain carrying this mutation suffers from a decrease in movement that becomes more severe with age. The mutation is also embryonic/larval lethal. To identify the gene responsible for these defects, we mated animals carrying the mutation to a *C. elegans* strain with known small nucleotide polymorphisms (SNPs). We then selected progeny exhibiting the mutant phenotype for whole genome sequencing (WGS). We aim to use the differences in SNP distribution to pinpoint the region of the gene with the mutation.

Kristy Choi, Computer Science-Statistics

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

Title: Profiling the Immune Landscape with Single-Cell RNA-Sequencing

Abstract: Single-cell RNA-sequencing technology offers a promising avenue for characterizing cell populations while preserving cell-to-cell heterogeneity. Ultimately, this project seeks to extend the functionality of a newly developed protocol, particularly in the context of cancer. With two different profiling approaches, we hope to gain a finer-resolution image of immune cell activity and response. First, we will sequence individual, sorted T-cells in order to capture both T-cell receptor (TCR) and targeted phenotypic transcripts. The resulting information will allow us to draw conclusions about TCR repertoire diversity as well as expressed pathways related to T-cell activation and cell-killing. In the second approach, we will target a wider variety of immune cells – ranging from peripheral blood mononuclear cells (PBMCs) to myeloid cells – in order to examine their cellular states and active pathways at a more granular level. As we are currently in the preliminary stages of experimental design, we have developed a pipeline to design primers such that we can capture our desired transcripts with high efficiency, while minimizing the formation of secondary structures such as primer-dimers in multiplex PCR. Upon finalizing the list of target phenotypic genes and completion of the experiment, we will proceed with error correction, TCR re-assembly, and differential gene expression analysis with the sequenced cell libraries.

Omid Cohensedgh, Neuroscience and Behavior

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Faculty Mentor: Amanda Fakira, PhD, Department of Anesthesiology, Columbia University Medical Center

Title: Morphine Conditioned Place Preference Induces Structural Plasticity of CA1 Pyramidal Neurons in the Hippocampus

Abstract: Opioid addiction affects 2.1 million people in the US, costing society \$56 billion a year. There is an 80% relapse rate in abstinent abusers, indicating the need to understand the mechanisms behind drug craving. Synaptic plasticity, a proposed mechanism for addiction and relapse, has been linked to morphological changes in dendritic spines. However, the underlying causes of opiate induced functional and structural plasticity in the hippocampus have not been investigated. Here, we investigate the role of context in the morphological changes in spines following morphine administration and the roles of RhoA and RhoA-inhibitor in affecting spine morphology.

Method: Mice were treated with saline or escalating doses of morphine every 24 hours, and placed in a CPP chamber for 30 minutes or back into their home cages. Mice placed in the CPP chambers had their saline or morphine treatment either paired or unpaired with a context. After four days, the hippocampi were removed to assay RhoA and Rac1 activity. Dendritic segments in the CA1 pyramidal neurons were imaged and dendritic spines were counted using 3D-reconstruction. A preference test was also administered following administration of H1152, a RhoA-inhibitor.

Results: Morphine administration caused a decrease in overall spines in both CPP paired and unpaired conditions from 2 spines/?m to 1.5 spines/?m. Morphine CPP increases RhoA but not Rac1 in the hippocampal synaptosomal fractions. Unpaired mice were found to have increases in Rac1 and RhoA expression in synaptosomal fractions. Morphine administered in the home cage did not cause an increase in RhoA in the synaptosome. Context preference was attenuated following RhoA-inhibitor (H1152) administration by about 10%.

Conclusion: Pairing morphine with any new environmental cues (e.g. CPP apparatus) decreases the number total spine. RhoA activation accompanied a decrease in spines in both paired and unpaired conditions, suggesting that RhoA activation mediates changes in spine morphology. When morphine was administered to mice in their home cages, RhoA did not increase, suggesting that the context in which morphine is administered plays an essential role in affecting synaptic plasticity. RhoA-inhibitor succeeded in attenuating preference suggesting potential therapeutic targets. These results suggest environmental cues play a role in opioid-induced morphological changes in the brain, and these morphological changes and their signaling pathways may serve as potential therapeutic targets for opioid addiction.

Eliza Cricco-Lizzaer, Biochemistry

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

Title: Investigation of Heterocyclic Sulfoxides: Synthesis and Application toward Dehydrative Catalysis

Abstract: This project concerns catalysis of dehydration reactions, which are widely utilized in industry and commonly crucial to many types of chemistry. Current catalysts are often limited in scope, such as strong acid and heat, or highly harmful and difficult to use, such as DEAD and DCC. It is in this context that we seek to identify a true catalyst of dehydrative chemistry, making use of the unique properties of certain mesocyclic sulfoxides capable of transannular activation. Our previous efforts involved a catalyst structure with Nitrogen as the activating heteroatom. After observation that this Nitrogen overly stabilized the species, a new design is here attempted with less electron-donating Sulfur as the heteroatom. Though its performance as a catalyst has not been confirmed, we have discovered additional potential for this structural framework as a highly reactive and broadly applicable ylide.

David Dai, Neuroscience and Behavior

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Faculty Mentor: Dr. Lloyd Greene, Department of Pathology and Cell Biology, Columbia University College of Physicians & Surgeons

Title: Guanabenz Derivatives Show Neuroprotective Effects in Two Cellular Models of Parkinson's Disease

Abstract: Parkinson's Disease (PD) is a neurodegenerative disorder that is characterized by the death of dopaminergic neurons in the brain's substantia nigra. Unfortunately, there are currently no effective cures for PD. Our lab previously found that Guanabenz (GA), an FDA-approved drug for hypertension, was capable of protecting neuronal PC12 cells from dying in the 6-hydroxydopamine (6-OHDA) cellular model of PD by increasing cellular levels of parkin protein, making GA an exciting candidate for PD-targeted neuroprotective therapies. However, GA's inherent effects on blood pressure and its instability in cell media exposed its limitations in clinical use. As a result, several GA derivatives (denoted 19, 55, and 63) were created. These compounds lack the cardiovascular effects of GA and were tested for their potential usage in PD-related neuroprotective therapies. My results indicate that compounds 19, 55, and 63 seemed to protect neuronal PC12 cells from 6-OHDA, while compounds 19 and 55 protected cells from 1-methyl-4-phenylpyridinium (MPP+), another PD-mimicking cellular model. In all cases, the GA derivatives showed enhanced protective ability when compared to GA. Furthermore, compound 19 protected cells after 48 hours of neurotoxin incubation and increased cellular parkin levels 48 hours after initial addition. These results suggest that compound 19 is more stable than GA, as GA is degraded within 24 hours of being added into cell media. Thus, without any cardiovascular side effects and with enhanced protective mechanisms, compound 19 is a good candidate for PD-targeted neuroprotective therapies.

Shirin Dey, Earth and Environmental Engineering

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Faculty Mentor: Ph.D. Candidate Maria Colmenares, DAAD RISE Scholarship Program, and Technische Universitat, Berlin

Title: What is Ordered Mesoporous Silica?

Abstract: Ordered mesoporous silica (OMS) is a versatile nano-carrier, having applications ranging from chemical catalysis to drug delivery. OMS is made of nano-sized, hexagonal crystals that have an intricate honeycomb structure of cylindrical pores. To the naked eye, these crystals look like powdered sugar. But, for example, when loaded with anti-cancer medication and tagged to attack specific targets, OMS particles act like Trojan horses, stealthily releasing cytotoxic agents inside unsuspecting cancer cells. OMS is unique in its biocompatibility, high surface area allowing for subsequently high drug loading, and ability to target cancer cells, thus sparing the healthy cells that chemotherapy normally destroys. OMS is therefore one example of nanotechnology in medicine that represents a paradigm shift from managing cancer to actually curing cancer.

Willie Dong, Mathematics

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Faculty Mentor: Dr. Joanna Nelson, Department of Mathematics, Columbia University

Title: Obstructions to Symplectic Embeddings

Abstract: We focus on obstructing symplectic embeddings of polydiscs into other 4-dimensional symplectic toric manifolds.

