UNDERGRADUATE RESEARCH SYMPOSIUM

Abstract Program

Saturday, October 13, 2018 | 9 AM - 4 PM
Guggenheim Pavillion
The Graduate School of Biomedical Sciences
1468 Madison Ave, New York, NY 10029

Icahn School of Medicine at Mount Sinai

Graduate School of Biomedical Sciences

Acknowledgements

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The Friedman Brain Institute

The Mindich Child Health and Development Institute

The Precision Immunology Institute

The Tisch Cancer Institute

The Mount Sinai Diabetes, Obesity and Metabolism Institute

Department of Microbiology

Department of Neuroscience

Department of Oncological Sciences

Division of Hematology and Medical Oncology

Program Agenda

9:00 AM – 10:00 AM	Registration, Breakfast and Poster Set-Up - Atrium
10:00 AM – 10:15 AM	Welcoming Remarks, Hatch Auditorium
10:15 AM – 11:30 AM	Poster Session 1 – odd numbers - Atrium
11:30 AM – 12:50 PM	Oral Session 1, Hatch Auditorium Chairs – Tim Kenny and Deppak Kaji Presenters: Burrell, Venkatesh, Mintz, Finke, Ramoni, Nemeth
12:50 PM – 1:30 PM	Lunch
1:30 PM – 2:45 PM	Poster Session 2 – even numbers
2:45 PM – 4:05 PM	Oral Session 2, Hatch Auditorium Chairs – Allison Kann and Nick Upright Presenters: Lo, Liu (Alice), Hung, De La Torre, Orozco, Nick
4:05 PM – 4:15 PM	Awards, Hatch Auditorium
4:15 PM	Close

Iurii Gurkov • *University of California San Francisco*

Mentor: Adam Frost
Biochimestry

How do mitochondria fuse?

Mitochondria are double membrane organelles that contain their own genome. Unlike nuclear DNA, mtDNA is highly prone to somatic mutagenesis due to high levels of reactive oxygen species (ROS) and inadequate DNA repair machinery. By balancing cycles of organelle fusion and fission, Eukaryotic cells exert dynamic control over mitochondrial connectivity and morphology. This regulated organelle morphology allows for the exchange of functional copies of mtDNA and other contents as well, including proteins, lipids and small metabolites. Together, this results in a homeostatic buffering mechanism connecting the entire mitochondrial network. Mfn1 (mitofusin 1) and Mfn2 (mitofusin 2) are dynamin-related GTPases that are essential for mitochondrial fusion. Deletion of these nuclear encoded genes causes mitochondrial fragmentation and embryonic lethality in mice. Moreover, hypomorphic mutations in Mfn22 are associated with Charcot-Marie-Tooth disease, a hereditary neuropathy in humans. However, the molecular mechanism of mitochondrial fusion remains poorly understood. We propose to purify human Mfn1 from bacterial cultures and to use cryo-EM (cryo-electron microscopy) to determine the 3D structure of full-length Mfn1 and to explore the effects of loss-of-function mutations within the GTPase domain of Mfn1. Our preliminary results suggest that purified Mfn1 is associated with contaminant proteins from bacterial cultures. Here we present our efforts to purify homogeneous sample suitable for future structural studies.

This work has been supported by the National Science Foundation and the Summer Research Training Program at the University of California San Francisco.

Allison Hung • *University of California, San Francisco*

Mentor: Alexander Johnson
Biochemistry

Candida albicans is an opportunistic fungal pathogen that lives asymptomatically in healthy individuals, but causes serious illness in immunocompromised patients. Previous studies have determined that the pathogenesis of C. albicans is linked to its morphological plasticity. C. albicans also exhibit distinct white and opaque cell types, although it is unclear how these distinct morphologies contribute to pathogenesis. White and opaque cells are known to interact differently with the innate immune system - macrophages preferentially phagocytose white cells over opaque cells. C. albicans strains that are heterozygous at the mating type locus (a/α) are unable to switch in lab strains. However, switching has recently been observed in clinical a/α isolates. We used a murine macrophage infection model to determine how such strains interact with the host immune response. We evaluated whether these strains are differentially phagocytosed by taking time-lapse images and quantifying the phagocytic index of white versus opaque cells. Further, we measured cytokine secretion to evaluate whether these strains induce different inflammatory responses. Finally, because C. albicans can survive in and rupture their host macrophages, we monitored survival of these clinical strains by counting cells within macrophages and survival of macrophages by measuring cytotoxicity following infection. We observed consistent differences between white and opaque cell interactions with macrophages, similar to differences observed in lab strains. Taken together, these results indicate that opaque cells induce a dampened macrophage immune response in comparison to white cells, thus suggesting that opaque C. albicans can evade the immune system during infection.

Andrea Orozco • *Williams College*

Mentor: David Lawrence
Biology

The Effect of Perinatal Diesel Exhaust Particulate (DEP) Exposure on the Developing Immune and Nervous Systems

Andrea Orozco1,2 , Kevin Manley1, and David Lawrence1

1. Department of Infectious Diseases, Wadsworth Center
2. Williams College

Individuals living near trafficked roads have increased incidence of certain disorders. With mouse models, exposure to environmental toxicants, such as particulate matter derived from diesel exhaust (DEP), have been shown to induce both behavioral and immunological changes. Our laboratory investigates the effect of perinatal DEP, characterized for its polyaromatic hydrocarbon and nitro-polyaromatic hydrocarbon composition, exposure on five inbred mouse strains. We selected these strains based on differences in their positions on the mouse phylogenetic tree and select immunological traits. I worked with the SJL/J and BALB/cByJ mouse strains. The differences in genetic makeup between the strains could potentially allow us to identify genetic susceptibilities to DEP exposure and any resultant immunopathology. We strive to explore the interconnectivity between the immune and nervous systems by identifying behavioral and immunological outcomes and then comparing them to the BTBR mouse model of ASD. We hypothesize that, through maternal immune activation, DEP exposure will result in neuroinflammation and oxidative stress which will then result in damage to the CNS. We predict that this damage will manifest as aberrant behaviors. We observed a large variation in the range of activities in behavioral assays, yielding limited apparent differences in exploratory, social and anxiety traits on the SJL/J and BALB/cByJ strains, regardless of DEP exposure, in comparison to those characteristic of the BTBR strain with ASD-like behavior. However, the differences that we did observe through our behavioral assays set general trends of hyperactivity and reduced sociability for the SJL/J mice and hypoactivity for the BALB/cByJ strain. Our behavioral assays have set the ground for extensive ex vivo studies, including gene and protein expression studies. In addition, we look forward to analyzing immunological responses at the cellular level, including T-cell, microglial, and macrophage activities.

Sarah Nick *• Columbia University (Research Conducted at University of California San Francisco)*

Mentor: William DeGrado
Biomedical Engineering

CHARACTERIZATION OF THE BINDING OF A COMPUTATIONALLY DESIGNED TRANSMEMBRANE PEPTIDE TO THE ERYTHROPOIETIN RECEPTOR

Membrane proteins regulate many essential cellular functions including transport, adhesion and signaling. Membrane-spanning α-helices dictate folding, protein-protein interactions, and ultimately the protein function. However, the link between primary sequence and transmembrane (TM) helix self-association is unclear. One frequently observed sequence motif, the repeat of small amino acids (Gly/Ala/Ser) every other helical turn (7-residues), was found to mediate both parallel and antiparallel helix association in many natural membrane proteins. This sequence motif occurs at the dimerization interface of the erythropoietin receptor (EpoR), a cytokine receptor that directly regulates the production of red blood cells.

Previously, an isolated TM α-helix mimicking the EpoR-TM domain was made repeating serine, and associated in a parallel geometry. Thus, to test if antiparallel geometry can be achieved outside of the context of a full-sized protein, a synthetic TM peptide was designed containing this motif named 'CHAMP' (Computed Helical Anti-Membrane Protein). The tested hypothesis was that CHAMP would form an antiparallel dimeric complex with EpoR-TM and inhibit parallel self-association of EpoR transmembrane domains. Antiparallel binding of CHAMP to EpoR-TM and inhibition of full-length EpoR signaling in cells was previously demonstrated.

Herein, the CHAMP-EpoR-TM complex was characterized by fluorescence resonance energy transfer (FRET) between fluorescently-labelled CHAMP and EpoR-TM in detergent micelles. These data were then fit to theoretical curves to determine binding affinity and complex stoichiometry. A clear association between CHAMP and EpoR-TM was detected, based on the concentration-dependent quenching of donor emission and increased acceptor emission. Initial experiments suggest that a weak monomer-trimer equilibrium model best describes the experimental binding curves. These results indicate that a small amino acid 7-residue repeat successfully promotes antiparallel dimeric TM helix association and refine our understanding of how sequence drives protein-protein interactions and folding within membranes.

Acknowledgements: S.E. Nick was funded by the UCSF Summer Research Training Program and Amgen Scholars.

Rachel Mintz • *Columbia University*

Mentor: Kam Leong
Biomedical Engineering

For patients carrying BRCA1 mutations, at least one-third develop triple negative breast cancer (TNBC). Not only is TNBC difficult to treat due to the lack of molecular target receptors, but BRCA1 mutations also result in chemotherapeutic resistance, making disease recurrence more likely. Although BRCA1 mutations are highly heterogenous and are therefore difficult to target, BRCA1 gene's synthetic lethal pair, PARP1, is conserved in the BRCA1-mutated (BRCA1m) cancer cells. Therefore, we hypothesize that targeting PARP1 might be a fruitful direction to sensitize BRCA1m cancer cells to chemotherapy. We used CRISPR/Cas9 technology in conjunction with Lipofectamine to conduct multiple clonal selections and generate PARP1 deficiency in two TNBC cell lines, MDA-MB-231 (BRCA1 wild-type) and MDA-MB-436 (BRCA1m). The PARP1 knockout was confirmed and quantified with Sanger Sequencing. We explored whether this PARP1 disruption could significantly lower the chemotherapeutic dose necessary to achieve therapeutic efficacy in 2D and in a 3D tumor-on-a-chip model. With both BRCA1 and PARP1 deficiency, the cancer cells were more sensitive to the three representative chemotherapeutic breast cancer drugs chosen, doxorubicin, gemcitabine, and docetaxel, compared with their PARP1 wild-type counterpart in 2D ($p<0.0001$). However, this chemotherapeutic sensitization by PARP1 knockout was not observed in the BRCA1 wild-type cells (MDA-MB-231). PARP1 knockout led to significant synthetic lethality in the 3D tumor-on-a-chip model but not in the 2D system, suggesting that the microenvironment may play a role. Thus, the drug dosage optimized for the 2D study could not be extrapolated to the tumor-on-a-chip model. The difference between the 2D and 3D systems will be next considered for defining the chemotherapeutic synergy. Collectively, these results highlight the selective synergism between PARP1 knockout and chemotherapy in the BRCAm cells, which may offer a potential approach to TNBC therapy.

