The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Exploring the Unfolded Protein Response in Calreticulin Mutations in Myeloproliferative Neoplasms

Nicole **Arellano**, 2nd-Year, Creative Writing
Mentor(s): Professor Shannon Elf, Ben May Department for Cancer Research

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Myeloproliferative neoplasms (MPNs) comprise a group of diseases of the bone marrow. They arise in the hematopoietic stem cell (HSC) compartment, where excess mature myeloid blood cells are produced. Most MPN patients harbor activation mutations in the non-receptor tyrosine kinase, JAK2 (JAK2V617F), while a small percentage of patients have activating mutations in the thrombopoietin receptor, MPL. Whole exome sequencing has revealed that a majority of non-mutated JAK2 and MPL MPN patients harbor somatic mutations in the calreticulin (CALR) gene, a calcium-binding chaperone protein that resides in the endoplasmic reticulum (ER). CALR consists of N, P, and C. The N and P domains control chaperone activity, and the P and C domains are locations for calcium binding. The two most common mutations are deletion-52 (DEL) and insertion-5 (INS). Previous data from our lab demonstrated upregulation of the unfolded protein response (UPR) in mutant CALR cells, which is activated by an abundance of unfolded/misfolded proteins. The UPR consists of three stress sensors: pancreatic ER kinase (PKR)-like ER kinase (PERK), inositol-requiring enzyme 1 (IRE1), and activating transcription factor 6 (ATF6). When unfolded proteins are present in the ER, binding immunoglobulin protein (BiP) binds to the unfolded proteins, thereby unbinding themselves from the UPR stress sensors which activates them. Downstream of both ATF6 and IRE1 is the protein x-box binding protein 1 (XBP1), whose gene is activated by ATF6 and mRNA transcript is spliced by activated IRE1. Spliced XBP1 goes on to activate transcription of other ER chaperones. RT-PCR and PST1- digestion assays have revealed increased splicing in DEL CALR mutants. Furthermore, cells with mutant CALR that have been overexpressed with P and C domains in an effort to recover calcium binding properties of CALR have shown to have decreased XBP1 splicing in DEL and thus reflect less activation of the UPR. Overexpression of N and P domains, however, does not have the same effect on DEL. While these findings provide biological insight into the varying mechanisms of how DEL and INS may activate the XBP1 arm of the UPR, a number of additional mechanistic questions remain to be answered to further elucidate the mechanisms behind how each CALR mutation activated the remaining UPR pathways.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Characterization of Fecal Microbiota of WT Mice Compared with Alzheimer's Tg Mice in Relevance to Alzheimer's Pathogenesis

Shayna **Cohen**, 2nd-Year, Neuroscience, Health and Society
Mentor(s): Professor Sangram Sisodia, Neurobiology; Dr. Hemraj Dodiya, Neurobiology

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An altered microbiome in the gut has been associated with many neurological disorders such as autism, depression, Parkinson's disease, and Alzheimer's Disease (AD). In our prior studies, we have shown that antibiotic cocktail (ABX)-perturbed altered gut microbiome results in reduced brain amyloidosis of two independent AD transgenic (Tg) lines. Additionally, these changes were restored after fecal microbiota transplantation (FMT) of age-matched APPPS1-21 mice into ABX- treated APPPS1-21 male mice. Even though this establishes a causal relationship between Aβ deposition and gut microbiome, studies investigating the differences in the gut microbiome of APPPS1-21 Tg and Wild-Type (Wt) mice and their effects on cerebral Aβ pathology are needed. To fill this gap, in our first set of studies, we compared the microbiota profile between male WT and APPPS1-21 Tg mice at the age of post-natal day 22 (P22) and 7 weeks. Fecal 16S ribosomal RNA (rRNA) amplicon sequencing at pre-weaning phase (P22) showed significantly higher abundance of *B. uniformis* at species taxonomy in Tg pups compared with WT pups. Additionally, at 7 weeks of age, *prevotella* and *lactobacillus* genera showed higher abundance in Tg male mice compared with WT. At 7 weeks of age, we observed trends of higher abundance (FDR-P=0.058) of *Akkermansia Muciniphila* at species taxonomy in Tg compared with WT mice. To confirm the role of WT vs Tg mice microbiota, we performed FMT studies using WT and Tg male fecal pellets into ABX–treated APPPS1-21 male mice. ABX treatment was performed using our established protocol from P14-P21. The control group was gavaged with 0.2ml of autoclaved water daily while the experimental groups were gavaged with 0.2 ml of either Tg or WT fecal slurry (5mg of fecal pellets dissolved in 1 ml of autoclaved water) daily from P24 till the day of sacrifice at 9 weeks of age. During necropsy, brain, cecum, large intestine, liver, plasma and fecal pellets were harvested and stored for further analysis. Microbiome profile from these studies (both cecal and fecal) will be evaluated. Brains will be sectioned and incubated with Aβ-specific monoclonal antibody in order to evaluate Aβ burden. The plasma obtained (~ 0.4 mL) will be used to quantify cytokines and chemokines levels. The data generated from these series of studies will be presented at the symposium.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Cell Surface IgSF Proteins are Required for Normal Larval Locomotion