Anjali Doshi, Biophysics

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Faculty Mentor: Dr. Teresa Head-Gordon, Amgen Scholars Program, Teresa Head-Gordon Laboratory, University of California, Berkeley

Title: Analysis of Star Diblock Copolymers Designed for Biomedical Applications

Abstract: Star polymers are a class of molecules that hold great promise as drug delivery vehicles due to their potential for delivering targeted and timed dosages for treating diseases such as cancer and rheumatoid arthritis. Careful study of these polymers is necessary to verify their ability to function properly and safely in physiological conditions. Therefore, we analyzed the behavior of two classes of star diblock copolymers, developed by IBM, which are the first of their kind to load and release hydrophobic drugs under different conditions. In the first class, designed to be degradable, the diblock arms are composed of a hydrophilic block of polyethylene glycol and a hydrophobic block of poly- δ valerolactone attached to a caprolactone core. The second class's non-degradable polymers consist of a divinylbenzene core with arms of polystyrene and polymethacrylate, which has varied amounts of polyethylene glycol and tertiary amine pendant groups. The size and shape of these molecules over a range of pH values was investigated using small angle x-ray scattering. Preliminary

analysis of the data showed that the polymers take on a globular shape. The data were then fitted to ideal geometric functions, which demonstrated that the polymers take on a “core-shell” shape in solution, with the hydrophobic blocks of the arms densely packing to create a spherical “core” and the hydrophilic blocks loosely creating a “shell.” The degradable series of polymers, as expected, was more polydisperse (heterogeneous in size) than the non-degradable series. The more basic non-degradable polymers were found to expand in size with decreasing pH. This trend is likely due to repulsion between the tertiary amine groups, which become positively charged in acidic conditions. Overall, the ability of these polymers to change shape and size in response to pH will make them attractive candidates for tunable drug uptake and release.

Britt Fossum, Chemistry

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Faculty Mentor: Professor Colin Nuckolls, Department of Chemistry, Columbia University

Title: Perylene Diimide Derivates for STM Break Junction

Abstract: We describe the study of several Perylene Diimide derivatives designed for obtaining single molecule conductivity measurements. Two synthetic routes were attempted to make a PDI monomer substituted at the bay positions with a thioanisole alkyne subunit, which is known to conduct based on previous measurements using an STM break junction technique. This PDI was then subjected to HPLC to isolate samples of 1,6 and 1,7 isomers. A 10 mg sample of the 1,7 isomer and a 2 mg sample of the 1,6 isomer were isolated, characterized, and submitted for STM break junction measurements.

Anna Fu, Biochemistry

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Faculty Mentor: Professor James T. Vosseller, Department of Orthopaedic Surgery, Columbia University Medical Center

Title: Impact of Delay in Ankle ORIF in Surgical Outcome

Abstract: 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 surgery. The effect of these small delays has not been overtly studied. The 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, Mathematics

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Faculty Mentor: Nicholas Tatonetti, Department of Biomedical Informatics, Columbia University Medical Center

Title: Compilation of a Condition–Symptom Database from Adverse Event Reports

Abstract: A useful condition–symptom database is currently not available for public use. Such a database could prove helpful in drug repurposing, among many other projects. This project seeks to develop such a database for public use. The Adverse Event Reporting System is managed by the FDA, and compiles non - PHI reports of interactions reported between different drugs. The reports only contain the indications being treated, the drug profile of the patient, and the drug dosages. Since the reports do not contain age, ethnicity, or medical background; removing selectional bias while forming a control group can prove difficult. Several studies have shown that forming control groups with similar drug profiles to the experimental group can vastly reduce the effects of these biases. This study uses and expands upon those bias-reduction techniques used and analyzed in other previously published studies. This study uses the same drug profile matching, but also adjusts for reporting errors by searching for ""key drugs"" that have nearly exclusive drug-indication relationships. Drug profile bias is then removed using a side effect database. This study uses this additional step to form control and experimental groups for every indication with at least 500 instances in the Adverse Event Reporting System database (about 4000 indications). The study then proceeds to find the reporting rates of every reaction reported on all the AERs for the control and experimental groups. By comparing the reporting rates of every reaction, the program then finds which reactions are statistically more prevalent in the experimental group. Since the experimental and control groups share the same drug profile, this study makes the claim that the supposed side effects that are more prevalent in the experimental group are actually just symptoms of the indication, being reported as reactions. Numerous case studies of individual indication - symptom profiles proves that this methodology holds much promise for the creation of a condition - symptom database, and the case studies also show the specific weaknesses of such an approach.

Graham Gobieski, Computer Science and Chemistry

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Faculty Mentor: Luis Campos, Department of Chemistry, Columbia University

Title: ClickabILs: Cyclopropenium Ion Containing Poly(ionic liquids) by Post Polymerization Click Reaction

Abstract: Recently there has been much research on the synthesis and characterization of organic polyelectrolytes for applications in organic capacitors, cationic polymer/DNA 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-transfected cell lines.

Tze Goh, Astrophysics

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Faculty Mentor: Dr. Michael Hahn, Department of Astrophysics, Columbia University

Title: Solar Coronal Oscillations and the Coronal Heating Problem

Abstract: The solar coronal heating problem asks why temperature is increasing away from the surface of the sun. We hypothesize that the dissipating waves along coronal loops is responsible for this extra energy. I analysed these waves in IDL to determine if they have enough energy to heat the coronal loops. We found that there is likely enough energy to heat the loops, but we still need a more accurate measurement of the proton density.

Cynthia Hajal, Mechanical Engineering

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Faculty Mentor: Professor James Hone, Department of Mechanical Engineering, Columbia University

Title: Mechanosensor in Integrin Signaling: The Emerging Role of EGFR

Abstract: Although the epidermal growth factor receptor (EGFR) is known to interact with integrins in the processes of cellular spreading and motility, little is known about the actual role of EGFR. Previous studies from our laboratory have shown that in the early interactions of cells with rigid Arg-Gly-Asp (RGD) ligands, EGFR activity is needed for normal cell spreading and for the assembly of local contraction units that sense rigidity. EGFR inhibitors blocked local contractions and normal spreading in media lacking serum and soluble EGF. Here, we test the hypothesis that EGFR is mechanically activated by substrate stiffness through selectively modulating stiffness of submicron pillar arrays and we analyze the correlation between local contraction force and EGFR phosphorylation. To verify our hypotheses, we used submicron pillars of different stiffnesses as mechanical tools to study the effect of EGFR on cellular growth. On the one hand, our results suggested that wild-type cells plated on pillar arrays exert more contraction forces on these pillars than EGFR-inhibitor cells plated on similar arrays. Thus, EGFR is correlated with cellular rigidity sensing. On the other hand, we also showed that paxillin and phosphorylated EGFR have higher concentrations in the cellular regions plated on stiffer pillars. From these findings, we concluded that EGFR is a mechano-sensor with a higher level of activation on stiffer substrates.

Ifeoma Irobunda, Biology

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Faculty Mentor: Professor Mimi Shirasu-Hiza, Department of Genetics and Development, Columbia University Medical Center

Title: The Influence of Pigment Dispersing Factor on Immune System Function and Metabolic Activity in *Drosophila melanogaster*

Abstract: Circadian rhythms within a host organism play a complex and not-well-understood role in the host organism's ability to survive bacterial infection. The circadian state of the host is directly tied to metabolic function—aberrant circadian rhythms have been shown to affect metabolic function in metabolically-dysregulated patients, and moreover significantly impact survival rates in *Drosophila melanogaster*. The neurohormone Pigment Dispersing Factor (PDF) in *Drosophila* is required for circadian rhythm and is thought to play a role in both immune function and metabolism, as PDF mutants have altered metabolic function. Fruit flies that are deficient in PDF have been previously shown to exhibit resistance to *S. pneumoniae* upon bacterial infection, suggesting that PDF inhibits resistance to *S. pneumoniae*, and knockdown of PDF receptors in the fat body has been shown to cause similar resistance to infection. The fat body in *Drosophila* controls immune system function and metabolism, and is analogous to the liver. It is moreover the main sight of antimicrobial peptide (AMP) production, a major immune response in *Drosophila* that occurs upon infection. The present study aims to help further elucidate the role of PDF in regulating immunity and metabolic function upon introduction to bacterial infection by performing survival assays with various pathogens and analyzing AMP levels in PDF mutants. Here, we further determine the profile of PDF mutant resistance to infection and use qRT-PCR to test AMP levels in PDF mutants and determine regulation levels both after bacterial infection and in the absence of infection, at zero hour timepoints. In addition to exhibiting *S. pneumoniae* resistance, PDF mutants are preliminarily shown to further be resistant to *P. rettgeri*, levels of at least one AMP are higher after bacterial infection, and basal levels of several AMPs are upregulated in PDF mutants at the zero hour timepoint. The results of these tests, though still pending, coupled with further manipulations of AMP levels in PDF mutants, will shed light onto the precise effects PDF signaling within the fat body has on overall immune function. Additionally, identifying the role of the fat body in metabolic function can have significant pharmacological implications for patients afflicted with illnesses characterized by metabolic dysregulation.