Bridget Weston • *Hofstra University, Fred DeMatteis School of Engineering and Applied Sciences*

Mentor: Roche De Guzman
Biomedical Engineering, Mechanical Concentration

Basic Galvanic Battery Measurements
Bridget Weston, 2019, Bioengineering - Biomechanics

Summary:

I. Introduction
Galvanic or voltaic electrochemical reactions are the basis of battery technology for storing and producing electricity. This project investigated the basic principles of a galvanic cell utilizing oxidation-reduction reactions to produce electrical currents.

II. Methods
A copper (Cu)-zinc (Zn) galvanic battery was assembled as follows. Solutions of 1 M copper sulfate (CuSO4) and 1 M zinc sulfate (ZnSO4) were prepared and placed in separate reservoirs. Metal electrode sheets: Cu (cathode) and Zn (anode) were immersed in CuSO4 and ZnSO4, respectively. A cotton twine with absorbed 2.5 M potassium chloride (KCl) was utilized as a salt bridge, connecting the separate solution chambers. The two electrodes (Cu and Zn) were connected to a copper wire via alligator clips to induce electricity. A multimeter (voltage, current, and resistance) and electrical components (LED and resistors) were placed in series to the copper wire and electrical measurements recorded.

III. Results
Experiments demonstrated that the Cu-Zn galvanic cell produced an output voltage of 1.08 V, 0.02 V off based on the expected 1.1 V of the two half-reactions: 0.76 V for the Zn(s) □ Zn2+(aq) + 2e- oxidation reaction and 0.34 V for the Cu2+(aq) + 2e- □ Cu(s) reduction reaction. Copper deposits were observed on the Cu cathode while zinc corrosion on the Zn anode. The electrical current of the system was recorded to be time-dependent and relatively low, insufficient to light an LED. The salt bridge was found to be essential for voltage difference production. In the absence of a salt bridge (replaced by a copper wire), only 0.1008 V was generated.

IV. Discussion
The project successfully tested the essential components of the galvanic battery. Future directions involve investigating the effect of different biomaterial solutions such as chitosan (polycationic polysaccharide), alginate (polyanionic polysaccharide), and gelatin (protein) to the electrical properties of the system, as well as producing biomaterial mineral deposits based on these galvanic reactions.

Paige Burrell *• Harrisburg University of Science and Technology*

Mentor: Mehran Makvandi
Biotechnology

FDG AND FTT UPTAKE IN RESPONSE TO PARP INHIBITION AND DNA DAMAGE

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Poly-(ADP)-ribose polymerase (PARP) is an enzyme that catalyzes DNA damage repair. PARP inhibitors (PARPi) have been developed currently to treat breast and ovarian cancers and are especially effective in cancers containing a BRCA mutation. BRCA mutations limit the ability to repair double stranded DNA breaks. In these cells, PARP is heavily relied upon to seal single stranded nicks before lethal double stranded DNA breaks occur. By inhibiting PARP activity, cancer cells must rely on the more error-prone non-homologous end joining to repair breaks in the DNA, leading to a high level of mutagenicity and eventually cell death.

F-18-FluorThanatrace ([18F]FTT) is a radio-labelled analogue of the PARPi rucaparib; it is currently in clinical trials as a tumor imaging agent and predictive marker of clinical response to PARPi therapy. Early trial results have shown some unexpected cases of discordant [18F]FDG (a measure of glucose metabolism) and [18F]FTT uptake in sites of disease in response to treatment. To better understand this, we undertook to measure [18F]FDG and [125I]KX1 (an iodinated analogue of [18F]FTT optimized for in vitro studies) uptake in breast and ovarian cancer cell lines in vitro at baseline, in response to DNA damaging agents cisplatin and doxorubicin and the PARPi rucaparib.

While cytotoxic therapy predictably reduced [18F]FDG uptake and rucaparib reduced binding of [125I]KX1, rucaparib treatment unexpectedly increased [18F]FDG uptake in ovarian cancer cells. These findings are important for understanding the clinical results of [18F]FDG and [18F]FTT scans as well as to better elucidate the mechanism of action and potential resistance pathways for PARPi therapy. Future studies on the topic should focus on the specific metabolic and cell cycle effects of cytotoxic and PARPi therapy, as well as clarifying the ability of [18F]FTT to monitor and predict the response of patients to PARPi therapy.

I would like to thank SUPERS@PENN for allowing me the opportunity to perform research at the University of Pennsylvania and for partially funding this project. I would like to thank Dr. Dan Pryma for his insight and guidance on this project, and Dr. Mehran Makvandi for his patience and mentorship throughout the summer. I would like to thank Dr. Hwan Lee for his aid in performing the radioligand binding and uptake studies, Dr. Aladdin Reid for his advice on western blotting, and Laura Puentes for her aid in many techniques. I would also like to thank Dr. Steve Tuttle, Dr. Costas Koumenis, and Dr. Sydney Evans for their mentorship throughout the program. Lastly, I would like to thank the entirety of the Pryma and Mach labs for their welcoming demeanor and support.

Katherine Lo • *Stony Brook University*

Mentor: Benjamin Martin
Biology-Developmental Genetics

Understanding the Role of cdh6 in Early Zebrafish Development via Generation of a cdh6 Mutant and Reporter Line

Katherine Lo1, Brian Kinney1, Benjamin Martin1
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The zebrafish tailbud contains a population of neuromesodermal progenitors (NMPs) which contribute to both neural and mesodermal lineages during posterior elongation, forming the posterior spinal cord and somites, respectively. The decision between neural and mesoderm fate in NMPs is made primarily by the canonical Wnt signaling pathway. In the presence of Wnt, NMPs become mesodermal progenitors. However, in the absence of Wnt signaling, the NMPs join the neural progenitor population. Our model predicts the combined activity of canonical Wnt signaling and the Sox2 transcription factor maintains the undifferentiated NMP state, however this mechanism is still poorly understood. Currently, we have identified cadherin-6 (cdh6), a homophilic cell-cell adhesion molecule, as a putative transcriptional target of combined Wnt and Sox2 activity in NMPs. As a potential regulator of NMP differentiation, this study focuses on creating a mutant and reporter line for cdh6 to better understand its role in development. Using CRISPR/Cas9, we insert fluorescent proteins such as Tomato into the cdh6 locus. Currently, we have identified a mutant cdh6 allele and will continue to screen for fluorescently tagged mutant zebrafish to be used as a reporter cdh6 zebrafish line.

Tristan Onek • *East Tennessee State University*

Mentor: Brian Bennett
Computing

Predicting how a population's genetic and social composition will change over time can be difficult even with sophisticated statistical methods and high-quality data. It is possible to utilize several machine learning methods to reduce uncertainty in determining which individuals in a species may be more likely to reproduce based on their genetic diversity and social standing within their population. This research examines a data set that tracks interactions between olive baboons (Papio anubis) in Kenya, with baboons in each recorded interaction having associated genetic and social rank values. Furthermore, the data records if each interaction leads to reproduction between the individuals. Machine learning methods applied to this data collectively form a model, which can predict if an individual baboon pairing will or will not lead to attempted reproduction. This research uses three major machine-learning methods: recursive feature elimination, decision trees, and neural networks. The primary model in this research is the multi-layer perceptron neural network, which predicts reproduction likelihood upon interaction between individuals. Recursive feature elimination supports the neural network by finding which features in the data set are insignificant. Decision trees find which data features are significant nodes in predicting reproduction. The neural network trains on a sample of the original data and then attempts to predict a different testing sample of the data without knowing if each testing instance leads to reproduction. Training and testing repeats until the neural network achieves an ideal accuracy rating. The current model can achieve 89% maximum accuracy for determining if a pair of individuals will attempt reproduction after training and testing on the data set. Applying several machine learning techniques within one structured model in biological research can allow for better understanding and evaluation on constantly changing and evolving populations.

Margish Ramani • *New York University School of Medicine*

Mentor: Henrieta Scholtzova
Neural Science

Alzheimer's Disease (AD) is the most common cause of dementia characterized by the presence of parenchymal amyloid-β (Aβ) plaques, cerebral amyloid angiopathy (CAA) and neurofibrillary tangles. Genome-wide association studies have demonstrated the importance of macrophage and microglia-the primary innate immune cells of the brain-in AD pathogenesis (Karch et al., 2014). Prior work has showed that stimulation of innate immunity with CpG ODN can reduce plaque pathologies without causing toxicity in mouse models based on cytokines, the molecules inciting an immune response (Scholtzova et al., 2009). Long-term safety of a well-characterized immunotherapeutic drug, TLR9 agonist CpG ODN 2006 (cytosine-phosphate-guanine oligodeoxynucleotides) is assessed in aged squirrel monkeys (SQMs) using peripheral cytokine concentrations. SQMs are small New World primates with cerebrovascular and immune systems similar to those in humans. An important feature is that cerebral amyloid deposition in SQMs has a predilection for abundant CAA and low levels of parenchymal Aβ deposition, supporting SQM as a translational model for Alzheimer's Disease. Hence, these exciting non-human primate data indicate that long-term treatment with TLR9 agonist CpG ODN results in amelioration of CAA and cognitive improvements in aged SQMs without inducing adverse events. Overall, these extensive preclinical research findings suggest that this innovative immunomodulation is effective at reducing all cardinal AD related pathologies without toxicity in multiple experimental models of AD. This study supports the viability of a Class B CpG ODN as a cure for Alzheimer's Disease and would have a significant chance of achieving clinical efficacy.