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Mentor(s): Professor Robert Carrillo, Molecular Genetics and Cell Biology

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Animal locomotion is required for escaping predators and finding food and suitable habitats. Motor circuits, including motor neurons and muscles, enable these behaviors. Cell surface proteins belonging to the immunoglobulin superfamily (IgSF) are required for assembling the motor circuits required for locomotion. The Dprs and DIPs are two subfamilies of the Drosophila IgSF and their interactions instruct motor neuron-muscle connectivity. However, whether subtle changes in connectivity translate to behavioral defects is unknown. We utilized loss- and gain-of- function genetics to test Dpr/DIP function in larval locomotion in a Raspberry Pi Virtual Reality system (PiVR). In this apparatus, we recorded average speed, distance travelled, displacement from start position, and head:tail (H:T) activity ratio. H:T ratio approximated the ratio of pause-turning to running. Custom R scripts were created to analyze each parameter and to present the data in graphical format. A subset of Dpr and DIP mutants were selected based on known expression patterns and functions, and preliminary results suggest that loss of DIP-α, DIP-κ, and DIP-□ increase larval locomotion compared to controls. We speculate that this phenotype may be due to non-specific connections at the neuromuscular junction, or instead, impaired inhibition at the level of the central nervous system. We will use the DIPs uncovered in this study to determine if loss-of-function mutants reveal neuromuscular circuit alterations. Also, electrophysiological studies of the neuromuscular junction will reveal if neurotransmission is affected. Overall, our studies will provide novel insights into how cell surface proteins modulate circuit assembly and behavior.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Evolution of Behavior in Insect Larvae

Yiqin **Gao**, 2nd-Year, Biology, Computational and Applied Math
Mentor(s): Professor Elizabeth S. Heckscher, Molecular Genetics and Cell Biology

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Evolution has given rise to diverse animal behaviors. In all animals, behavior is driven by the sensorimotor system, consisting primarily of muscles and motoneurons. A major question in evolution is how behavior (and sensorimotor systems) differs across species. Among insects, neurons that populate the sensorimotor system are generated by an invariant pool of neuronal stem cells. Therefore, changes in stem cell number are not a contributor to evolution of behavior, and evolutionary modifications of later development must be associated with differences in anatomy and function of sensorimotor system. A comparative analysis among closely-related insect species is needed to uncover diverging and conserved development, which will provide insight into generation of novel behavior. We are comparing larvae of dipterian insects, or two-winged flies in part because this Order contains the genetic model fruit fly, *Drosophila melanogaster*. Drosophila has well-characterized, neurons, muscles, and behaviors. We compare Drosophila with its dipteran relative, *Megaselia scalaris*, the Scuttle or Coffin fly. At the level of behavior, our initial observations suggest that when flipped onto their dorsal sides, Megaselia larvae are able to make a dorsal crawl, whereas Drosophila usually self-right within 30 seconds under similar conditions. This difference in behavior implies the existence of differences at the anatomical and molecular levels. Anatomically, in Drosophila larvae, there are seven motoneurons, which send their axons to nine dorsal muscles in each segments of its body wall. We performed immunofluorescent staining on both Megaselia and Drosophila body wall musculature and Central Nervous System. Interestingly, Megaselia larvae have the same type and number of motoneurons, but their dorsal muscle structure appears very different. Hence, our data suggests that the innervation from motoneurons to dorsal muscles is adapted to support the different behaviors among dipteran larvae. This research uses comparison between two close species to provide insight into how sensorimotor systems are adjusted over evolution. Further investigation at the molecular level will be required and essential to gain insights about the differences in circuit development for both species.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Inhibition of ADAM10 Increases Density of Endothelial Cells in Murine Retina Model Treated with *Staphylococcus aureus* Toxin α-Hemolysin