Isaac Jiffar, Computer Science

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Faculty Mentor: Professor Gregg Harry, Department of Physics, American University

Title: Continuous Q Measurement of Mechanical Resonators

Abstract: The focus of my work at American University was developing a feedback loop in order to continuously measure the quality factor (Q) of a resonant system. More precisely, we were measuring the quality factor of a silica mirror that resonates at specific mode frequencies. The purpose of these measurements were to test different materials for use in the Laser Interferometric Gravitational-wave Observatory (LIGO). LIGO is a project with two

operational detectors that aim to directly detect a gravitational wave, and one of the main obstacles to optimal performance is reducing the thermal noise of the system, which corresponds to the quality factor of the materials used. In order to do this, however, we need a good way of measuring quality factor. The method of measuring the quality factor that we are working on, which is an update on a system originally created by Nicolas-Smith Lefebvre, aims to measure the quality factor by driving the mirror at resonance and then measuring the amount of energy you need to continue to put into the system to keep it oscillating with the same amplitude (which is equal to the mechanical loss and will give you the quality factor). This is opposed to the current method of measuring the quality factor, which requires you to excite the mirror at resonance and then withdraw the stimulus, measuring the amount of time the system takes to return to normal. The benefits of our system is while the current system requires the detector to be shut down during testing, our system would allow the detector to continue operation during testing because it would be kept at the same level of oscillation with a feedback loop rather than being excited and then removing the exciter.

Lara Karaaslan, Neuroscience and Behavior

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Faculty Mentor: Dr. John Loike, Physiology and Cell Biophysics, Columbia University Medical Center, College of Physicians and Surgeons

Title: Microglial Cells in Parkinson's Disease: Cellular Assassins with a Double Edged Sword

Abstract: Parkinson's disease (PD) is a progressive, late-onset neurodegenerative disorder that affects approximately 1 million people in the United States. Parkinson disease is a process mediated by inflammation and marked by a progressive loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpc) region of the brain. This study seeks to examine the role of microglial cells in PD pathology. We hypothesize that in non-affected individuals, the cellular release of alpha-synuclein from neurons into the SNpc is rapidly and effectively cleared by glial cells without activating a robust inflammatory response. In Parkinson's patients, this clearance is altered and results in the activation of glial cells, triggering inflammation and the production of reactive oxygen species, which promotes further neurodegeneration. Our lab has identified SR-B2 scavenger receptors and CD-11b beta-2 integrins as crucial mediators of microglial cell interactions with matrix bound synuclein. We show that the efficiency of glial cells in clearing modified and mutated forms of alpha-synuclein is markedly reduced as compared to wild type alpha-synuclein. Additionally, oligomeric species of alpha-synuclein are shown to be less effectively cleared from the extracellular matrix as compared to wild type monomeric alpha-synuclein. The abnormal accumulation of uncleared modified, mutated, and oligomerized alpha-synuclein results in activation of microglial cells as well as the production of neurodegenerative biologicals. In order to attenuate Parkinson's pathology we must direct microglia to up-regulate alpha-synuclein clearance without triggering the inflammatory response, thus balancing the double-edged sword properties of microglial cells.

Hyeon Jin Koo, Biology

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Faculty Mentor: Professor Gerard A. Ateshian, Department of Mechanical Engineering, Columbia University

Title: Initiating and Characterizing Cartilage Damage under Physiologic Loading Conditions

Abstract: This experimental study tests two hypotheses that address the wear mechanism of Osteoarthritis (OA) in physiologic conditions: friction coefficient alone is not a robust measure of cartilage damage; fatigue wear, not abrasive wear, is the chief wear mechanism of OA. Our preliminary data was inconsistent with the conclusions reached by previous studies. This study aimed to resolve the conflict. Design: To analyze the effect of different loading configurations on the friction response of immature bovine knee joints, 24 explants were harvested and subjected to migrating sliding motion with either glass lens or cartilage contact surface. All explants were submerged in a culture medium of either synovial fluid (SF) or saline. Results: Friction coefficient underwent a temporal evolution, frequently changing during a damage event. As hypothesized, fatigue wear accurately described the mechanism of initial cartilage damage under physiologic conditions. To induce damage to cartilage, both the choice of boundary lubricant and the choice of load material were considered. Conclusions: These results shed light on the disagreement between prior research vs. our preliminary data and a recent 2009 study. Friction coefficient ? was revealed a better measure of cartilage damage if recorded during a damage event. As hypothesized, fatigue wear prevailed as the characteristic wear mechanism even in physiologic loading configurations. Fatigue damage resulted in visible delamination of the middle zone (MZ) due to fatigue failure.

Elizaveta Kulko, Chemistry

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Faculty Mentor: Dalibor Sames, Department of Chemistry, Columbia University

Title: Synthetic and Biochemical explorations of Iboga Alkaloid Scaffold

Abstract: Morphine and related opiate analgesics are among the most effective drugs for the treatment of severe pain. The analgesic action of these drugs is due to their ability to activate the mu-opioid receptor (MOR) in the spinal cord, brain stem, and forebrain pathways involved in transmission of painful stimuli from the peripheral sensory system into the central nervous system (CNS). Unfortunately, classical opioid analgesics suffer from serious disadvantages, namely high addiction liability, the rapid development of tolerance, and respiratory depression. Accordingly, novel opioid agonists with reduced potential for abuse remain of high interest. Selective kappa-opioid receptor (KOR) agonists hold potential as alternative analgesics and antidepressants with less potential for addiction or physical dependence since KOR is not connected to dopamine reward circuit. However, there are unwanted side effects associated with full KOR agonism, including dysphoria and hallucinogenic effects. We and others hypothesize that a partial or low potency agonist of the receptor may avoid the aversive effects of the full KOR agonist while retaining the beneficial analgesic effects. Recently, the Sames Lab found that benzofuran analogs of ibogamine are potent agonists and antagonists of the opioid receptor system, with modest selectivity for KOR, which makes them

desirable lead compounds for further exploration. The novel analog with β -ethyl substituent in relation to N-atom appears to be a promising selective antagonist of KOR in our biological assays ($IC_{50} = 8.2 \pm 0.5 \mu M$), which may hold potential for targeting depression. We therefore report the synthesis and biological activity of additional iboga analogs with a methyl substituent at other positions on the isoquinuclidine core in order to further explore the strong SAR found in this region in the hopes of finding new therapeutics for pain and depression.

Daniel Lee, Mathematics-Statistics

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Faculty Mentor: Professor Laura Kaufman, Department of Chemistry, Columbia University

Title: Simulation of Breast Cancer Cells

Abstract: Shape of breast cancer cells is known to influence the invasiveness and rate of tumor growth. Although there are physical, chemical, genetic, and other factors that are believed to influence cell morphology, we use simulation of the two-dimensional Potts model to determine the minimum physical factors needed to create four major breast cancer cell shapes: round, mass, grape-like, and stellate. Cell-cell contact, cell-environment contact, and curvature of the cell surface are the energy values in the Potts model that are optimized in an effort to produce different morphologies. This research has yet to produce the desired shapes, but is ongoing with consideration for the modification of the Hamiltonian equation.

Hyunwook Lee, Biochemistry

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Faculty Mentor: Professor Virginia Cornish, Department of Chemistry, Columbia University

Title: Screening of Vitamin D Derivatives Using a Yeast Two Hybrid System

Abstract: The yeast two hybrid (Y2H) system has been shown to be an important and valuable tool for investigating protein-protein interactions in a high-throughput manner. The aim of this study is to use the yeast *Saccharomyces cerevisiae*, as a heterologous host for discovery and production of biologically active vitamin D derivatives, such as 1 α ,25-dihydroxyvitamin D3 (calcitriol). The selection of yeast cells that produce calcitriol and other vitamin D derivatives can be achieved with the Y2H system. Previously, a Y2H system that successfully screened for vitamin D has been reported, in which a lacZ reporter gene and GAL4 transcription factors were used. For our Y2H system, one integration plasmid containing the LexA DNA binding domain fused to the vitamin D receptor ligand binding domain (LexA-VDR) and an expression plasmid containing B42 activation domain fused to the retinoid X receptor β ligand binding domain (B42-RXR β) were constructed, both located downstream of a GAL1 promoter. The LexA DNA binding domain and B42 activation domain allow compatibility with Gal activation of the cytochrome P450 hydroxylating enzymes. We hypothesized that the vitamin D-dependent heterodimerization of the VDR-LBD and the RXR β -LBD will induce transcription of the reporter gene. Two different reporter genes, HIS3 and lacZ, were placed downstream of a minimal GAL1 promoter and multiple LexA operons. The HIS3 gene allows for selection of the cells of interest rather than screening, which can be more work-intensive.

We demonstrated a 7-fold difference in optical density between the cultures with 100 nM calcitriol and no calcitriol. In addition, we demonstrated that the two hybrid system was at least 10 times more sensitive to calcitriol than other vitamin D derivatives, including calcidiol, calcipotriol, and vitamin D3, using a beta-galactosidase assay. These results show promise in our yeast two hybrid strain's ability to be selected for calcitriol production. We are currently working on heterologously expressing in the same strain 25-hydroxylase (CYP2R1) and 1?-hydroxylase (CYP27B1), mammalian enzymes for calcitriol production from vitamin D3, and using the Y2H system to optimize production of active vitamin D derivatives.