Salma Youssef • *Gerstner Sloan Kettering Graduate School, Memorial Sloan Kettering Cancer Center*

Mentor: Jennifer Tsai
Biology

Nrf2 regulates T cell function and graft-versus-host-disease

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Gerstner Sloan Kettering Graduate School,
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Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a primary therapy for several hematologic malignancies. A common complication of allo-HSCT is graft-versus-host disease (GVHD) which accounts for 10% of post-transplant deaths. GVHD is mediated by donor alloreactive T cells that cause inflammation in the skin, thymus, liver, and gut. Nuclear factor erythroid-derived 2-like 2 (Nrf2) is a master regulator of the redox pathway that has been shown to have a role during T cell activation. Here, we sought to evaluate the role of Nrf2 in the pathophysiology of GVHD. We found that transplantation of T-cell depleted bone marrow and Nrf2-/- T cells in our major and minor MHC-mismatched GVHD mouse models leads to decreased GVHD mortality, as compared to mice receiving wildtype (WT) T cells. We discovered that the increased survival is through the expansion of anti-inflammatory regulatory T cells (Tregs) in the absence of Nrf2. Our data show a greater fraction of donor-derived CD4+ Helios+ Tregs. In addition, Nrf2-/- donor T cell recipients had significantly decreased CD8+ cytotoxic T cell infiltration into the liver, small intestine, and large intestine and comparable CD4+ helper T cell counts following allo-HSCT consistent with the reduced GVHD effect. Our proposed mechanism is the absence of Nrf2 allows the increased expression of Helios which stabilizes Foxp3 leading to increased Tregs. To validate that the decrease in GVHD is not through increased apoptosis of alloreactive T cells, we measured the expression of apoptotic genes in WT and Nrf2-/- CD25+ Tregs after allo-HSCT and found analogous levels of pro- and anti-apoptotic genes using qPCR. Our findings in addition to elucidate the role of Nrf2 in regulating T cells also show that Nrf2 inhibition can be used as a therapy to decrease GVHD in allo-HSCT.

Nailya Khalizova • *CUNY Hunter College*

Mentor: Ana Rodriguez
Biology

DETERMINING THE SIGNALING PATHWAYS IN ENDOTHELIAL DYSFUNCTION DURING CEREBRAL MALARIA

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Each year, malaria kills more than 400,000 people and remains a global health problem. Malaria is caused by the parasite Plasmodium. There are five species of Plasmodium known to infect humans. From the five, Plasmodium falciparum is considered to be the deadliest due to the development of the severe pathology, cerebral malaria. It has been previously shown that the rupture of P. falciparum infected red blood cells (iRBCs) and release of its contents in vitro induces the disruption of the inter-cellular junctions of human brain microvascular endothelial cells (HBMECs), mirroring the pathology observed in patients with cerebral malaria. However, the signaling induced by iRBCs that leads to this disruption is not clear. To begin to elucidate the signaling cascade, we have determined whether the rupture of iRBCs induces calcium (Ca2+) signaling in HBMECs. Using a fluorescent Ca2+-sensitive dye detected by microscopy, we have found that the lysates of iRBCs induce an increase in intracellular Ca2+ levels in HBMEC in vitro that is not observed when control lysates of uninfected RBC were used. These results suggest that Ca2+ signaling may play a role in the signaling cascade involved in the disruption of HBMEC junctions. Eventually, understanding the basic principles of signaling between P. falciparum and endothelial cells may lead to the development of a treatment of cerebral malaria.
This work was conducted with the funding by by NIH/NHLBI, grant 1R01HL130630.

Soham Ghoshal • *City University of New York, Hunter College*

Mentor: Alexander Smith
Biology

The dorsal striatum is a brain structure that integrates motor and limbic information and is critical for action selection and reinforcement learning. We examine the innervations to and functions of two populations of medium spiny neurons (MSNs) in the anterior dorsolateral striatum (aDLS) to understand their roles in instrumental conditioning. MSNs comprise 95% of the total cell population in the striatum, and they are categorized by their dopamine receptor expression and neuroanatomical projections. MSNs expressing D1 receptors are part of a 'direct pathway' that stimulate locomotion, while neurons expressing D2 receptors are part of an 'indirect pathway' that inhibit locomotion, although it is less understood how each MSN acts in reward-related behaviors. The aDLS is considered a 'habit center' of the brain, and is thought to be more involved with motor than limbic circuits.

Data from our laboratory contradicts this view, indicating that the aDLS becomes activated in mice following a single instrumental acquisition (IA) task. Our data utilizing D1- and D2-Cre mice shows that aDLS D1-MSNs are required for the memory consolidation of IA, whereas D2-MSNs inhibit new learning and are required for habitual responding. In order to examine the cell-type specific contributions to this behavioral paradigm, we utilized in-vivo Ca2+ imaging in D1- and D2-Cre mice to further characterize control by the aDLS in goal-directed A-O IA and habitual S-R responding. Our imaging data support the hypothesis that D2-MSNs oppose new learning, as their activity is decreased following IA. Thus, we hypothesize that D2-MSNs contribute to development of habitual behaviors through suppression of alternative actions.
It is also unknown which cell populations project to the two MSNs and whether these afferents differ between the two types. We investigate the inputs into each of these cell types utilizing retrograde tracing techniques, building upon on our laboratory's data on the different MSNs' roles in instrumental acquisition. Our tracing indicates several cell-type specific afferents to D1- and D2- MSNs in the including the parafascicular nucleus of the thalamus (PfN), and the basolateral amygdala (BLA). Further investigation into control by these regions may allow us to better understand IA and support these experiments' data which indicate that the D1- and D2-MSNs in the aDLS are critical and necessary for regulating both novel learning and in habitual responding.

Chethana Gallage Dona • *LaGuardia Community College*

Mentor: Richa Gupta
Biology

Role of RecO in the DNA Break Repair Mechanisms of Mycobacteria

Mycobacterium includes both pathogenic and non-pathogenic bacteria, and DNA repair genes are highly homologous across the species of this genus. A break in both strands of the DNA, termed as the "double-strand break (DSB)", is particularly lethal if not repaired to maintain the integrity of chromosomal DNA. Recent studies have indicated that mycobacteria employ three DSB repair pathways to ensure survival: (i) Homologous recombination (HR), (ii) Nonhomologous end joining (NHEJ), and (iii) Single-strand annealing (SSA). Several distinctive features of HR repair are evident in mycobacteria compared to other model bacteria, with a multitude of proteins involved. Of special note is the RecO protein, which plays a dual role in mycobacterial DSB repair by participating in both HR and SSA mechanisms but its exact molecular function is yet unclear. We propose to investigate genetically which activities of this key player are pertinent to its role in vivo. By sequence alignment, we have identified amino acid residues in the RecO protein which when mutated are predicted to disrupt specific domains critical for its activity. We are in the process of making chromosomal mutants of recO and will be investigating the effects of these mutations on the DSB repair mechanisms. The findings of this project can also help in the identification of a new drug-target against mycobacteria.

Hira Peracha • *University of Delaware*

Mentor: Shunji Tomatsu
Biological Sciences

Mucopolysaccharidosis IVA (MPS IVA, Morquio A syndrome) is an autosomal recessive disorder caused by the deficiency of N-acetylgalactosamine-6-sulfate sulfatase. Deficiency of this enzyme leads to the accumulation of specific glycosaminoglycans (GAGs), chondroitin-6-sulfate (C6S) and keratan sulfate (KS), which are mainly synthesized in the cartilage. Therefore, the substrates are stored primarily in the cartilage and its extracellular matrix (ECM), leading to a direct impact on bone development and successive systemic skeletal spondylepiphyseal dysplasia. The skeletal-related symptoms for MPS IVA include short stature with short neck and trunk, odontoid hypoplasia, spinal cord compression, tracheal obstruction, obstructive airway, pectus carinatum, restrictive lung, kyphoscoliosis, platyspondyly, coxa valga, genu valgum, waddling gait, and laxity of joints. The degree of imbalance of growth in bone and other organs and tissues largely contributes to unique skeletal dysplasia and clinical severity. Diagnosis of MPS IVA needs clinical, radiographic, and laboratory testing to make a complete conclusion. To diagnose MPS IVA, total urinary GAG analysis which has been used is problematic since the values overlap with those in age-matched controls. Currently, urinary and blood KS and C6S, the enzyme activity of GALNS, and GALNS molecular analysis are used for diagnosis and prognosis of clinical phenotype in MPS IVA. MPS IVA can be diagnosed with unique characters although this disorder relates closely to other disorders in some characteristics. The aim of this study was to describe clinical, radiographic, biochemical, and molecular diagnosis and clinical assessment tests for MPS IVA. The aim of this study was also to compare MPS IVA to other closely related disorders to differentiate MPS IVA. Overall, imbalance of growth in MPS IVA patients underlies unique skeletal manifestations leading to a critical indicator for diagnosis.