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Mentor(s): Dr. Sonia Hernandez, Surgery, Division of Pediatric Surgery

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Protein A Disintegrin And Metalloproteinase domain-containing protein 10 (ADAM10) is an essential cleavage-site protein in the Notch signaling pathway, a well-established pathway in angiogenesis. We have recently discovered that the α-Hemolysin (Hla) toxin of *Staphylococcus aureu*s is an activator of the Notch signaling pathway in endothelial cells. Furthermore, preliminary data collected by our lab indicates that Hla induces greater endothelial cell density and proliferation as well as disrupted pericyte coverage of arteries. We therefore hypothesized that ADAM10 is essential to the increased endothelial cell proliferation stimulated by Hla. Using the well-established murine retinal model, the treatment group of mice was injected subcutaneously at three days old with ADAM10 inhibitor GI254023X as well as either Hla or Hla-H35l (a genetically inactivated version of Hla). The retinas were harvested at day-of-life 5, then they were stained for endothelial cell imaging and quantification. Endothelial cell density was measured via quantification of Isolectin B4, an endothelial cell marker for non-primates. Our results demonstrate an increase in endothelial cell density when ADAM10 is inhibited. This increase is observed in both the Hla and Hla-H35l groups. Based on our images, arterial development appears to be stunted when ADAM10 is inhibited. These findings indicate that Hla's effects on endothelial cell density are mediated by multiple factors and that ADAM10 plays multiple roles in vascular development.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Interpregnancy Interval and Adverse Pregnancy Outcome-Analysis on U.S. Birth Data

Khadija **Haleem**, 2nd-Year, Neuroscience
Mentor(s): Dr. Yuzuru Anzai, NY Midtown OB/GYN; Dr. Maria Teresa Benedetto, NY Midtown OB/GYN; Dr. Teresa Cheon, NY Midtown OB/GYN; Dr. W. Spencer McClelland, NY Midtown OB/GYN

Inter-pregnancy interval (IPI) is defined as the spacing between live birth and the beginning of the next pregnancy. Past research has found that IPIs shorter than 18 months (M) are associated with adverse pregnancy outcomes. However, it is unclear whether IPI is an independent risk factor or a marker of other confounding risk factors, such as race, socioeconomic status, and age. This makes it difficult to accurately counsel patients as to their individual risk based on IPI. CDC WONDER is a database which contains all the U.S. birth data and open to public access. Using this database for 2016-2017 (the first years to contain more expanded information including IPI), we analyzed IPI in relation to adverse pregnancy outcomes—preterm birth (PTB), gestational hypertension (gHTN), low birth weight (LBW), and gestational diabetes (GDM)–accounting for race, pre-pregnancy BMI, education, marital status, and maternal age. We focused our analysis to singleton pregnancies. Short IPI (less than 18 M) increased the rates of PTB and LBW, with stronger association with PTB rates. The highest PTB risk was seen among patients with IPI less than 12 M, modest increase was seen between 12-17 M, and rates plateaued at 18-23 M. This pattern was consistent in subgroup analysis by risk factor, indicating that IPI is an independent risk factor for PTB. In this analysis of a nationwide birth database, short IPI, particularly less than 12 M, is an independent risk factor for PTB and LBW, whereas no association was seen between IPI and gHTN or GDM. It is important to educate the patients about this modifiable risk factor of pregnancy complications.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

α7 Nicotinic Acetylcholine Receptor Modulation of Descending Pain Control Pathways

Emma **Hovanec**, 4th-Year, Neuroscience
Mentor(s): Professor Daniel McGehee, Anesthesia and Critical Care; Shivang Sullere, Neurobiology