Cameron Lemley, Astrophysics

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Faculty Mentor: Professor David Schiminovich, Department of Astronomy, Columbia University

Title: Galaxy Evolution Explorer (GALEX): Galactic Plane Survey

Abstract: The Galaxy Evolution Explorer (GALEX) completed its survey of the Galactic plane in the near-ultraviolet during 2012. Although preliminary data were released shortly after the completion of the survey, the full dataset was reanalyzed during 2014 using refined attitude correction techniques that yield angular resolution-limited images. The GALEX Galactic plane survey includes more than 75% of the sky between $10 > b > -10$ degrees. The initial photon dataset contains about 400 individual scans, each of which is a vertical slice of the Galactic plane. Each slice spans 1500-1700 seconds, during which the 1.24 degree diameter field of view performed a double-pass sweep across the Galactic plane. The Galactic Plane survey was the only time this non-standard, high scan rate acquisition mode was exercised during the mission, and required specialized processing and astrometric refinement to produce high quality sky maps. We present the first high-resolution map of the Galactic plane in the near-ultraviolet as well as a catalogue of thousands of sources for follow-up with HST. This work was partially supported by the Keck Institute for Space Studies.

Charles H. Liang, Applied Physics

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Faculty Mentor: Professor Elizabeth M.C. Hillman, Egleston Scholar Fellowship, Laboratory for Functional Optical Imaging (LFOI), Columbia University

Title: Structured Light Sheet Microscopy for High-speed, Volumetric Imaging

Abstract: Over the past decade, light sheet microscopy (LSM) has emerged as a promising volumetric (3D) imaging modality, particularly in the field of developmental biology and neuroscience. Swept confocally aligned planar excitation (SCAPE) microscopy is a novel LSM variant that permits the imaging of large fields of view at high speeds () over a diverse set of samples, from freely crawling *Drosophila* larvae to *in vivo* mouse brain. A major challenge in imaging thick samples is degradation of image quality due to light scattering caused by the sample's tissue. Here, we present an implementation of SCAPE with HiLo, a type of structured LSM that reduces out of background components and improves contrast. Although the implementation is still under development, SCAPE with HiLo does somewhat reduce out of

background focus and improve optical sectioning (i.e producing clearer images in the deeper parts of the sample versus typical uniform illumination) in an ex vivo mouse brain of with a field of view of. To improve the novel SCAPE with HiLo imaging method, further work is still needed to eliminate the introduced horizontal streaking and artifacts.

Maggie Mallernee, Computer Science-Mathematics

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Faculty Mentor: Professor Brian Metzger, Department of Physics, Columbia University

Title: Resonant Migration and Tidal Disruption of Stars by Inspiraling Supermassive Black Hole Binaries

Abstract: The goal of this project is to better observe supermassive black hole (SMBH) binaries in galaxy mergers, and the gravitational waves emitted by them, by quantifying the role of mean motion resonances in the tidal disruption of stars. If a significant number of stars trap into these resonances as the black holes spiral inward, we expect that some of them will be tidally disrupted as their orbits harden and evolve in resonance. Even a single such disruption releases a large amount of electromagnetic (EM) radiation that is identifiable as a characteristic optical/UV/X-ray flare. A sequence of such flares could identify a SMBH binary through EM radiation alone, and a single flare could serve as an EM counterpart to gravitational wave radiation picked up by future detectors like LISA to signal the merger of a SMBH binary. Additionally, stars interacting with SMBH binaries can be ejected at relativistic velocities, and mean motion resonant migration may dominate the rate of production of such relativistic stars.

Tatini Mal-Sarkar, Biology

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Faculty Mentor: Dr. Adam Ratner, Department of Infectious Pediatrics, Columbia University College of Physicians and Surgeons

Title: Establishing A Murine Model of Group B Streptococcus

Abstract: The number one source of sepsis in vaginally delivered infants, Group B Streptococcus is a little-known, but deadly killer. Acquisition of GBS results in traversal of newborn intestinal barriers via colonization of intestinal tract. Creating an in vivo model will allow the scientists to eventually generate some form of protection scheme against the deadly bacteria. It will also provide a space through which previously existant intervention schemes can be compared and analyzed, including probiotic treatments. The model was studied through the technique of polymerase chain reaction of infected and uninfected mouse infant stools. Infected mouse stools were to result in positive identification of GBS DNA, while uninfected stools resulted in negative. The methods worked for enough samples such that the subsequent steps of experimentation will be DNA sequencing of the present murine model.

John Paul Mester, Chemical Engineering

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Faculty Mentor: Professor Gerard Parkin, Department of Chemistry, Columbia University

Title: Synthesis and Characterization of Novel Heterobimetallic Compounds: Reactions of [TpBut,Me]MgMe and [TpBut,Me]ZnH towards CpM(CO)3H (M = Cr, Mo, W)

Abstract: There is significant current interest in the synthesis of heterobimetallic compounds due to their unique structures, potential use in catalysis, and roles in bioinorganic chemistry. We have investigated the use of the tris(3-tert-butyl-5-pyrazolyl)hydroborato magnesium and zinc compounds, [TpBut,Me]MgMe and [TpBut,Me]ZnH, to afford such compounds via their reactivity towards transition metal hydride complexes, namely CpM(CO)3H (M= Cr, Mo, W). For example, CpW(CO)3Mg[TpBut,Me] was synthesized via the reaction of [TpBut,Me]MgMe and CpW(CO)3H, accompanied by the elimination of methane. The molecular structure of CpW(CO)3Mg[TpBut,Me] was determined by single crystal X-ray diffraction, thereby demonstrating that the magnesium coordinates to the [CpW(CO)3] moiety via the oxygen atom of one of the carbonyl ligands, rather than form a direct Cr-Mg bond.

Noah Miller, Physics and Mathematics

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Faculty Mentor: Professor Szabolcs Marka, Department of Physics, Columbia University

Title: Constraining the Jet Structure of Gamma-Ray Bursts

Abstract: The angular dependence of emission in gamma-ray burst (GRB) is of fundamental importance in understanding the underlying physical mechanisms. We examine the prospects of using reconstructed GRB jet opening angles and off-axis observer angles in determining the jet structure. We lay out a new general method for determining what the GRB jet structure should look like based on the distribution of observation angles. We show that recent reconstructed angles are inconsistent with uniform jet structure. We further calculate the number of GRBs with accurately reconstructed opening and observer angles necessary to differentiate between some phenomenological non-uniform structures.

Aditya Nair, Biochemistry

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Faculty Mentor: Oliver Hobert, Department of Biochemistry and Molecular Biophysics, Columbia University

Title: Neuronally Regulated Sexually Dimorphic Behaviors in *C. Elegans*

Abstract: The mechanisms underlying the modification of neuronal circuits in generating sexually dimorphic behaviors remain largely unexplored. While some studies have addressed the development of sexual dimorphisms in mating or pheromone-chemotaxis related behaviors, fewer studies have addressed sexually dimorphic shared locomotory behaviors. To identify behavioral dimorphisms established by the nervous system, we compared the locomotory behavior of nervous-system masculinized animals (animals overexpressing the

masculinizing *fem-3* protein in all neurons) to non-transgenic controls, and compared the behavior of male worms to hermaphrodite worms. Behavior was quantified using Worm Tracker 2 hardware and software. The crawling frequency of worms was found to be increased in both males and masculinized animals, compared to non-transgenic hermaphrodites. We conclude that the canonical sex-determination pathway helps to establish the crawling frequency phenotype. Other sexually dimorphic phenotypes could not be sex-reversed with the overexpression of *fem-3*. Transgenic animals at the fourth larval stage (L4) demonstrated no significant differences compared to their non-transgenic siblings. Future studies will address potential neural and molecular mechanisms by which this dimorphic phenotype is established. Potential mechanisms include a rewiring of the circuit involved in generating movement, expressing different or altered levels of receptors in the neurons involved, or altered transcription levels of the aforementioned neural genes. One interesting potential explanation of our inability to sex-modify the majority of dimorphic behaviors is the presence of an alternate sex-determining pathway, besides the canonical tra-1 pathway, in the nervous system.