Samvida Venkatesh • *Princeton University*

Mentor: Ileana Cristea
Molecular Biology

Human cytomegalovirus (HCMV) is among the most prevalent infectious agents in humans and is life-threatening in immunocompromised individuals. For successful infection and spread, the virus must reorganize and redirect the functions of various host cell organelles at the right times, yet molecular mechanisms of cellular infection remain to be elucidated. To see these organelle alterations during HCMV infection from a proteomic perspective, I constructed a web-accessible visualization of translocations of host and pathogen proteins with previously determined protein localization data during infection. The versatile tool is not limited to this dataset alone, as it allows users to input any proteomic data with subcellular localization information to highlight dynamic spatiotemporal localization in their own data. By visualizing the spatial and temporal proteome of HCMV-infected cells, we uncovered an important role for a less-studied organelle in infection, the peroxisome. Lipid metabolism in the peroxisome is thought to be important for enveloped viruses such as HCMV to form their host-derived lipid envelope, yet peroxisomes remain poorly characterized as they cannot be adequately resolved by biochemical fractionation. Therefore, I adapted a proximity labeling approach using APEX to identify host and viral proteins in the peroxisome throughout infection. APEX is an engineered peroxidase that biotinylates proteins in its vicinity upon the addition of biotin-phenol. The newly biotinylated proteins can then be enriched by immunoaffinity purification against the biotin tag and identified by mass spectrometry. I demonstrated that APEX constructs can be modified to include a peroxisomal targeting signal and consequently be localized to peroxisomes via transient transfection. Experiments utilizing APEX in HCMV-infected cells to identify and functionally characterize proteins localized to the peroxisome are ongoing. Through an integrated visualization tool and peroxisomal proteome-labeling method, I have provided novel techniques to illuminate the complex proteome of HCMV-infected cells.

Nhung Hoang • *Swarthmore College*

Mentor: Sara Mathieson
Computer Science

The evolutionary histories of human populations are traditionally studied and inferred using summary statistics. This quantitative approach yields simplistic and nearly comprehensive results, but it is computationally expensive and usually undermined by confounding variables, as well as lossy compression. Recent work in population genetics has turned to machine learning to take advantage of the current abundance of genetic data available. We propose a Hidden Markov Model (HMM) to Convolutional Neural Network (CNN) pipeline that improves upon the summary statistics approach. HMMs are unsupervised statistical models that are effective at generalizing global trends across the genome. CNNs, a class of machine learning models, are trained to extract local patterns within a given set of data and to represent the data by its most informative features. Our objective is to integrate the advantages of the two models into one pipeline for making evolutionary inferences about populations. Specifically, our integrated method is designed to take in samples of genetic regions from a population and produce a prediction for how strongly natural selection has affected the population in that genetic region. Our results, for population data generated using coalescent simulators, show that the global information learned by the HMM helps the CNN in capturing local information about the genetic data, thus producing consistently high accuracies for inferring natural selection strengths.

Syed Daniyal • *Icahn School of Medicine at Mount Sinai*

Mentor: William Howe
Human Biology

Control of Cocaine Reward by the Alpha5 Subunit of the Nicotinic Acetylcholine Receptor

Syed A. Daniyal1, William M. Howe2 ,Paul J. Kenny2
CUNY Hunter College1, Icahn School of Medicine at Mount Sinai2

Genome-wide association studies have identified a single nucleotide polymorphism (SNP) in the gene coding for the α5 nicotinic receptor subunit (CHRNA5; nAChR) that causes a loss of receptor function and is linked to the development of nicotine dependence. Paradoxically, this same SNP also appears to be protective against the development of cocaine dependence. The circuit-level mechanisms underlying the disparate role of this SNP in modulating the rewarding aspects of different drugs of abuse are unknown. Here, we used a combination of methods to investigate this question, including mice genetically modified to express the same CHRNA5 SNP, behavioral assays of cocaine reward, designer receptors exclusively activated by designer drugs (DREADDs), optogenetics, electrophysiology, and in vivo calcium imaging to identify the specific brain circuits that contribute to α5-mediated coding of drug reward. In previous studies, we found evidence to suggest that the α5 nAChR SNP supports pathological nicotine seeking by reducing activity in brain pathways that signal aversion. In the current study, we found that the same loss of function mutation can reduce cocaine seeking by negatively modulating brain reward circuits. Specifically, we found that by selectively inhibiting α5 nAChRs in the parafasicular nucleus of the thalamus, we could reduce the rewarding effects of cocaine to the same extent observed in mice lacking the α5 nAChR, or those expressing the loss-of-function SNP in the human population. Furthermore, we found that the activity of cholinergic interneurons (CINs) in the nucleus accumbens (NAcc), which are known to be key in signaling cocaine reward, was drastically altered at baseline, and in response to cocaine, in mice lacking the α5 nAChR. Given that CINs receive input from that parafasicular thalamus and play a major role in cocaine reward, our combined data suggest that loss of α5 nAChR leads to altered recruitment of this distributed circuit, which in turn diminishes the ability of cocaine to motivate future behavior. Our on-going studies are aimed at testing this hypothesis in vivo using a novel, multi-region calcium imaging approach. Together, these data highlight the importance of thalamic modulation of striatal CINs in regulating cocaine reward, provide a mechanism through which cocaine efficacy is reduced in the α5 SNP population, and importantly demonstrate the importance of different brain circuits in supporting use of different drugs of abuse.

Max Elikan • *Columbia University*

Mentor: Harris Wang
Biology

Improved characterization of the cas13a protein provides the opportunity to build a cheap, rapid non-technical diagnostic tool that has point-of-care applications in resource-poor settings through the use of an Escherichia coli –based transcription-translation (TX-TL) cell-free expression system. This self-contained platform encodes all components for diagnosis from detection to a readout in a cell-free solution. By combining the collateral cleavage of CRISPR-cas13a and small molecule sensing via metal sensitive operons, this system becomes modular, allowing for multiple diagnostic targets. To demonstrate, gene fragments of Chlamydia trachomatis and Neisseria gonorrhoeae were detected through the creation of specific targeting guide RNAs. CRISPR-cas13a's collateral cleavage and its preferential cleaving towards certain motifs allowed for the development of a ratiometric read-out due to the preferential degradation of chromoprotein expressing mRNA. The diagnostic system provides a simple in vitro platform that can be used for the versatile detection of pathogenic bacteria in clinical or field settings.

Aneesa Valentine • *Weill Cornell Graduate School of Medical Sciences*

Mentor: Iliyan Iliev
Biology

The Infectivity of IBD Patient Isolated Gut Mycobiota Species

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Background
Inflammatory bowel disease (IBD) is a heterogeneous group of chronic inflammation disorders that result from the dysbiotic interaction of the intestinal immune system with the gut microbiome. Until recently, most investigative efforts were centered on understanding and manipulating the altered mucosal immune response that characterizes these diseases. However, more recent studies have highlighted the important role of the microbiota in disease onset and disease exacerbation.

Methodology
Using a sterile fungal culturing approach with the highest quality control taken, alongside DNA isolation and qPCR, we identified 4 fungal species from a cohort of 5 active Ulcerative Colitis (UC) patients.

Hypothesis
Knowing that Candida colonization in particular is significantly augmented in IBD cases, we hypothesized that different fungal species are both able to be cultured and characterized from the human IBD gut.

Results
A total of 82 fungal isolates were obtained from both mouse and human samples. Preliminary Real-Time PCR revealed Candida tropicalis, Candida albicans, Saccharomyces cerevisiae and Sacchromycopsis fibuligera species in both our healthy and active UC cohorts. These fungal isolates were observed at a much higher incidence in our active UC cohort than in our healthy cohort.

Conclusion
These associations warrant further investigation into the fungal communities and species identification within the IBD gut, as well as the factors contributing to the efficacy of human commensals to colonize the GI tract. Our results provided us potential basis for novel therapeutic avenues to combat IBD.

Carlos Jeronimo • *Memorial Sloan Kettering Cancer Center*

Mentor: Morgan Huse
Biology

The role of cofilin-mediated F-actin clearance at the Immunological Synapse upon T cell activation

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Cytotoxic T-Lymphocytes (CTLs) recognize and kill virally infected cells and tumorigenic cells (target cells). Binding of the T cell to the target cell results in the secretion of cytotoxic proteins, promoting apoptosis of the target cell. CTL killing is potentiated by the formation of the Immunological Synapse (IS) at the cell interface between the CTL and target cell. IS formation is associated with F-actin clearance at the center of the contact. The T cell centrosome reorients to the center of this F-actin cleared region, bringing with it lytic granules containing cytotoxic proteins. Previous work in the lab has shown that centrosome reorientation to the center of the IS requires F-actin clearance. To further understand how F-actin clearance promotes centrosome reorientation, a better understanding of how F-actin clears is necessary. Cofilin (CFL), an actin-severing protein, has been shown to sever F-actin at the IS in B cells, another immune lymphocyte that exhibits centrosome polarization. Therefore, we hypothesized that CFL promotes F-actin clearance at the T cell IS. To investigate whether CFL promotes F-actin clearance, we sought to characterize the localization of CFL at the IS using various imaging approaches. Additionally, we examined the requirement of CFL for F-actin depolymerization using a CRISPR-CAS9 knock out approach. Using TIRF microscopy we saw that cofilin correlated with F-actin clearance at the center of the synapse. While results are in progress, we expect to see a disruption of F-actin clearance at the IS upon knockout of CFL.