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The ventrolateral Periaqueductal Gray (vlPAG) is an important midbrain structure in the descending pathway that modulates chronic pain perception. vlPAG plays a critical role in pain information transmission via projections to the Rostral Ventromedial Medulla (RVM), which projects to spinal cord. Existing research demonstrates that neurons in vlPAG express α7 nicotinic acetylcholine receptors (α7 nAChRs), and activation of these receptors produces anti-nociceptive effects with efficacy similar to opioid drugs. Recent studies have shown that chemogenetic excitation of glutamatergic neurons or inhibition of GABAergic neurons in vlPAG produced anti-nociception, however, the role of α7 nAChRs in producing this effect remains uncertain. The neurotransmitter phenotype of vlPAG neurons that express α7 nAChRs has not been characterized, and it is unclear if α7 nAChRs are expressed predominantly on local interneurons or on projection neurons from vlPAG to RVM. To address these issues, we have conducted mRNA and protein labeling experiments and identified that α7 nAChRs are predominantly expressed on GABAergic neurons. We also found that α7 nAChR expressing GABAergic neurons co-express u-opioid receptors (MORs). In most physiology studies, α7 nAChRs are excitatory, while MORs are inhibitory. In light of the high degree of overlapping expression, we hypothesize that in this system, α7 nAChRs are inhibiting neuronal activity. We are testing this hypothesis by assaying the immediate early gene, c-fos, in identified vlPAG neurons that express α7 nAChRs. We expect that α7 agonist treatment will decrease pain- induced c-fos expression in α7 neurons, and increase c-fos expression in RVM-projecting vlPAG neurons. We expect these data to support the hypothesis that α7 nAChRs are expressed on local GABAergic interneurons in vlPAG, where their activation disinhibits the glutamatergic projections to RVM to cause pain relief. These findings signify the ongoing relevance of α7 nAChRs as potential non-opioid therapeutic targets for pain relief.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Water Dynamics and Interactions Inside B-Amyloid Fibrils

Alexander (Alex) **Hummels**, 4th-Year, Computational & Applied Math/Statistics
Mentor(s): Dr. Esmael Haddadian, Biological Sciences

Aggregation of Aβ-peptides is important in the etiology of Alzheimer's Disease (AD). Studies have documented the presence of mobile water molecules in Aβ-fibrils, even in relatively anhydrous areas. One main proposed mechanism of Aβ toxicity is the disruption of water and ion fluxes at neuronal cell membranes. We compared multiple long all-atom explicit solvent molecular dynamics simulations starting from two structural models of Aβ (1-40 residues) fibrils having 3-fold rotational symmetry (PDB-ID's: 2LMP, 2M4J). The 2M4J structure is based on an AD brain-seeded fibril whereas 2LMP is synthetic. Consistent with hollow amyloid fiber hypothesis, the brain-seeded fibril exhibited large cavities within the fibril that would plausibly facilitate water along the central longitudinal core of the fibril. This structure rapidly develops gaps at the sides of the fibril, allowing bidirectional diffusion of water and ions from the bulk phase in and out the central longitudinal core of the fibril. We observed similar but less marked changes in the synthetic 2LMP fibril. We also find that the protein residues around the cavity regions largely coincide with residues exhibiting rapid hydrogen-deuterium exchange in experimental NMR studies, which is again consistent with the existence of channels within the amyloid fibers. We suggest a link between the presence of D23-K28 salt bridges and gap openings, as this salt bridge is mostly absent in 2LMP. The K28 residues partially block the 2LMP gaps, as they are not linked to the D23 residues via salt bridges, preventing the water flow to the core of the fibril. The diffusion of water molecules beginning in the core is biphasic and can be separated into two regimes: confined motion and directed diffusion in the presence of obstacles. Waters reside in the 2M4J core for an average of 767±135 picoseconds, and in the 2LMP core for 1581±374 picoseconds. Of these core waters, those closer to the protein are less mobile than those further away as measured by Debye-Waller factor. These observations suggest that Aβ-fibrils may act as aqueous pores that might disrupt water and ion fluxes if inserted into a cell membrane.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Ties that Bind: Mixed-Status Immigrant Families, Stress Response Dysregulation, and Cardiometabolic Health

Woorin **Jang**, 4th-Year, Computer Science
Mentor(s): Dr. Aresha Martinez-Cardoso, Public Health Sciences