Neha Nataraj, Biology

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Faculty Mentor: Professor Lance Kam, Department of Biomedical Engineering, Columbia University

Title: The Effect of Substrate Rigidity on ex vivo Treg Induction

Abstract: Regulatory T cells (Tregs) act as the crucial brake mechanism on the immune system by suppressing the function of conventional T cells. Treg inactivity can result in an overactive immune system and complications involving autoimmune diseases, such as diabetes. Clearly, Tregs play a critical and non-redundant role in the immune system. Adoptive immunotherapy is a method to train the body's own immune cells against a specific target. Recent work by our lab demonstrated that improved T cell stimulation can be achieved using softer poly(dimethyl siloxane) (PDMS) substrates ($\sim 30 \text{ kPa} - 2 \text{ MPa}$) compared to the current clinical gold standard which sees expansion performed on more rigid (GPa range) substrates. In this study, we seek to apply this mechanosensing property of T cells as an avenue for promoting Treg induction from naïve populations of CD4+ T cells. Specifically, we examine herein the effect of rigidity and antibody coating concentration on short-term (48 hour) Treg induction by studying the induction of Tregs on surfaces of varying rigidity on the order of 104 – 106 Pa. Here we show that rigidity appears to play an important role in the induction of Tregs. Results are preliminary, but this study will help us better understand how to optimally and most efficiently induce Tregs ex vivo, which will eventually help us develop treatments for autoimmune diseases.

Richard Nederlander, Astrophysics

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

Title: Analysis of Fermi-Detected AGN Sources as Potential Observable VERITAS Candidates

Abstract: Gamma-ray astronomy in the Very-High-Energy range (VHE, $E > 100$ GeV) is conducted from the ground using Imaging Air Cherenkov Telescope (IACT) arrays such as the VERITAS observatory. So far, 163 VHE sources have been identified across the entire sky. Meanwhile, the most recent FERMI LAT 4-Year catalogue (3FGL) contains over 3000 sources recorded at lower energies (20 MeV $< E < 300$ GeV) by the Fermi gamma-ray space telescope. VERITAS is therefore always searching for new observable sources of VHE gamma rays. In our study we carried out a search for potentially new VHE sources in the Fermi Catalog. 31 VHE source candidates were selected based on a Fermi detection threshold of 5 sigma above 30 GeV, and an integrated flux above 50 GeV higher than 5% of the Crab nebula gamma-ray flux. The majority of the sources analyzed were Active Galactic Nuclei (AGNs), specifically blazars. By using the FERMI toolset Enrico, fluxes were extrapolated to the TeV energy range. A Python code was created to carry out a maximum likelihood analysis and compare the extrapolated flux at TeV energies in terms of the flux of the Crab Nebula. This allowed us to statistically identify the probability of VERITAS being able to observe a source. Analysis of the selected sources is ongoing, and we hope to find promising sources candidates that may be observable with the VERITAS VHE gamma-ray telescopes.

Tiago Palmisano, Biology

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Faculty Mentor: Professor Uttiya Basu, Department of Microbiology and Immunology, Columbia University

Title: Does the RNA Exosome Complex Interact with its Potential Cofactors C1D and MPP6?

Abstract: The RNA exosome complex is the primary 3' to 5' RNA degradation molecule in eukaryotes. Composed of 11 subunits, the RNA exosome plays important roles in post-transcriptional RNA modification, immunologic somatic hypermutation, and class switch recombination. Here we utilize size-exclusion chromatography to show that the RNA exosome complex interacts with the proteins C1D and MPP6 within an in-vitro environment. The observed binding indicates that C1D and MPP6 are indeed likely cofactors for the RNA exosome complex.

Lia Parkin, Biology

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Faculty Mentor: Professor Ann McDermott, Department of Chemistry, Columbia University

Title: Development of Methods to Study Synthetic Phospholipid and Liposome Degradation

Abstract: We report studies of the chemical stability of lipids with respect to oxidation or hydrolysis. Lipids are important components of cell membranes, and were studied here in the form of liposomes, simplistic models of cell membranes frequently used to obtain important experimental data regarding membrane proteins. For example, the McDermott group has conducted structural, dynamic and thermodynamic studies of the potassium channel, KcsA, using DOPE and DOPS phospholipid containing liposomes, wherein the KcsA protein was embedded in the membrane through a dialysis protocol. In the present study, lipids and liposomes were chemically treated to characterize “forced” chemical degradation: specifically lipids were treated with perchloric acid, hydrogen peroxide, hypochlorous acid, or a pH 3.5 buffer. Lipid degradation was characterized by ^1H and COSY NMR spectroscopy and also by TLC. Hydrolysis of the head groups was observed on an hours timescale due to perchloric acid treatment, but the other conditions studied did not result in hydrolysis. Oxidation of the double bonds in lipids is a known phenomenon. Arnhold used hypochlorous acid to “force” oxidation of the double bond, and developed methods to analyze oxidation via ^1H NMR (Arnhold 1995). Under our conditions, however, we did not observe oxidation of the double bonds in the fatty-acid chains of DOPE and DOPS. Therefore, these lipids are surprisingly durable and resistant to chemical changes. This study established methods to detect degradation by NMR and TLC including the extraction of lipid from protein-containing liposomes. In the future, we will use these methods to monitor lipids in proteoliposome samples used in structural and dynamic analysis.

Sachi Patil, Biology

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Faculty Mentor: Professor Chloe Bulinski, Department of Biological Sciences, Columbia University

Title: Investigating the Role of CD73 on Electric Field Induced Motility of Chondrocytes for Cartilage Regeneration

Abstract: This project was focused on understanding the role of CD73, a cell surface ecto-5'-nucleotidase, on electric field induced motility of chondrocyte cells. Chondrocytes were chosen due to their function in maintaining and producing functional cartilage. Chondrocytes were cultured and experiments consisted of applying electric fields through a specially constructed chamber and taking photos of cells at various time points in order to quantify both direction and speed of the cells over time. The preliminary parts of this project focused on finding the best conditions for the experiment, and included varying cell passage number, buffer concentrations, and length of the application of electric field. After trials consisting of over 100 cells, we have found that the chondrocyte cells do polarize and move in the direction towards the cathode to a greater extent with the electric field than control trials. The ongoing phase of the experiment includes transfecting and over-expressing the CD73 protein on the

surface of chondrocytes. These early trials of transfection trials have shown a positive anodal velocity, which is opposite in direction to that of the cells with and without the electric field.

Maya Ramachandran, Biology and Statistics

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Faculty Mentor: Professor Ruben L. Gonzalez, Department of Chemistry, Columbia University

Title: Real-Time Probing of a Pro-Angiogenic Translational Switch

Abstract: As a tumor expands, it rapidly outgrows its blood supply, creating an oxygen-starved environment. Low oxygen levels suppress the canonical biochemical pathway through which the translation of messenger RNAs (mRNAs) into proteins by the ribosome is typically initiated. Despite shutting down this general mechanism for initiating protein synthesis, the tumor can continue to initiate translation of a subset of mRNAs that are involved in angiogenesis and tumor survival. To explain this observation, it has been proposed that this subset of mRNAs, of which the pro-angiogenic mRNA, encoding the Fibroblast Growth Factor-9 (FGF9) is a prototypical member, contain highly stable structures in their 5' untranslated regions in addition to the eukaryotic mRNA-specific 7-methyl guanosine cap at the 5' end. These structures, also referred to as Cap Independent Translation Enhancers (CITEs), form part of a switch that activates a non-canonical pathway for initiating translation, distinct from the canonical 5' cap-dependent mechanism. Here we report the design and synthesis of a library of FGF9 mRNA variants in which the 5' untranslated region has been mutated in order to systematically alter its structure and thus its ability to initiate CITE-mediated translation initiation. By using multi-color, single-molecule fluorescence microscopy techniques to visualize the process of translation initiation on these mRNA variants, we will elucidate if and how the structure of the 5' untranslated region of the pro-angiogenic FGF9 mRNA activates the proposed non-canonical pathway for translation initiation during tumor growth.

Lindsey Remark, Neuroscience and Behavior

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Faculty Mentor: Dr. Benjamin Ohlstein, Genetics and Development, Columbia University

Title: Investigating the Role of Secreted and Adhesion Molecules in Order to Identify Possible Mechanisms of Migration in Larval Drosop

Abstract: The larval midgut of Drosophila does not yet contain active adult stem cells but contains adult midgut progenitors (AMPs), precursors of adult stem cells. These precursory stem cells specify their own niche cell, the peripheral cell (PC), during larval development via Notch signaling. The PC surrounds the islands of AMPs keeping them undifferentiated. The adult intestinal stem cells (ISC) are generated when the PC breaks down and large clustered AMP islands fuse during metamorphosis to make the adult midgut epithelium. Many cancers and diseases pertaining to the gut are due to imbalances in regenerative processes. Therefore, an understanding of intestinal stem cells and their progenitors has significance with intestinal stem cells of Drosophila being similar to vertebrates. The larval gut is significant because an understanding of its novel autonomous progenitor cell that is able to both generate its own niche and thought to migrate to assist with damage could be useful in models in stem cell

biology. It is likely that secreted and adhesion molecules play a role in cell communication between AMP islands and basement membrane, visceral muscle, or other cells of the larval midgut as they do in ISCs. In this study, a screen of RNAi lines for adhesion and secreted molecules was performed using a specific driver for AMP-islands. We have identified four adhesion molecules that may be involved in structure, signaling, or migratory aspects of AMP islands: dlg1, santa-maria, rab-rp4, and peste. Dlg1 is of particular significance because when mutated, most AMP islands disappear. Our data suggest that Dlg1 may have a role in cell survival.