Shivani Vyas • *Rutgers University - New Brunswick*

Mentor: Nada Boustany
Biomedical Engineering

Our goal is to investigate how vinculin protein distribution in neurons alters over time. In preliminary data collected in isolated neurons overexpressing vinculin fused to a fluorescent protein, we find that when comparing images from day-in-vitro (DIV) 7 of growth to DIV 14, there is a significant and noticeable difference between the appearance and distribution of the protein in the cell. At the earlier DIV, vinculin appears continuous throughout the neuron and its processes. At the later DIV, the protein is more punctate and seems to gather at specific spots throughout the cell processes, especially at the edges of the process. To find out whether this change in vinculin distribution occurs with endogenous vinculin, we used immunofluorescence to image the distribution of the native vinculin in cultured neurons. By immunostaining for vinculin, establishing an ideal incubation procedure, and confirming the visibility of the protein by comparing it to MAP2, it is clear that vinculin in neurons gathers at regions throughout the cell and has a spotted appearance when imaged with a fluorescent microscope after immunostaining. Quantitatively, with MATLAB image analysis, neurons randomly sampled from the earlier DIV contained less circles and dots representing the vinculin protein in comparison to the later DIV images. Additionally, the density of vinculin distribution was greater in the later DIV than the earlier DIV. However, as compared to epithelial cells, neurons seem to have less vinculin, yielding a much dimmer image. The general protocol for immunostaining is to stain both primary and secondary for two hours each, however, this protocol did not yield images with intensities that were high enough to image properly. A MATLAB image analysis regarding neuron image intensities based on varied incubation periods was conducted, demonstrating that the longer incubation periods previously stated were producing significantly brighter images. In the future, reasons for why vinculin appearance within neurons is changing over time need to be determined. Although neuronal vinculin immunostaining procedure was improved upon, it still appears dimmer when compared to other types of cells. Therefore, the immunostaining methods still need to be developed further to yield optimal results when imaging.

Brenda Okereke • *Rutgers University-New Brunswick*

Mentor: Dr. Li Cai
Biomedical Engineering

Secondary data analysis reveals changes in gene expression after spinal cord injury
Brenda Okereke, Dr. Li Cai, Rutgers University, New Brunswick.

This study focused on global and temporal changes in gene expression following contusion spinal cord injury (SCI). Secondary data analysis was performed on two published studies [GSE5286 and GSE47681] and over 10,000 genes using Expander (EXpression Analyzer and DisplayER), a java-based tool for analysis of gene expression. The combined datasets contain a total of 22 samples (Affymetrix Mouse Genome 430 2.0 Array) and three time points: 1, 3, and 7 day after injury with corresponding sham control (sham: 2 samples/time point; SCI: 4 samples/time point). In addition, the dataset also includes 4 samples from the Naïve animals. The dataset was first normalized, log scaled, and filtered with 1.5 fold changes in gene expression using naïve group as baseline resulting in 266 highly differentially expressed genes (DEGs). Further clustering, gene ontology and pathway analyses reveal these DEGs involved in spinal cord injury, cytokines and inflammatory response, chemokine signaling pathway.

Gabrielle Paniccia • *Stony Brook University*

Mentor: Laurie Krug
Biochemistry

Epstein-Barr virus and Kaposi's Sarcoma-associated herpesvirus are cancer-causing viruses capable of establishing lifelong infections in humans. These viruses cycle between active, lytic replication and a resting state called latency. It is challenging to treat these herpesvirus infections because current therapeutics only inhibit actively replicating virus, making them ineffective against the resting, latent virus. Our goal is to create a system to target these viruses using a CRISPR-Cas9 gene-editing system, eradicating the infection through the disruption of essential viral genes. We designed a series of guideRNAs to target genes essential to both the latent and lytic replication of murine gammaherpesvirus 68, a mouse gammaherpesvirus that served as a model for Epstein-Barr virus and Kaposi's Sarcoma-associated herpesvirus. In addition to pairing these guideRNAs with wild-type Cas9, which causes double stranded breaks, we also utilized an alternate form of Cas9, called Cas9N, which generates single stranded nicks. Because gene editing with Cas9N requires two different guide-RNAs, it reduces the risk of off-target effects. We transduced mouse fibroblast cells with lentiviral vectors encoding each CRISPR-Cas9 or -Cas9N construct in mouse fibroblast cells, creating cell lines with CRISPR-Cas9 capable of targeting a specific virus gene. We then drug-selected for stable cell lines using puromycin. We performed a de novo infection at low and high multiplicity of infection, and examined for the reduction in infectious particle production by plaque assay. From this data, we identified that fibroblast cells expressing guideRNAs against genes ORF50 and ORF73 have a drastic defect in replication. These defects are less severe in the Cas9N system, indicating that the wild-type form of Cas9 is more effective at disrupting the virus. Future experiments will test cell lines expressing combinations of guideRNAs that target multiple viral genes with the goal of creating a more effective therapeutic against the virus. This work was supported with funding from NIH 1R43AI131958.

Gizem Dursuk Osmanoglu • *University of Pennsylvania*

Mentor: Jonathan Katz
Biology

Cells are exposed to internal and external stresses that can cause different cellular responses such as cell survival or cell death depending on the nature, severity, and duration of the stress. The tumor suppressor protein p53 along with the zinc finger transcription factor KLF5 play significant roles in mediating cell fate decisions upon stress exposure. In this study, we examine the cellular response to common stressors, ethanol, and cigarette smoke. Furthermore, we investigate the functions of p53 and KLF5 upon treatment with ethanol and cigarette smoke. Exposure to both stressors resulted in increased cellular death in primary human esophageal epithelial cells. Relative mRNA expressions of p53 and KLF5 changed depending on the severity
of ethanol treatment, indicating their importance in the mechanism behind mediating cell fate decisions.

Jessica Kuppan • *CUNY Hunter College*

Mentor: Mandë Holford
Chemistry and Bioinformatics

Developing a Dissociative Viral Nanocontainer for Peptide Drug Delivery
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Chronic pain is a global health concern affecting over 1.5 billion people and the prescription opioid crisis has propelled scientist to identify novel therapeutics that are non-addictive and selective. Such novel therapeutics have included bioactive venom peptides which are highly potent, extremely specific to their molecular targets, and whose rigid disulfide-rich structure enhances their stability. While there are significant advantages to pursuing peptide therapeutics, delivering peptides to their targets is challenging due to their varying pharmacokinetics in vivo and inability to cross the blood brain barrier. For example, Prialt® (MVIIA), a venom peptide from Conus magus, is the only FDA approved and non-narcotic conopeptide recommended to treat chronic pain. However Prialt® can only be administered via intrathecal infusion. Here we describe a drug delivery strategy using nanocontainers to encapsulate bioactive peptides for delivery and induce the disassembly of the nanocontainer to release the bioactive peptide to its target. While it has been possible to load nanocontainers with peptides, triggering the release under physiological conditions remains challenging. Using this strategy, recombinant and chemical techniques were used to create P22 viral nanocontainers loaded with a peptide cargo and with site specific unnatural norbornene lysine amino acid inserted for triggered disassembly. Specifically, P22-GFP and P22-MVIIA nanocontainers were developed and characterized by gel electrophoresis, mass spectrometry, transmission electron microscopy (TEM), and dynamic light scattering (DLS). The P22-GFP nanocontainers were then tested for release of the cargo, by an Inverse Electron Demand Diels-Alder (IEDDA) reaction, where the unnatural amino acid norbornene lysine reacts with an arbitrary tetrazine molecule. This reaction was then characterized by TEM and DLS where morphological changes in the appearance of the capsid suggest disassembly may have occured. Our results provide proof in principle for applying P22 nanocontainers to deliver MVIIA in a less invasive manner than the current intrathecal injection.

Rufina Kamaletdinova • *Hunter College*

Mentor: Danny Winder
Biology

Chronic Stress Post Chronic Alcohol Exposure Alters the Rewarding Effects of Cocaine

Rufina Kamaletdinova 1, Anel A. Jaramillo 2,3,4,5, Rafael Perez 3,4,6, Oliver Vranjkovic 2,3,4,5, Brett Nabit 3,4, Danny G. Winder 2,3,4,5,7
1 CUNY Hunter College, 2 Mol. Physiol. and Biophysics, 3 Brain Inst., 4 Center for Addiction Research, 5 Kennedy Ctr., Vanderbilt Univ., Nashville, TN, 6 Department of Pharmacology, 7 Dept. of Psychiatry, VUMC

Depression is a mental illness that is a leading cause of disability in the United States and worldwide and is often comorbid with drug addiction. However, the question of how a combination of previous drug-exposure and depression affect the rewarding effects of a novel drug remains to be fully understood.
The goal of our study was to investigate whether a negative affect state induced by a recent history of chronic alcohol exposure followed by a period of chronic stress produces a modified response to the rewarding effects of cocaine. Specifically, we examined the impact of an alcohol-withdrawal and stress-induced negative affect state on cocaine preference in mice. We hypothesized that mice with a recent history of alcohol and stress exposure would exhibit a depression-like phenotype and would have a stronger preference for a cocaine-associated context. To induce a negative affect state composed of both depressive- and anxiety-like symptoms, mice underwent a chronic period of intermittent alcohol exposure for 2 weeks, followed by a period of forced abstinence. During the alcohol withdrawal period, mice underwent 4 days of exposure to restraint stress, and a novelty-suppressed feeding test (NSFT) was used to assess affective state. After the desired phenotype was established, mice were exposed to cocaine conditioned place preference (CPP) training followed by testing for preference for the cocaine-associated context.
We found a trend for a positive correlation between negative affect (as measured by the NSFT) and cocaine preference (measured by the change in preference for the cocaine-paired context). These observations give us more insight into depression and substance abuse comorbidity, as they show a potential interaction between forced alcohol abstinence/stress-induced negative affect and preference for a novel drug such as cocaine.

Kelly Finke • *Swarthmore College*

Mentor: Sara Mathieson
Cognitive Science

Endogamous Pedigree Reconstruction Using Identity By Descent

As DNA sequencing decreases in cost, genetic studies of individuals and families becomes increasingly accessible for biologists investigating disease inheritance; still, however, it is often impossible to obtain genetic information for an entire family tree, especially if that pedigree extends many generations back in time. Since it is often useful for biologists to examine complete, multigenerational pedigrees, a number of algorithms attempt to fill these gaps by using known genotypes of living individuals to construct estimations of unknown genotypes of recent ancestors. However, many of these algorithms fail when working with complicated pedigrees, such as pedigrees that involve inbreeding, cross-generational marriages, or remarriage. When working with endogamous pedigrees - pedigrees marked by a close sharing of DNA due to the practice of marrying within a small, contained group - all of these complications are common. Our endogamous pedigree reconstruction algorithm, therefore, is designed to take these factors into account, allowing users to work both with typical pedigrees and more complex, endogamous pedigrees. By probabilistically analysing the most likely sources of DNA segments shared between related individuals (identity by descent segments), our algorithm is able to reconstruct ancestral genotypes for even very complicated pedigrees. This algorithm allows biologists to better gain insights from these genetically unique populations which can inform studies of rare traits and diseases that are disproportionately expressed in endogamous communities.