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The U.S. has been experiencing a mounting immigration enforcement regime which has heightened the risks and costs of being undocumented. Research suggests that living in a mixed-status household (MSH), where some members of the family are undocumented, can have taxing effects on the health of members who may not necessarily be undocumented themselves. While current works have been mainly focused on investigating outcomes in mental health and social service utilization, such sociopolitical stressors can also manifest in physical health outcomes caused by a cascade of physiological processes that disrupt the stress-response systems in the body. This research explores the association between living in a MSH, disruption in the stress regulation system as indicated by stress-response biomarkers, and cardiometabolic risk among samples of adults and children. The three specific aims are as follows: 1. determine the relationship between residence in a MSH and stress-response biomarkers in children and adults, 2. confirm the relationship between stress-response biomarkers and cardiometabolic risk, and 3. model the pathway between these biomarkers and cardiometabolic risk among children and adults in MSHs. The study will use the second wave of the Los Angeles Family and Neighborhood Study (LAFANS 2) for statistical analysis, which provides adult and child data on household composition, immigration/documentation statuses, general demographics, and health variables including stress-response biomarkers (c-reactive protein, cortisol) and cardiometabolic risk factors (HbA1c, cholesterol, BMI, WHR) across 65 neighborhoods in L.A. Analyses will be performed in two sub studies: the health of adults with respect to the documentation status of their spouse, and the health of children with respect to the documentation status of their primary caregiver. We hypothesize that children and adults in MSHs will have elevated stress-response biomarkers and cardiometabolic risk in comparison to those in documented households. This work will help elucidate the unintended health consequences of contemporary immigration policies for adults and children who are embedded in social networks with undocumented immigrants.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Modeling Selective Trapping of Weak Bases inside Intra-cellular Vesicles

Phillip **Jordache**, 4th-Year, Statistics, Biological Sciences
Mentor(s): Dr. Esmael Haddadian, Biological Sciences

Recent work from our group has characterized selective trapping of nicotinic acetylcholine receptor (nAChR) ligands within neurons in the brain (Govind et al. eLife 2017). The ligands are weak bases that bind with high-affinity to α4β2-type nAChRs (α4β2Rs), such as the anti-smoking drug varenicline (Chantix) and epibatidine. Selective trapping occurs within α4β2s-containing acidic vesicles of cells and neurons. Slow release of trapped varenicline reduces effects of long-term nicotine exposure. Selective trapping is further regulated by nicotine exposure, which increases the number of α4β2s-containing acidic vesicles. Nicotine, also a weak base, is not trapped due to its lower pKa and lower affinity for α4β2Rs. Here, we present a kinetic model that accounts for the biphasic behavior of these weak bases leaving the cell after accumulating in the acidic vesicles and binding to the nAChRs on the surface of the vesicles, within intracellular membranes, and on the exterior of the cell. Intracellular accumulation and release of molecules by diffusion into and out of cytosol and vesicles is calculated using Fick's Law of diffusion (neutral molecule) and the Nernst-Planck equation for ions (Trapp and Horobin 2005). Ligand binding to α4β2Rs is modeled using empirical receptor-ligand kinetics. Solving our coupled differential equations numerically has accurately approximated experimental data for epibatidine accumulation and release in vesicles. The model is mainly limited by inclusion of pKa and binding affinity as the only parameters directly causing the trapping. Our model also suggests that the vesicle membrane receptor concentration is an important factor, a notion that we hope to verify experimentally. Using this model, we have been able to model kinetic trapping of the weak-base α4β2 ligands Nifene and 2-F-A8538, and to explain differences in their kinetics during positron emission tomography.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Comparative Biogeography of the Filefishes (family *Monacanthidae*)

Kelly **Kang**, 1st-Year, Geophysical Sciences
Mentor(s): Chloe Nash, Committee on Evolutionary Biology; Professor Mark Westneat, Organismal Biology and Anatomy

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The filefishes (Monacanthidae) are a geographically widespread family of coral reef fishes that consist of 111 species. Typically inhabiting the tropical to subtropical waters of the Atlantic, Pacific, and Indian Oceans, species of filefish exhibit interesting patterns in their geographic distributions. For example, the distributions of different filefish species range from being globally distributed to being restricted to a single island. Understanding the geographic distribution of the Monacanthidae will provide key insights into how communities are structured, and how this relates to the evolutionary history within this family. In this study, our main questions were 1) how are communities of Monacanthidae geographically clustered, 2) do the clusters differ in species composition and geographic structuring, and 3) what are the evolutionary relationships among species within and among each community cluster? We hypothesized that species that inhabit similar clusters will be more closely related to each other, which may indicate their ability to exist in similar habitats. Upon downloading and cleaning georeferenced coordinate data for each filefish species from online databases (GBIF, VertNet, and OBIS), we generated novel community clusters based on the amount of species turnover. These clusters show the geographical areas where the distributions intersect in unique ways, forming a distinct assemblage. Using the phylogeny of the Monacanthidae family, we analyzed the relationship among the geographic distribution, cluster composition, and phylogenetic diversity. Our results show that the clusters appear to be geographically consistent. Additionally, there appears to be different evolutionary dynamics within and among clusters. These results highlight the important role that geographical distributions play in understanding the evolutionary history of species. Future directions include 1) a deeper analysis of how the specific geological features and other abiotic factors of the clusters may have influenced evolution, and 2) conducting a larger study encompassing the entire Tetraodontiformes order.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Curvature as an Indicator of Successful Aortic Dissection Endovascular Repair