Sarah Ricklan, Evolutionary Biology of the Human Species

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Faculty Mentor: Dr. Laura Johnston, Genetics and Development, Columbia University Medical Center

Title: Cell Competition Patterns are Highly Context-Dependent

Abstract: As tissues develop, some cells prove to be stronger than others. The strong cells compete with the weaker cells, ultimately killing the weak and taking over the tissue. While many details of cell competition are well-studied, the precise reasons why some cells are stronger than others remain unknown. Understanding the contexts in which cells compete and their patterns of competition might help the scientific community understand why some cells, such as cancer cells, become too strong. To better understand patterns of cell competition in diverse contexts, I examined levels of cell competition when some cells express low levels of Myc, a transcription factor, and RpL14 and RpS3, ribosomal proteins. Myc has been implicated and extensively studied in the field of cell competition. Mutations in ribosomal proteins have been shown to induce cell competition, but the effects of low expression levels without mutations have not been well-studied. Examining the patterns of competition in these contexts reveals that the intensity of competition differs considerably; the differences in competition depend on the identity of the proteins expressed. This indicates that the nature of cell competition is highly context-dependent.

Emanuelle Rizk, Biology and Human Rights

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Faculty Mentor: Dr. Rodney Rothstein, Department of Biological Sciences, Columbia University Medical Center

Title: Phenotypic Sensitivity to the DNA Damage Drug Cisplatin in Mutant Yeast Strains

Abstract: Cisplatin is a chemotherapy drug that is used to treat testicular, bladder, ovarian, and lung cancers. It causes multiple types of DNA lesions, including – but not limited to – intrastrand and interstrand crosslinks. Here, we identify genes that affect sensitivity to cisplatin in *Saccharomyces cerevisiae*. Through crosses of various query strains to an array of sensitive genes, we define affected double mutants to characterize epistasis within several genetic pathways. This allowed us to then identify synergistic sensitivities between the single mutant strains and the double mutant strains, with which we then built a network of interconnected genes sensitive to cisplatin. Because these genes are sensitive to cisplatin – a

DNA-damaging agent – they are also involved in DNA repair pathways. Oftentimes, a factor leading to cancer is mutations in such DNA repair genes, so it is important to understand how they function. Furthermore, these results allow for a better understanding of which genes are implicated in the success of cisplatin therapy.

Esther Roh, Chemistry

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Faculty Mentor: Greeshma Gadikota, Chemical Engineering, Park Lab

Title: Preparation of Sodium Silicate from Magnesium-rich Silicate

Abstract: Sodium silicate, also well-known as water glass, is a widely used material in our everyday lives (including the preparation of concrete, detergent, etc.). The currently used process for the synthesis of sodium silicate requires a high temperature (~1400-1500°C) and high pressure, which is considered as a pricy process since it consumes a large amount of energy. In this experiment sodium silicate was synthesized by reacting magnesium-rich silicate (forsterite, Mg₂SiO₄) and sodium hydroxide to produce brucite (Mg(OH)₂) and sodium silicate. This process requires a lower temperature and pressure (~15atm and ~200°C). Not only does this process save energy but also is the first step of preparing brucite, which can be used for long-term carbon dioxide sequestration. The main objective of this experiment is to find the exact reaction conditions (temperature, pressure, agitation, time, concentration of sodium hydroxide) for this process.

Natalia Romano Spica, Biology and Medicine, Literature, and Society

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Faculty Mentor: Dr. Julie C. Canman, Pathology and Cell Biology, Columbia University Medical Center (Columbia P&S)

Title: Role of the Formin Actin Polymerase in Early *C. elegans* Embryonic Cell Divisions

Abstract: Cytokinesis is the physical division of one cell into two, driven by constriction of an actomyosin contractile ring. Understanding its mechanisms can have applications in a wide variety of disorders resulting from cytokinesis failure, ranging from developmental defects to cancer. The diaphanous-type formin CYK-1, involved in the creation of filamentous actin (f-actin) that composes the contractile ring, is known to be essential for cytokinesis in the first division of the *C. elegans* embryo. However, less detailed information is available about CYK-1 and other formins in later cell divisions, once cells have begun to develop specific identities. To investigate formin mediated f-actin assembly in other cells, we analyzed cytokinesis at the 4-cell stage in a cyk-1(ts) mutant. This allowed us to determine requirement for CYK-1 at this developmental stage and identify potential redundancy with other f-actin assembly factors. Initially we observed that this fast acting (~20 sec) temperature-sensitive (ts) allele of cyk-1 caused failure of cytokinesis in two of the four cells (ABa and ABp) while the other two cells (EMS and P2) were still able to divide ~40% of the time. We then combined the cyk-1(ts) mutant with null alleles of two other formins, exc-6 and inft-2, to see if they acted redundantly with CYK-1 in EMS and P2. We did not find a role for EXC-6 or INFT-2 during cytokinesis in the 4-cell embryo, and our data instead suggests a lower overall requirement for CYK-1

formin activity in EMS and P2 blastomeres. We are currently testing if any of the other 7 f-actin assembly factors (DAAM-1, FHOD-1, F59E12.9, FRL-1, FOZI-1, SYND-1, and/or the Arp2/3 Complex) in *C. elegans* may coordinate with CYK-1 in these later divisions.

Diana Ruan, Biochemistry

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Faculty Mentor: Professor Brent Stockwell, Departments of Biological Sciences and Chemistry, Columbia University

Title: Nrf2 Mediates an Adaptive Mechanism of Resistance to Ferroptosis

Abstract: Ferroptosis is an iron-dependent form of regulated, non-apoptotic cell death that can be induced by small molecules such as erastin. Cancer cells develop resistance to apoptosis, which complicates treatment by cell death inducing agents. Ferroptosis circumvents this barrier, as a non-apoptotic cell death program, but application of ferroptosis requires understanding of differential sensitivity of a population to treatment. In this study, ferroptosis-resistant cell lines, FR1 and FR3, were generated by isolating single cell, resistant clones, capable of growing in media supplemented with a lethal concentration of ferroptosis inducer erastin, of the originally ferroptosis-sensitive DU145 prostate carcinoma cell line. We conducted a mutational analysis to determine different pathways for resistance to ferroptosis and identified the transcription factor Nrf2, which mediates survival signaling in response to diverse stress factors and is a critical determinant of redox homeostasis. Differential gene expression analysis showed significant enrichment of Nrf2-target genes among most up-regulated genes in the resistant lines, including ~500 fold up-regulation of members of the alpha-keto reductase family (AKR1C), whose overexpression is a canonical marker of Nrf2 activation. Quantitative polymerase chain reaction was used to validate the up-regulation of said Nrf2 target genes. Culturing the resistant lines without erastin resulted in decreased up-regulation of Nrf2 target genes, and subsequent exposure to erastin did not induce ferroptotic cell death, indicating an adaptive resistance mechanism. Knockdown of NFE2L2, the gene that codes for Nrf2, using siRNA re-sensitized cells to erastin and other ferroptosis inducers, while pre-treatment of sulphoraphane, an Nrf2 activator, resulted in resistance to erastin in DU145, indicating that Nrf2 is functionally involved in the resistance phenotype. We have found that resistance to ferroptosis is dependent on Nrf2-mediated suppression of lipogenesis. RNA-seq and metabolomic data indicated perturbation of fatty acid import, synthesis, and long chain elongation in an Nrf2-overactive context. Depletion of available substrates for lipid peroxidation resulted in selective resistance to ferroptosis inducers over other oxidative lethal small molecules, which is consistent with polyunsaturated fatty acids being the primary lipid substrate for ferroptosis. These results suggest that Nrf2 mediates an adaptive resistance to ferroptosis. Future work involves using CRISPR knockdown of Nrf2 to further validate these results and investigating a possible alternate resistance mechanism involving aquaporin 3 and determining its possible connection with Nrf2 for conferring resistance to ferroptosis.

Daniel Sawyer, Electrical Engineering

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Faculty Mentor: Dr. Kenneth Shepard, Summer Undergraduate Research Program, Bioelectronic Systems Laboratory, Columbia University

Title: Area-Efficient Hardware Design of a Tunable Digital Filter for Ultra-High Density Neural Recording Systems

Abstract: As microelectrode arrays (MEAs) with rapidly increasing channel densities are developed to investigate increasingly large ensembles of neurons, the challenges of processing the data in real time has scaled accordingly. For our target 256x256 channel recording system, the data rate of approximately 3 GB/s renders processing schemes considered efficient in conventional applications entirely infeasible for this device. Here, we propose a highly efficient and modular infinite-impulse response (IIR) filter design implemented on field-programmable gate arrays (FPGAs) with stringent chip area and processing latency constraints. Strategic optimization of tradeoffs in area, timing, and precision allow for the implementation, in inexpensive FPGAs, of a pipelined band-pass IIR filter with tunable cutoff frequencies for all channels on the device.