Calvin Herman • *Macaulay Honors College, Hunter College, CUNY*

Mentor: Alan Grossman
Biological Sciences

Differences in Conjugation Efficiencies Between Two Integrative and Conjugative Elements in Bacillus subtilis

Horizontal gene transfer (HGT) drives bacterial evolution through the sharing of genetic material among cells. Traits conferred include: antibiotic resistance, pathogenicity, and various metabolic capabilities. Conjugation, one type of HGT, is the transfer of DNA from a donor to a recipient through a type-IV secretion system (conjugation machinery). Integrative and conjugative elements (ICEs) reside integrated in a host cell's chromosome, and can excise and transfer to recipients via conjugation. Following excision, ICEs replicate autonomously, transfer DNA via the element-encoded conjugation machinery, and integrate into the chromosome. Our work evaluates two different ICEs from Gram-positive bacteria: ICEBs1 and Tn916. ICEBs1's conjugation efficiency is ~10,000-fold greater than that of Tn916, due partly to more efficient excision of ICEBs1. To elucidate which additional steps of the ICE lifecycle contribute to the difference in conjugation efficiencies, we constructed hybrids that utilize ICEBs1 gene expression, excision, and integration functions and Tn916 replication and conjugation functions. With similar excision frequencies, the transfer efficiency of the ICEBs1-Tn916 hybrid was ~300-fold greater than that of Tn916 and ~20-fold less than that of ICEBs1, indicating that Tn916 replication and/or conjugation machineries were less efficient than those of ICEBs1. Furthermore, the hybrid's ability to transfer a heterologous plasmid, independently of its excision, replication, or integration functions, was 20-40-fold lower than that of ICEBs1, indicating that Tn916's conjugation machinery is less efficient than ICEBs1's. This work provides a basis for determining the mechanism(s) underlying differences in conjugation efficiencies, and will aid our understanding of an important process that drives bacterial evolution.

Shubhi Singh • *CUNY School of Medicine / Sophie Davis Program in Biomedical Sciences*

Mentor: Samantha Barrick
Biomedical Sciences

"Give It to Me Straight" is an educational review of the Sophie Davis School of Biomedical Education surrounding implicit bias and narrative medicine. Students were split into two groups: Group A who was aware of the authors' sexual orientation and Group B who was not aware. Both groups participated in a regular narrative medicine workshop. Pre and post surveys were distributed to measure the levels of homophobia before this intervention was implemented. The post survey was qualitatively coded as to see if there was a change in people's perspective and comfort with the LGBTQ+ community after the workshop.

Danielle Xie • *Children's Hospital Colorado, Anschutz Medical Campus*

Mentor: Melanie Cree-Green
Biochemistry and Molecular Biology

VALIDATION OF SURROGATE MODELS TO ASSESS TISSUE-SPECIFIC INSULIN RESISTANCE AMONG HIGH-RISK ADOLESCENT GIRLS

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Polycystic Ovarian Syndrome (PCOS) is a common endocrine disorder which develops in adolescence and affects 6-10% of women. PCOS is associated with insulin resistance (IR), which can occur in multiple tissues, in particular skeletal muscle and liver. Reliable assessment of tissue-specific IR in youth with PCOS is important for development of new therapies. The gold-standard method to assess tissue-IR is the hyper-insulinemic euglycemic clamp, a method which is too intensive for use in routine research. We aimed to validate surrogate indices (the oral minimal model (OMM)-derived muscle index and the Abdul-Ghani model-derived muscle index and liver index) against their respective clamp measurements in a population of high-IR-risk adolescent girls. 45 adolescent girls (14.6 ± 1.7 years; BMI %ile 23.3%-98.2%) underwent a standard 2-hour oral glucose tolerance test (OGTT) (75g glucose) and a hyper-insulinemic euglycemic clamp (80 mU/m2/min). This study was a secondary analysis. OMM total Si was computed using SAAM II software, and Abdul-Ghani muscle and liver insulin resistant indices (IRIs) were calculated as previously described. Correlation analyses were performed using Spearman's (nonlinear association) or Pearson's (linear association) correlation, as appropriate. OMM total Si correlated with clamp-measured insulin sensitivity ($r=0.65$; $p<0.0001$), whereas muscle IRI did not correlate ($p=0.4523$). Liver IRI correlated modestly with clamp-derived IC 50 Glucose ($r=0.35$; $p=0.0319$). In adolescent girls at high risk of IR, the OMM provided a strong surrogate characterization of muscle IR, when evaluated against the clamp. Whereas the Abdul-Ghani model indices are simpler to calculate and don't require the use of a modeling software, they may not be adequate for describing and distinguishing among those within a narrower IR range, such as that found in our study population. The OMM is an OGTT-based model, and may offer a cheaper and less time-intensive procedure to be used in research studies for characterizing tissue-IR.

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Jordy Sepulveda • *Hunter College - City University of New York*

Mentor: Arie Kaffman
Biological Sciences

Microglia are specialized immune cells in the central nervous system whose role in various neurodegenerative disorders has been studied extensively. However, the function of microglia in guiding myelination, astrocytic maturation, neurogenesis, and axonal growth during the postnatal period remains unclear. To investigate these issues, we developed a method to ablate postnatal microglia in a cell-specific, efficient, and non-toxic manner. We explore this by inducing the expression of the Diphtheria Toxin fragment A (DTA) in microglia at P10 and P13 using mice that express the inducible Cre recombinase from the CX3CR1 promoter (CX3CR1creER/DTA). Here we show that this method causes efficient ablation of microglia at P17 but with no significant changes in the expression of the myelin marker MBP, the synaptic markers PSD95, and Synaptophysin. Understanding this mechanism could allow us to investigate the role of complete ablation of microglia in neuronal development during early life stress.

Nana-Hawwa Abdul-Rahman • *University at Albany, State University of New York*

Mentor: Rabi Musah
Chemical Biology

In an effort to circumvent current drug laws or avoid the well-known dangers of highly addictive substances such as cocaine, heroin and methamphetamine among other compounds, an increasing number of drug users are resorting to the ingestion of unscheduled psychoactive plants as a means to get high. However, many of these plants are themselves toxic and contain banned psychoactive substances. Examples include plants that contain the drugs atropine and scopolamine, both of which are scheduled, while the plants from which they are derived are not. The ability to legislate the use of these substances is hampered by the absence of methods that can be used by law enforcement to identify these plant materials when they are discovered in a crime scene context. Reported here is the development of a method that can be used by law enforcement to rapidly identify and distinguish between plant drugs that contain atropine and scopolamine. Our hypothesis is that, these psychoactive seeds contain muscarinic receptor antagonist atropine and scopolamine.The seeds of 24 species representing the genera that contain both compounds (i.e. Atropa, Hyoscyamus, Brugmansia, Datura, and Mandragora) were analyzed by direct analysis in real-time mass spectrometry (DART-MS) in order to determine the unique chemical fingerprint that characterized each. Analyses were conducted in replicates of 8-10 and a total of 240 spectra were acquired. The presence of the key biomarkers atropine at m/z 290.369 and scopolamine at m/z 304.353 was confirmed in all the seed spectra. Kernel Discriminant Analysis (KDA) of the data yielded a diagram that shows clustering of like species and separation between species. The observed leave-one-out cross validation was 91.34% and an external validation of 100%. The results provide the first database of atropine and scopolamine-containing seeds that can be used by crime labs to identify them. Advantages of the method include the ability to analyze samples in their native form, its speed, and its accuracy.

Iris Liu • *Bryn Mawr College*

Mentor: Karen Greif
Biology

SYTAPTOTAGMIN 1 REGULATES AXONAL BRANCHING DURING EARLY NEURONAL DEVELOPMENT

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Synaptotagmin-1 (syt1) is a calcium-binding protein traditionally known for its role in vesicular exocytosis at the synapse. However, syt1 is also expressed in many types of neurons well before synaptogenesis. We hypothesize that syt1 mediates exocytosis along developing axons in response to localized calcium transients. This process could provide axons with the membranes needed for neuronal growth and branching, which includes the formation of filopodia: cytoplasmic projections that play a major role in migration and cell-cell interaction during early neuronal development.
Our past research has shown that overexpressing syt1 in the neurons cultured from E8 chicken embryo leads to an increase in filopodia formed during axonal development. This increase is dependent on the presence of functional syt1 calcium binding domain. In addition, shRNA (short hairpin RNA) knockdown of syt1 leads to a significant decrease in filopodia. In our summer experiments, we continued the syt1 shRNA knockdown experiment and quantified the percent knockdown of syt1 as well as the number of filopodia. We focused on analyzing the neurons with above 50% knockdown and found that there was no correlation between the efficacy of syt1 knockdown and the number of filopodia. These results suggested that a knockdown greater than 50% may not be necessary to produce a strong phenotype of reduced filopodia. Furthermore, we conducted a pilot double transfection of GFP and scrambled (Scr) shRNA plasmids to finalize methods for our future rescue experiment.