Kameel **Khabaz**, 1st-Year, Biological Sciences
Mentor(s): Dr. Luka Pocivavsek, Vascular Surgery & Endovascular Therapy, Medicine

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Aortic dissection is a life-threatening condition marked by the formation of a tear in the aortic wall, allowing blood to enter between the layers of the wall and create a false lumen of blood flow. The condition can be divided into two types, type A and type B, depending on where the tear forms. Type A dissections are often fatal and treated by open surgery, while type B dissections can be treated by medical management or endovascular repair (TEVAR), a minimally invasive procedure marked by the insertion of a stent graft. A major challenge with TEVAR is monitoring its success in de-pressurizing the false lumen. This is critical for determining and minimizing the risk of complications, which are often fatal, before they arise. We hypothesize that changes in the curvature distribution of the surface of an aorta can be used as an indicator of false lumen status after a TEVAR operation. We studied two patients with type B dissections, one who had a successful TEVAR operation and another who had an unsuccessful operation. We created pre- and post-operation models of each patient's aorta from computed tomography (CT) scans and compared the curvature distributions of the different models. Specifically, we compared Gaussian curvature, an intrinsic measure of curvature directly connected to elastic strain, and the shape index, a measure of shape that is independent of scale. We found that the successful patient's aorta's shape index distribution narrowed after the procedure, converging to a value characteristic of a cylinder. However, the unsuccessful patient's aorta's shape index distribution widened after the procedure. We also found that the successful patient's aorta had a narrowing of the Gaussian curvature distribution in the descending thoracic aorta, while the unsuccessful patient had no significant observable changes in Gaussian curvature. These observations indicate that the shape of the aorta changes to decrease the stress on its wall after a successful TEVAR operation. Our next steps include investigating for the aforementioned changes in different sets of patients as well as elucidating the mechanism of false lumen depressurization through finite element analysis.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Convergent Epicardial-Endocardial Ablation for Treatment of Long-Standing Persistent Atrial Fibrillation

Zoheb **Khan**, 2nd-Year, Biological Sciences and Economics
Mentor(s): Dr. Mohanad Hamandi, Cardiovascular Research, Baylor Scott & White The Heart Hospital; Dr. Hafiza Khan, Electrophysiology, Baylor Scott & White The Heart Hospital; Dr. Tung Cai, Cardiothoracic Surgery, Baylor Scott & White The Heart Hospital Denton; Dr. Michael DiMaio, Cardiovascular Research Baylor Scott & White The Heart Hospital; Dr. Matthew Evans, Electrophysiology, Baylor Scott & White The Heart Hospital Denton

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The Convergent Procedure (CVP) is a hybrid ablation technique via subxiphoid incision that has recently emerged as a treatment option for non-paroxysmal atrial fibrillation (npAF). By combining endocardial and epicardial ablation into a simultaneous or staged procedure, the pulmonary vein and posterior left atrium can be isolated with transmural lesion sets while minimizing the risk of proarrhythmic gaps that are a known limitation with endocardial linear lesion sets. We reviewed the 12-month outcomes in patients who underwent CVP compared to those who underwent endocardial catheter ablation (CA) and surgical ablation (SA). A literature search was conducted using PubMed database for publications related to CVP. Selected studies included a detailed 12-month follow-up of patients, patient characteristics, periprocedural complications, use of antiarrhythmic drugs (AADs), and monitoring method. Five studies with 340 patients who underwent CVP between January 2009 and March 2017 were selected for this review. 8.5% of patients had paroxysmal AF (pAF), 42.2% had persistent AF (peAF), and 49.1% had long-standing persistent AF (lspAF). At 12 months, 81.9% of patients were in sinus rhythm, while 54.1% of patients were in sinus rhythm while not taking AADs. The overall complication rate was 10%. CVP had better 1-year efficacy in eliminating AF when compared to CA. However, SA, specifically the Cox Maze IV, had lower rates of AF recurrence in the npAF patient population. Despite its promising 1-year efficacy rates, the periprocedural complication rate for CVP was significantly higher than both CA and SA. The prevalence of atrial fibrillation (AF) in the United States was estimated to be 5.9 million in 2010, with that number expecting to rise to 15 million by 2050. AF care and treatment costs approximately $15,000 annually per patient, creating an economic burden on the United States healthcare system. If the complication rate of CVP can be mitigated, the hybrid ablation procedure can ultimately provide an opportunity to improve the quality of life for patients' with npAF with a high-efficacy, less invasive operation that prevents long-term AF recurrence.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