Shannon Shipley, Neuroscience and Behavior

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Faculty Mentor: Dr. Christine A. Denny, Department of Psychiatry; Division of Integrative Neuroscience, Columbia University Medical Center; New York State Psychiatric Institute

Title: Optimization of iDISCO and CLARITY for Indelibly Labeled Memory Traces in ArcCreERT2 Mice

Abstract: Intact whole tissue imaging is a new and rapidly growing area of focus. Using immunolabeling-enabled three-dimensional imaging of solvent-cleared organs (iDISCO) and CLARITY—the leading precedents for whole brain clearing and imaging—we developed a modified whole brain clearing and imaging technique optimized for preservation of endogenous fluorescence and for green fluorescent protein (GFP) staining and co-staining with Arc and c-fos in the ArcCreERT2 mouse model. Previously used fixing and clearing solutions quenched immunolabeling, particularly of GFP, and disrupted proteins within the tissue. Alternative fixing and clearing solutions, such as tert-butanol, circumvented these harmful affects on immunolabeling, while still effectively clearing whole tissue. Buffering these alternative solutions to pH 9.5 further enhanced their efficacy. Additionally, a GFP nanobody, a functionally similar but physically smaller alternative to a GFP IgG antibody, penetrated deep tissue better than its whole antibody counterpart, making it a viable candidate for GFP immunolabeling. These modifications collectively provide an improved whole brain clearing and imaging method that is compatible with the ArcCreERT2 mouse line, offering a novel approach to studying indelibly labeled memory traces across the whole brain.

Cosmas Sibindi, Biomedical Engineering

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Faculty Mentor: Bruce Walker, Ragon Institute of MGH, MIT and Harvard University

Title: Development of Fluorescent HIV

Abstract: HIV/AIDS is a global pandemic with up to 35 million people living with HIV in the world. Treatment is now available to people with the disease which allows the disease to be suppressed and the immune system to rebound. However, the biggest impediment to HIV/AIDS cure remains the presence of a reservoir of infected immune cells located in various tissues which are latently infected and not expressing any HIV proteins on their cell surfaces. This summer, I designed and made six constructs of the HIV virus cloned with a Blue Fluorescent Protein (BFP) gene alongside one of the following three Internal Ribosome Entry Sites (IRES); Encelocardiomegalovirus (EMCV), Enterovirus 71(EV71) and the self-cleaving peptide F2A located on either side of the Nef construct. I used Gibson cloning to introduce them into the HIV genome. I sought to assess long term infection in humanized mice and ultimately the viral reservoir. I produced virus using mammalian HEK293Ts and tested the efficacy of infection from these virus constructs using flow cytometry of cells infected by spinoculation. I then selected the construct which imposed the minimum fitness cost on the virus and lead to the least changes in its infection ability and Nef downregulation. I found that the construct with BFP followed by the IRES from EV71 had the minimal fitness cost on the virus.

Maxim Sigalov, Computer Science; Linguistics; Mathematics

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Faculty Mentor: Mirella Lapata, School of Informatics, University Of Edinburgh

Title: Methods in Semantic Role Labeling

Abstract: Semantic Role Labeling is a task in Natural Language Processing that pertains to classifying the semantic (meaning-related) roles of words in a text. Algorithms can take into account a variety of factors, such as syntactic position, relationship to predicates, or word vectors. Computer predictions are generally tested against a human-annotated ""gold standard"". I implemented and tested several different algorithms on a corpus of German texts. These were then compared with expected results from previous trials on English and German corpora.

Jonnell Small, Biochemistry

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Faculty Mentor: Professor Brent R. Stockwell, Departments of Biological Sciences and Chemistry, Columbia University

Title: The Identification of Small Molecule Compounds Selectively Lethal to MYCN-Amplified Neuroblastomas

Abstract: Neuroblastoma ranks as the most common cancer in infants and is responsible for about 15% of cancer deaths in children. It has previously been shown that the oncogene MYCN when overexpressed becomes a driver of tumorigenesis in neuroblastomas. Using a high-throughput screen, we interrogated 5,500 compounds for their ability to selectively kill MYCN-amplified neuroblastoma cell lines expressing the N-Myc protein. Five cell lines were used: EBC1, IMR32, NLF, SKNAS, and SKNBe2. Of the five, only three were MYCN-amplified: IMR32, NLF, and SKNBe2, but only IMR32 and SKNBe2 expressed the gene. We identified several known compounds with selective activity, including Fludarabine, Erastin, Nutlin-3, and 6-Azauridine. Fludarabine, a purine analog that interferes with DNA synthesis, proved to be especially selective against the overexpressed N-Myc genotype; as did 6-Azauridine, a triazine nucleoside that interferes with pyrimidine biosynthesis. Dosage response assays revealed that both these drugs maintained selectivity against the IMR32 and SKNBe2 cell lines even at a low concentration of 2.5?M. The nature of these two drugs suggests that antimetabolites that interfere with DNA synthesis are more lethal to the overexpressed N-Myc genotype. Nutlin-3, a small molecule inhibitor of the MDM2/p53 interaction appeared to be lethal mostly to the IMR32 cell line at low concentrations. Its lethality suggests that small molecules targeted towards the p53 pathway are potentially promising agents for MYCN-amplified neuroblastomas. Erastin, an inducer of ferroptosis, appeared to be lethal to IMR32 only at high concentrations.

Katy Su, Neuroscience and Behavior

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Faculty Mentor: René Hen, Biological Sciences, NYSPI

Title: Projection-Specific Cellular Heterogeneity within the Ventral Hippocampus

Abstract: The hippocampus has become progressively implicated in the pathophysiology of anxiety disorders, yet its role in modulating emotions and mood is not well understood. We characterized ventral hippocampal (vHPC) neurons projecting to the hypothalamus (HT) and amygdala (AM), two regions important in anxiety-related behaviors, to determine if these projections arise from separate cell populations. We then examined the recruitment of these neurons in two different behaviors involving innate and learned fear (elevated plus maze [EPM] and contextual fear conditioning [CFC]). Hippocampal neurons were primarily found to project to a single region, rather than to both. However, the biggest proportion of vHPC neurons that were also activated in EPM and CFC behaviors, as measured by the immediate early gene cFOS, were vHPC neurons that had projections in both HT and AM. This indicates that vHPC neurons that can communicate with both regions may be especially important in orchestrating fear behavior.

Srikanth Varadaraj, Mathematics

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Faculty Mentor: Professor David Hansen, Department of Mathematics, Columbia University

Title: On the Numerators of Hurwitz Numbers

Abstract: The Hurwitz numbers are a sequence of rational numbers with interesting number-theoretic properties. (In fact, from their definition, it is not even obvious that they are rational.) In the 1970's, Nicholas Katz used algebraic geometry to prove some divisibility properties of the denominators of the Hurwitz numbers. In this project, we will develop a new way to compute Hurwitz numbers and characterize their numerators completely using p-adic analysis and other number theoretic techniques.

Kaylee Wedderburn-Pugh, Biochemistry

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Faculty Mentor: Dr. Joseph Hill, Columbia Undergraduate Scholars Program, Hill Cardiology Research Laboratory, University of Texas Southwestern Medical Center

Title: Hungry Hearts: Histone Deacetylase Regulation of Autophagy

Abstract: The general medical category of "heart disease" includes many health conditions including hypertension (high blood pressure), myocardial infarction, and heart failure. Collectively, these conditions and many others that fall under heart disease are the leading cause of death in the United States of America. Cardiology research now focuses on mechanisms that result in these diseases and ways to limit, stop, or even reverse their damaging effects. The research conducted in this study hinged on three key areas of research in the field. The first area is pathological cardiac hypertrophy, which is a type of growth the heart undergoes due to prolonged sickness or stress on the heart system. This form of growth differs from physiological hypertrophy that occurs after exercise or pregnancy in that prolonged pathological growth ultimately results in heart failure. Previous experiments have linked pathological hypertrophy to a second area of research – autophagy, which is a process that cells undergo to recycle existing organelles into new material for cell growth. Autophagy is a key process in the growth of heart cells since these cells are unable to multiply through traditional processes of mitosis. Finally, autophagy has also been linked to histone deacetylases (HDACs), which are proteins in the cell that regulate gene expression. Therefore, the aim of this study was to take these three branches of cardiology research and see the correlation amongst them in different cell environments. Using synthetic RNA (siRNA), various HDACs were "knocked-down" in Neonatal Rat Ventricular Myocytes (NRVMs). Then the levels of autophagic flux and therefore hypertrophy were measured as a result of these HDAC knockdowns. Although the data collected is not yet conclusive, the preliminary findings indicate that the HDACs (organized into two pre-established classes) do have an effect on autophagy in heart cells. These findings point to the conclusion that in the future HDACs could be (further) used to regulate heart growth and to prevent heart disease in patients.