Acknowledgement
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Antonia Ekerdt • *Bryn Mawr College*

Mentor: Melanie Cree-Green
Biology

Purpose of Study: The combination of obesity and adolescence greatly increases the risk of insulin resistance and dysglycemia. Idiopathic reactive hypoglycemia (RHG) has been observed to be common in adult populations with obesity, but its mechanisms and prevalence have not been well studied in adolescent populations, in particular females. Thus our goals were twofold: to document rates of RHG in a group of adolescent girls with obesity and to identify markers associated with the presence of RHG.
Methods: 98 sedentary adolescents with obesity (BMI, Age) were enrolled. Participants taking medications that altered glucose metabolism or regulated hormones were excluded. Girls were administered a 6h oral sugar tolerance test (OSTT) of 75 g glucose and 25 g fructose and indices of glucose metabolism were measured. MRI for visceral and hepatic fat was performed. Glycemia was categorized as follows: blood glucose (BG) ≥ 70 mg/dL normoglycemic; 69 mg/dL ≥ BG ≥ 62 mg/dL indeterminate and were excluded from analysis; BG ≤ 61 mg/dL RHG. Normoglycemic and RGH demographics and baseline metabolic labs were compared with t-test or Mann-Whitney. OSTT curves were compared with two-way ANOVA with repeated measures and area under the curve.
Summary of Results: 16% of girls had RGH and 35% had normoglycemia. Meantime for RHG was 240 min post-OSTT drink. The AUC of insulin and glucose in the first 3 hours was higher in RHG group ($p = 0.04$ for both). 42% of participants with RHG showed impaired glucose tolerance. RHG group had central obesity with higher amounts of visceral fat and a higher waist-to-hip ratio ($p = 0.04$ for both) and a high rate of familial history of type 2 diabetes (81%).
Conclusions: RHG was relatively common in this population. RHG is associated with other warning signs of IR and hyperglycemia. Further studies should be conducted to understand the long-term effects and outcomes of RHG and its prediction for the development of type 2 diabetes.

Paul Lee *• University of Pennsylvania*

Mentor: Daniel Rader
Biochemistry, Biophysics

EVALUATING FUNCTIONALITY OF PUTATIVE GAIN-OF-FUNCTION VARIANTS OF LOW DENSITY LIPOPROTEIN RECEPTOR

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Low density lipoprotein receptor (LDLR) is an endocytic receptor critical for uptake of LDL cholesterol from the bloodstream. Dysfunction in LDLR results in a genetic disorder called familial hypercholesterolemia (FH), greatly increasing the level of plasma cholesterol and elevating the risk of cardiovascular disease. While numerous pathogenic loss-of-function mutations in LDLR have been identified, no studies have yet examined naturally occurring gain-of-function mutations of LDLR. Recently, two variants of LDLR (G324S and S849X) have been shown to be associated with lower levels of plasma LDL cholesterol. Investigating such variants may aid in identification of clinically suitable variants for gene therapy for FH.

The present study examined the stability and functionality of these two LDLR gene variants through protein expression analysis and in vitro cholesterol uptake assay. Amino acid substitutions corresponding to the variants were introduced to human LDLR cDNA, and the variants were transiently overexpressed in HEK293T cells in conjunction with E3 ligase IDOL. All the variants demonstrated comparable level of gene and protein expression compared to the wild-type with or without IDOL, suggesting that the variants were prone to ubiquitin-mediated degradation at a level similar to the wild type. In addition, overexpression of LDLR variants in HEK293T cells did not result in increased uptake of fluorescent or radiolabeled LDL compared to the wild type, suggesting that the mutations did not enhance the uptake functionality of the receptor. Further in vivo validation through AAV-mediated expression of the variants in mice will be required to test whether these trends persist in a more physiological setting.

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Erika Nemeth • *Stony Brook University*

Mentor: Peter Brink
Biochemistry

It has been shown that microRNAs (miRNA) have tumor suppressive effects in an array of human cancers, are highly specific, and are able to be passed through intercellular gap junction channels. However, an effective delivery system for such gene-silencing products has yet to be optimized for therapeutic applications. This study investigated the regulatory effects of miRNA in human prostate cancer cells (PC3) and the potential of a cell-based delivery system of miRNA from a donor cell to a recipient cancer cell. Human mesenchymal precursor cells (huMPC) were selected as donor cells because they enable gap junction-mediated communication with PC3s and do not elicit an immune response in vivo. Results showed that microRNA-16 (miR-16) is a significant regulator of PC3 cell growth in monoculture as miR-16-transfected PC3s experienced the onset of a round morphology, decreased proliferation, increased apoptosis, and downregulation of the anti-apoptotic protein BCL-2. Co-culture of miR-16-transfected huMPCs (donor cells) and normal PC3s (recipient cells) resulted in successful delivery of miR-16, with the regulatory effects preserved. Additionally, in vivo proof-of-concept of this cell-based delivery system was demonstrated by significantly reduced tumor volume in nude mice after treatment with miR-16-transfected huMPCs. This study presents a preliminary model for therapeutic applications of a mesenchymal stem cell-based miRNA delivery system in cancer.

Yuqiao Wang • *Cooper Union*

Mentor: Robert Topper
Chemical Engineering

Applying Machine Learning Heuristics To Discover New Organic Chemistry Reactions

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Organic total synthesis has long been the gem of organic chemistry. Particularly, for those natural products that are sparse and limited in nature, total synthesis is promising and indispensable in light of both environmental sustainability and the economy. However, the tediousness and high complexity of total synthesis constraint the planning of efficient synthetic routes to form the desired molecules, thereby restricting the promising applications of numerous kinds of substance. Thus, to achieve appreciable efficiency and convenience of reaction planning, the concept of in silico reaction design toolbox came into the horizon. Machine learning heuristics, combined with the simplified molecular-input line-entry system (SMILE) language, were applied to discover new types of organic reactions by supervised learning. After the database (e.g. ASKCOS) was constructed, the computer would plan the pathways to build the desired product from the given starting molecules. Several searching filters (excessive angular and ring strain, undefined equilibrium condition, etc.) were applied to banish specific patterns from the reactions provided by the template library. A list of possible reaction routes would then be generated according to the likelihood of the occurrence of each reaction. After undergoing some advanced training, the computer was expected to deduce new options of reaction that are beyond the existing content of the reaction database.

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Thilaka Arunachalam • *Memorial Sloan Kettering Cancer Center*

Mentor: Frederic Geissmann
Biology

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder characterized by inflammation of healthy tissue and antinuclear autoantibodies in the blood circulation. Although clinical manifestations of SLE are widely documented, the underlying molecular and cellular mechanisms remain poorly understood. Previous mouse models have proposed that defective engulfment of apoptotic cells, leading to extracellular leakage of nuclear fragments, may trigger SLE development. We performed whole exome sequencing in a cohort of SLE patients and healthy relatives from multiplex families. Rare loss-of-function mutations were identified in two, non-receptor tyrosine-kinases: TNK2/ACK1 and PTK6/BRK. Based on their molecular pathways, we hypothesized that mutations in ACK1 and BRK kinases may cause defective engulfment of apoptotic cells. To elucidate the functional and pathologic mechanisms of these kinases in the phagocytic pathway, we have been using CRISPR/Cas9 technology to generate ACK1 and/or BRK induced pluripotent stem cell (iPSC) knock out (KO) lines. We first designed and constructed sgRNA-Cas9 plasmids targeting TNK2 or PTK6 genes. The plasmids were then introduced in iPSCs using electroporation. Electroporated iPSCs were FACS sorted based on GFP fluorescence, cultivated as single colonies, and screened for mutations using Sanger sequencing. The newly derived KO iPSC lines will be differentiated into macrophages and tested for phagocytic activity in the presence of apoptotic cells. Our preliminary data, involving selective kinase inhibitors, suggests that ACK1 and BRK kinases link phosphatidylserine recognition to the Rac1-Actin phagocytic pathway via p130CAS phosphorylation. Taken together, these studies identify novel disease-causing genes, explore the phagocytic pathways for apoptotic clearance, and provide a valuable in vitro knockout model for characterizing SLE pathogenesis.

Rodrigo De La Torre • *Brown University*

Mentor: Anne Hart
Neuroscience

Amyotrophic lateral sclerosis (ALS) is a late-onset fatal neurodegenerative disease characterized by muscle wasting due to degeneration of corticospinal and lower motor neurons. Despite the identification of genes implicated in ALS, the mechanisms by which neurodegeneration occurs remains elusive. A common cause of familial ALS is a missense mutation in the gene coding for the enzyme Cu/Zn superoxide dismutase (SOD1), which accounts for 20% of familial cases through both loss and gain of function mechanisms. This study had two specific aims: 1) to develop a higher throughput screen for mutant SOD1 suppressors, and 2) assess interactions between two mutant alleles known to be linked to ALS. In the first part of the study, we utilized one single copy insertion (A4V) and two knock-in (G85R & G93A) models of mutant SOD-1 in C. elegans carrying the transgene vtIs1, which expresses the mutant ROL-6 protein at low levels and has little impact on locomotion. Preliminary results in our lab suggested that in transgenic C. elegans carrying the knock-in ALS-associated sod-1 mutation, G85R, and the GFP-expressing transgene, vtIs1 there might be increased accumulation of the rol-6 gene product. We hypothesized that if sod-1 mutant alleles impair proteostasis, then worms with vtIs1 and other sod-1 mutant alleles would also show a roller phenotype. The proteostasis network is sensitive to cumulative protein damage, therefore, a genetic background which impairs proteostasis may modulate expression of misfolded proteins. In the second part of this study, we looked at interactions between fust-1 and pfn-1. Our findings indicate that loss of profilin function induces coiling locomotion in C. elegans, but when worms contain the profilin loss-of-function allele (ok808) as well as a FUS mutant allele (corresponding to patient FUS R524S), coiling is significantly reduced. These findings may advance therapeutic strategies targeting ALS neurodegeneration by increasing efficiency of SOD1 suppressor identification and elucidating genetic interactions involved in ALS pathology.