α7 Nicotinic Acetylcholine Receptors Relieve Pain Via Modulation of the Descending Pain Pathway

Alissa **Kunczt**, 4th-Year, Biological Sciences
Mentor(s): Shivang Sullere, Committee on Neurobiology; Professor Daniel McGehee, Anesthesia & Critical Care, Committee on Neurobiology

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Over 20% of adults in the U.S. suffer from chronic pain conditions, which highlights the need for more effective and sustainable treatment strategies. Pain signaling depends upon specific neural pathways, including ascending sensory circuitry stimulated by noxious stimuli and descending pain modulatory pathways that either enhance or suppress those signals. The descending pathway includes the ventrolateral periaqueductal grey (vlPAG) and the rostroventromedial medulla (RVM), which projects to the spinal cord to modulate pain transmission. Manipulation of vlPAG activity can induce analgesia, which is one mechanism that opioids use to relieve pain. In addition to opioid receptors, vlPAG neurons also express α7 nicotinic acetylcholine receptors (nAChR), which are excitatory cation channels. Our lab and others have shown that drugs that activate α7 nAChRs relieve tonic inflammatory pain. In this study, our first objective was to test how α7 receptor activity influences the sensory and affective components of acute and chronic pain states in mouse models. We found that α7 nAChR agonists was efficacious in relieving pain in these studies. Our second objective was to monitor neuronal activity in the vlPAG in vivo using an intracellular calcium sensor, GCaMP6, and fiber photometry. With these methods, we found that during induction of a pain state vlPAG neuronal activity increased, and after systemic α7 nAChR agonist administration there was a decrease in vlPAG neuronal activity. Our final objective was to study the effects of altering activity of α7 nAChR-expressing cells on a mouse's pain state using optogenetics. We determined that inhibition of α7 nAChR-expressing cells was analgesic. Together, these data will provide novel insights into the interaction of α7 receptors and vlPAG neuronal activity during pain, which will help develop better treatments for pain conditions.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Evaluating the Racial and Ethnic Distribution of Study Participants in Published Ob/Gyn Randomized Controlled Trials

Seoho **Lee**, 3rd-Year, Biological Sciences
Jasmine **Gulati**, 4th-Year, Biological Sciences, History
Mentor(s): Dr. Maria Teresa Benedetto, Lenox Hill Hospital; Dr. Teresa Cheon, Lenox Hill Hospital; Dr. Spencer McClelland, Lenox Hill Hospital; Dr. Lavinia Anzai, NYU Langone Medical Center; Dr. Yuzuru Anzai, Lenox Hill Hospital

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Randomized controlled trials (RCTs) are the gold standard in evaluating cause-effect relationships as they eliminate bias and minimize confounding factors. The generalizability of the findings in an RCT will depend on the extent to which the study's population is reflective of the general population. The objective of this research was to examine a cohort of RCTs and determine the degree to which the distributions of ethnic populations are correctly represented. A retrospective review was conducted on RCTs published in the Obstetrics and Gynecology Journal (The Green Journal) from 1990-2018 and the American Journal of Obstetrics & Gynecology (AJOG) from 1993-2018. Studies that were performed in the United States and provided information on ethnic backgrounds of the study participants were included. For each journal, studies that met inclusion criteria were categorized as "obstetric" or "gynecologic" by topic and were analyzed separately. Subjects of the included RCTs were separated into four major ethnic groups: Non-Hispanic White, Non-Hispanic Black, Hispanic, and Other. The distribution of individuals in these categories was then compared to the general US population. 140 studies met inclusion criteria. 41% papers were gynecologic and 59% were obstetric. Amongst the obstetrics papers, an average of 34% of the analyzed population identified as White, 30% Black, 29% Hispanic and 7% Other, compared to gynecologic papers where 63% identified as White, 18% Black, 14% Hispanic and 5% Other. While on c-square analysis, the distribution of ethnicities amongst gynecologic papers was found to be similar to published U.S. demographic data ($p=0.50$), this distribution was found to significantly deviate amongst obstetric papers ($p<0.001$, Table 1). Furthermore, the obstetrics papers demonstrate an overrepresentation of the Non-Hispanic Black population and an under-representation of the Non-Hispanic White population. When analyzing two of the leading journals in the field, published gynecologic papers revealed a study population similar to that of the general U.S.; however, interestingly, the distribution of subjects included in the obstetrics papers was shown to be less representative. While the reason for this deviation from general U.S. demographics is unclear, based on these results, readers should be cautioned in their interpretation of these RCTs and their generalizability.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Using Fluorescence Microscopy to Characterize the Role of Mechanosensation in Cell Division