Eric Wei, Neuroscience and Behavior

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Faculty Mentor: Professor Joachim Scholz, Department of Anesthesiology and Pharmacology, Columbia University Medical Center

Title: Investigating the Mechanisms of Peripheral Nerve Damage Caused by Hyperglycemia

Abstract: One of the most prominent complications of type 2 diabetes is diabetic polyneuropathy (DPN). DPN begins most often in somatosensory neurons, producing pain and numbness in the feet and hands, but the disease also affects motor and autonomic neurons. In order to understand the cellular mechanisms of DPN, it is important to distinguish between cell death and axonal degeneration. DRG neurons from C57BL/6 adult male mice were cultured for 1 thru 4 days to determine the optimal level of growth of each neuronal biochemical subtype for morphological analysis using NeuroLucida (MBF Bioscience). A pilot NeuroLucida experiment was performed to characterize the growth of a peptidergic pain responsive (nociceptive) neuron at 1 day of cell culture. The Campenot compartmented culture system was optimized for mouse dorsal root ganglia (DRG) neurons as a future tool to understand how elevated glucose levels affect somatosensory neurons.

Helen Yang, Biochemistry

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

Title: Organic Ligands for Nanoparticles in Cell Imaging

Abstract: I looked into phosphonic acid ligand binding on the surface of cadmium selenide quantum dots. My ultimate goal was to conduct a surface ligand exchange on the dots to render them water-soluble. The application of these fluorescent, water-soluble dots is cell-imaging, and hopefully in the future live brain-cell imaging. Water-soluble quantum dots attached to individual cells would have much better temporal and spatial resolution than current brain-imaging techniques such as calcium imaging and electrode insertion. I fine-tuned a phosphonic acid synthesis procedure. With this procedure I synthesized my own phosphonic acids and used them to exchange for existing ligands on the nanocrystals surfaces, namely cadmium-oleate and cadmium-tetradecanoate. My preliminary exchanges ran with tetradecylphosphonic acid, a molecule I synthesized and purified. I also synthesized and cleaned cadmium selenide dots. By doing tetradecylphosphonic acid exchanges at varying concentrations, heat, time, and other conditions, I attempted to pin down ideal exchange conditions for my next molecule, a phosphonated polyethylene glycol chain (phosphonated PEG). With a successful exchange, this phosphonated PEG should render the dots water-soluble and organic-soluble, and the next step is to quantify what ratio the ligands were being exchanged at. I made headway in characterizing what happens in these exchanges when not enough ligands are added, or too much excess of ligands are added. Some CdSe dots aggregated immediately with a high excess of phosphonated PEG ligand, suggesting that perhaps the excess ligand is stripping too much cadmium from the surface of the dot and creating free cadmium-phosphonate. This is key information in finding the ideal ratio of ligands for exchange on the surface of quantum dots, and I am working on continuing to

exchange quantum dots with different phosphonated ligands, perhaps commercially bought or I can learn to synthesize some. I'd also like to try an exchange on shelled quantum dots with a higher photoluminescence quantum yield than plain CdSe dots and observe how that affects the quantum yield.

George Yu, Mathematics-Computer Science

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Faculty Mentor: Professor Tim Leung, Department of IEOR, Columbia University

Title: Optimal Liquidation of Options with Learning

Abstract: Options are a widely traded financial asset around the world. Much work has gone into developing methods of evaluating these instruments, leading to results like the Black-Scholes method of pricing options. In this project we develop a mathematical model to determine the optimal time for an option holder to liquidate her position, taking into account her prior beliefs on how the underlying asset will move. In this way we also allow our holder to learn from the underlying price movements up to the present time and adjust the optimal selling time accordingly. In addition to analyzing the properties of the drift function of our model, we also implement a finite difference scheme based on the Crank-Nicolson method to solve the resultant variational inequality.

Luke Zhan, Biochemistry

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Faculty Mentor: Professor Brent Stockwell, Departments of Chemistry and Biological Sciences, Columbia University

Title: A Fluorescent Probe for Ferroptosis

Abstract: Ferroptosis is a non-apoptotic, iron-dependent form of cell death that can selectively kill tumor cells or be present in diverse pathological conditions. Because few molecular tools exist to distinguish ferroptotic populations, the goal of this project was to identify a fluorescent probe that selectively marks cells undergoing ferroptosis, as opposed to other types of cell death. We focused on four candidate probes discovered in a high-throughput screen. We used three distinct cell lines: OCI-LY7 (lymphoma), HT-1080 (fibrosarcoma), and BJeLR (foreskin fibroblast). By incubating these with a diverse array of ferroptotic and non-ferroptotic lethal molecules, we could evaluate the specificity and robustness of the probes. Flow cytometry analysis quantified the fluorescence change of the probes across different cell line and lethal molecule combinations. One probe in particular demonstrated sensitivity for ferroptosis in OCI-LY7 and HT-1080 but not BJeLR. However, we suspect that this discrepancy could be attributed to different rates at which each cell line undergoes ferroptosis, rather than the specificity of the probe itself. Further experiments, mostly attempting to optimize drug treatment time points, are currently in progress.

Catherine Zhang, Biology and Environmental Science

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Faculty Mentor: Professor Laura Kaufman, Department of Chemistry, Columbia University

Title: Advancing an In-Vitro 3D Breast Cancer Model: Creating a Homogeneous Basement Membrane Shell

Abstract: The purpose of this project was to further develop an existing in-vitro 3D breast cancer model. The model consists of a multicellular tumor spheroid coated with a layer of basement membrane extract (BME) implanted in a collagen I gel, mimicking the in vivo surroundings of an early stage breast tumor. This in vitro model allows controlled study of the invasion of tumor cells into breast tissue. To create the spheroid coated with BME, tumor cells are added to a 96-well Lipidure plate with BME and are centrifuged, creating a tightly packed spheroid of tumor cells with a thin basement membrane shell surrounding the spheroid. After 24 hours of incubation, the spheroids are implanted into collagen I gels and then imaged at multiple time points. Previously, it was shown that this approach resulted in an inhomogeneous BME shell, and cells were initially in contact with collagen I, a situation distinct from the physiological situation. The aim of this project was to create a homogeneous shell around the spheroid and better understand how tumor cells breach this basement membrane shell. It was found that the addition of collagen IV to the BME before centrifuging resulted in a homogeneous shell, as demonstrated through direct visualization of the shell. It was found that the concentration of collagen IV directly affected the thickness of the shell. It was also found that the presence of a complete, homogeneous BME shell changed the morphology of invading cells; cells that breach the shell are rounder than those in direct contact with collagen I. The effect of MMP inhibitors and beta1 integrin antibodies was also investigated: the addition of MMP inhibitors led to decreased cell invasion while the addition of the beta1 integrin antibody disrupted shell formation. Further experiments will confirm and elaborate on these findings.

Frank Zhong, Mathematics

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Faculty Mentor: Professor Yuan Zhong, Department of Industrial Engineering and Operations Research, Columbia University

Title: Study of Interbank Tiering

Abstract: Within financial networks and especially banking institutions is a study of the structure of these networks. Many networks exhibit a tiering structure where certain nodes may be more important than others, whether it be that node is larger in terms of amount of edges or whether the edge itself between two nodes is larger in terms of its worth. The study that we undertook is to examine the German and Dutch Banking systems and attempted to define institutions based on their size and net worth. From this we were able to determine that certain institutions exhibit a property that render them as integral to the structure of the network, without them, the network would collapse significantly. Such networks are seen in many banking networks and we present a method to categorize the different tiers of banks within a network using a Gibbs-Sampler based on total liabilities and assets of each bank.

Using this we are able to recreate the network and determine which banks are critical to the network.

Frank Zhu, Biology

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

Title: Neural Networks in Hydra Vulgaris

Abstract: Hydra Vulgaris is an emerging model organism in the field of neurobiology. Its unique physiological properties present opportunities such as the ability to see all the neurons of an organism at the same time, which may yield a more comprehensive view of a neuro-system. Our goal is to use computer vision algorithms to track the development of the neurons in a growing hydra vulgaris and to investigate how different stages of a hydra, such as budding affect the movement of the neurons. One of the problems with imaging the hydra is its constantly changing network presents a challenge to track each individual neuron long-term. Thus, I spent the summer trying to find a biological marker that doesn't bleach without perturbing the neuron. I successfully electroporated both cadmium nanoparticles and various dextrans but are now continuing investigating methods to make these photo-sensors last long-term.