Kristen Buscemi • *Saint Joseph's University*

Mentor: Matthew Nelson
Biology

THE ORCOKININ NEUROPEPTIDE NLP-14 REGULATES STRESS-INDUCED SLEEP

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Sleep/wake cycles are largely regulated by neurons that release protein messengers called neuropeptides. Neuropeptide genes often encode for an assortment of peptides with distinct amino acid sequences. Stress-induced sleep (SIS) in Caenorhabditis elegans is induced by a number of neuropeptides which are encoded for by distinct genes, such as flp-13 and flp-24 (Nelson et al 2013; Nath et al 2016). However, the specific role of distinct peptides encoded for within the same gene has not been explored. We report that NLP-14 neuropeptides, which are homologous to arthropod orcokinins, regulate SIS. Ectopic over-expression of all 11 NLP-14 peptides (5 distinct) induces quiescence of locomotion and defecation in normally active animals. Additionally, an nlp-14 mutant strain carrying a deletion allele, tm1880, displays a strong reduction in both locomotion and defecation quiescence during SIS. We find that nlp-14(tm1880) animals only produce 5 peptides: NLP-14-2(2) , NLP-14-4(2) and NLP-14-5(1). To begin to determine the roles of individual peptides within the same gene we used the CRISPR/Cas9 system to make a mutation which results in truncated pre-proteins containing only a single copy of NLP-14-1,2 and 3. These worms display defects in SIS that are similar but not identical to those of the nlp-14(tm1880) mutants. Additionally, over-expression of NLP-14-1 by itself induces quiescence of locomotion but not defecation. We are currently making more mutations to alter the number of peptides expressed and over-expressing other individual peptides.

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Abigail Shtekler • *Johns Hopkins*

Mentor: Robert Hobbs
Integrative Neuroscience

Alpha-particle emitters have become an interest for targeted cancer therapies. They have a short range in tissues and high energy deposit, which allows for optimization of cell kill and minimal damage to healthy surrounding tissue. The emitted alpha-particles generate DNA double strand breaks making them affective against radio- and chemo- resistant cancer cells. For these reasons, the alpha particle emitter Ac-225 was used alone and in combination with 17-AAG or Nu7441 in a colony formation assay. Relative biological efficacy (RBE) is then a calculated measure of increased cell kill in these treatments compared to radiation alone.

Kimberly Wei *• Yale University*

Mentor: Michael Koelle
Molecular Biophysics and Biochemistry

The model organism C. elegans is an excellent system to study neurotransmitter signaling as the wiring diagram mapped the synaptic connectivity between all 302 neurons and a C. elegans neurotransmitter map shows the neurons that release each of the seven small-molecule neurotransmitters1. We are adding to these neurotransmitter signaling maps a Neurotransmitter GPCR Atlas, where the overall goal of this project is to map out which cells express each of C. elegans' 27 small-molecule G-protein coupled receptors (GPCRs). Through the Atlas, we have found 18 neurotransmitter GPCRs in the egg-laying circuit, while previous studies have shown there was only six GPCRs in this circuit2,3,4. We are currently crossing RFP markers strains to the GPCR::GFP transgenes to confirm the expression pattern of these GPCRs in the C. elegans egg-laying circuit. We want to determine the function of these receptors in this circuit by testing 18 neurotransmitter GPCR mutants in egg-laying assays to look for behavioral defects. My specific project is to determine the function G□O-coupled GPCRs in the neuroendocrine cells, uv1s, of the egg-laying circuit, which are known to inhibit egg-laying events. Previous work has shown that mutants for the G protein, G□O, have a strong hyperactive egg-laying defect. Using single knockouts of G□O-coupled GPCRs, we will generate combinations of these knockouts to look for egg-laying defects matching that of the G□O mutant. With the completion of the "neurotransmitter GPCR Atlas", we hope to achieve a big-picture understanding of how neurotransmitter signaling controls the activity of neural circuits.

Diviya Rajesh • *Hospital For Special Surgery*

Mentor: Chitra Dahia
Race/Ethnicity Studies and Biological Sciences

ROLE OF SHH IN DETERMINING RATE OF SACRUM FORMATION IN MOUSE

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Degeneration of the intervertebral discs (IVDs or discs) is associated with aging and is a major cause of chronic lower back pain worldwide. Understanding the role of intracellular pathways that regulate post-natal disc growth and maintenance is of clinical interest for the development of therapy for disc regeneration. Structurally, the intervertebral disc is comprised of centrally located nucleus pulposus (NP) cells surrounded by annulus fibrosus (AF) cells, which are together sandwiched between cartilaginous endplate. Previously, we showed that the Hedgehog (Hh) signaling pathway, activated endogenously in the disc by Sonic hedgehog (Shh) secreted by the NP cells, plays a critical role in the development and maintenance of lumbar IVDs. Recently, we have demonstrated that SHH expression decreases rapidly during the postnatal growth period in mouse models and that this change in expression is associated with collapse of sacral discs by skeletal maturity.
In this study, we test the hypothesis that loss of Shh can accelerate the collapse of the sacral disc in neonatal mice by conditional targeting of Shh flx/flx allele using NP-specific Ck19CreERT2 line. Tamoxifen was administered at postnatal days 7, 9, and 12 and sacral spine sections were dissected two and four weeks later. Tamoxifen-treated littermates carrying only Shh flx/flx alleles were used as controls. Cryosections were prepared in coronal plane and stained with hematoxylin and eosin. Histomorphometric analysis was performed to compare changes in three parameters of disc growth: NP height, NP area and NP cell count.
Our results showed decrease in NP height, NP area, and NP cell count for all three sacral disc levels at both ages. Furthermore, the magnitude of this decrease was amplified with aging. These results suggest that loss of SHH can delay or slow the disc growth. However, further studies are required at a later time point to determine whether loss of Shh can accelerate sacral disc collapse before skeletal maturity in comparison to littermate controls.

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***Alice Liu** • University of Pennsylvania*

Mentor: Anthony Fouad
Biochemistry

PHASE RESPONSE CURVES FOR OPTOGENETIC MANIPULATION DURING C. ELEGANS FORWARD LOCOMOTION SUPPORT A THRESHOLD MODEL FOR RHYTHM GENERATION

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Despite the roundworm C. elegans' compact and well-mapped nervous system, the basic mechanisms underlying locomotory rhythm generation and coordination remain largely unknown. To gain insight into motor coordination during forward movement, we delivered brief optogenetic perturbations to muscles and neurons of freely moving worms in viscous liquids while quantifying their behavioral responses in the form of curvature over body coordinate and time. We then calculated phase response curves indicating the magnitude of phase delay or advance as a function of the phase within the locomotory cycle at which a manipulation occurred. We found that briefly relaxing the head body wall muscles shifts the phase of the locomotory wave in a highly phase-dependent manner, ranging from cycle delays of π/2 to small phase advances. The phase response curve had a highly asymmetric sawtooth-like shape, with a falling phase approximately five times steeper than the rising phase. We show computationally that the asymmetry and periodicity of the phase response curve can be explained by a model in which the active moment generated by body wall muscles switches between fixed values in the dorsal and ventral directions upon the curvature reaching thresholds in either direction. This model predicts an asymmetry between the slopes of the rising and falling absolute curvature, which we also verify experimentally. Transiently inhibiting motor neurons exclusively delayed the locomotor cycle, as did transient activation of neurons that inhibit locomotion. These results suggest that rhythm generation in C. elegans is highly dependent on proprioceptive feedback and occurs via a threshold-based mechanism.

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Shannon Teaw • *Yale University*

Mentor: Angelique Bordey
Molecular Cellular Developmental Biology

Examining the role of exosomes on neuronal morphology in the context of TSC disease

Tuberous sclerosis complex (TSC) is an autosomal dominant genetic disorder that causes cortical malformations. Phenotypes of TSC patients include seizures, autism spectrum disorders, developmental delay, and epilepsy. TSC is caused by inactivating mutations in the tsc1 or tsc2 genes, which subsequently cause the hyperactivity of the mechanistic target of rapamycin (mTOR), a major converging point in cell signaling. TSC is characterized by cortical tubers, which are composed of a mosaic of wildtype and mutant cells. While tubers can be removed in TSC patients, it is possible that neighboring wildtype cells are affected by surrounding mutant neurons. Whether and how mutant neurons impact the properties of wild type neighboring neurons is unknown. As such, exosomes, or vesicles that transfer molecules for cell-cell communication, are a possible signaling modality contributing to these alterations. We will examine whether exosomes from mutant neurons affect neuronal morphology of surrounding cells. Defects on neuronal properties will be investigated following the addition of exosomes from tsc mutant cells to wildtype neurons. This project aims to investigate whether exosomes from mutant tsc neurons alter the morphogenesis and synaptic integration of neighboring wildtype neurons. By understanding the effects of exosomes secreted by mutant cells on surrounding wildtype neurons, the mechanism behind TSC malformations and disease could be better understood, allowing for more targeted therapeutic intervention.

Maiko Sho • *Bryn Mawr College*

Mentor: Gregory Davis
Biochemistry and Molecular Biology

The pea aphid Acyrthosiphon pisum is cyclically parthenogenetic, with asexual generations of viviparous females being cued by short nights during the spring/summer and sexual generations of oviparous females cued by long nights during the fall. This effect of photoperiod is mediated by the mother, who transmits an asexual-promoting signal to her developing progeny under short night conditions, with the loss of this signal under long nights specifying sexual fate. Previous data showing the successful conversion of sexual females to asexuals under long night conditions upon topical administration of juvenile hormone (JH) has shown JH to be sufficient in inducing asexual fate. It has thus long been assumed that the asexual-promoting maternal signal transmitted from mother to embryonic progeny is JH. If so, JH should not only be sufficient but also required to specify asexual fate. I tested this putative requirement by creating JH-free mothers and examining the fate of their progeny. If maternal JH is required for asexual fate specification, JH-free mothers should not produce any asexual progeny. Interestingly, examining 25 JH-free mothers, created by destroying the corpora allatum, the source of JH, with the compound precocene III revealed no sexual progeny among the 197 embryonic progeny examined. Since JH-free mothers still produce high percentages of asexual progeny, we conclude that a requirement for maternal JH is unlikely. This finding encourages us to reconsider past assumptions about the currently accepted model of reproductive fate specification in A. pisum and further investigate the precise timing of fate specification, as well as the exact role of JH in this process.

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