Allen **Lu**, 3rd-Year, Biochemistry & Chemistry, English/Creative Writing
Mentor(s): Professor Eduardo Perozo, Biochemistry and Molecular Biology, Institute for Biophysical Dynamics

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MscS is a bacterial mechanosensitive channel linked to the cell's response to turgor pressure during hypoosmotic shock. MscS opens when the membrane stretches from water influx, functioning by a force-from-lipids model independent from direct interactions with any cytoskeletal elements. FtsZ is a cytoplasmic protein involved in the formation of the contractile Z-ring and cell wall synthesis during bacterial cell division. FtsZ subunits polymerize in the presence of GTP, anchoring to the membrane through its C-terminus with membrane chaperone proteins in order to form the Z-ring, while simultaneously recruiting cell division chaperones involved in cell wall synthesis and DNA repair. Prior research has demonstrated that the α/β domain (ABDOM) at the cytoplasmic ''ballon'' of MscS appears to directly interact with FtsZ and that overexpression of MscS ABDOM alone hinders cell division, creating long, filamentous cells. Using fluorescence microscopy, we show that upon overexpression of epitope- tagged MscS in E. coli in the presence of β-lactam antibiotics, different elongation phenotypes were observed when tags were placed on the N or C terminus. C-terminal tagging resulted in long filamentous cells while N-terminal tagging or no tagging resulted in regular length cells. This phenotype was observed regardless of the type of epitope tag used. Furthermore, it has been shown that cells expressing FtsZ with C-terminal obstructions induces cell filamentation. Co-expression with MscS showed that higher normalized expression levels of MscS allowed for increased "rescue" of this defective FtsZ mutant, producing more regular-length cells. This data sheds light on possible roles for MscS in cell wall repair or as an anchor for FtsZ during Z-ring formation. The interaction between mechanosensitive channels and contractile motors together with the dynamics of the bacterial cell wall points to an intriguing new role for mechanotransduction in the processes of cell elongation and division.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Ecomorphological Relationships of the Goatfishes (Family *Mullidae*)

Linnea **Lungstrom,** 4th-Year, Biological Sciences
Mentor(s): Chloe Nash, Committee on Evolutionary Biology; Professor Mark Westneat, Organismal Biology and Anatomy

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The ability of an organism to interact and adapt to their environment is critical for species survival. As such, the integration of ecology and morphology is important when investigating the evolution of a variety of behavioral adaptations. The goatfishes (*Mullidae*) are an ideal family to study these relationships because of their unique feeding behaviors. This family consists of 95 species of coral reef associated fishes that are united by a unique morphological structure called the barbel. Goatfish barbels are a pair of fleshy chin extensions that are capable of taste and prey excavation from loose sediment on the ocean floor. Previous research has shown that there is variation in foraging behaviors and substrate type preferences among species. Our research is focused on 1) quantifying the amount of variation in morphology among species of goatfish, 2) investigating how this variation correlates to the phylogenetic history of the family, and 3) analyzing the relationship among morphology, ecology, and feeding behavior. We hypothesize that the morphology of the goatfishes will correlate with their phylogeny and ecology. Using a robust photo database of approximately 350 images spanning the majority of species in *Mullidae*, we placed ~50 landmarks on each image to analyze the variation of important morphological structures on the head, body and barbel. To examine the key sources of morphological variation among species, we performed a geometric morphometric analysis using a principal component analysis (PCA). Additionally, we compiled a comprehensive trait database that contains information such as preferred substrate type and diet. Integrated with the morphological data, we used phylogenetic comparative methods to investigate the relationships among morphology, phylogeny and ecological characteristics. Preliminary results suggest that there is a relationship among morphology, phylogeny and ecology. Providing evidence that organisms' morphology correlates with their feeding mechanisms and ecology is important considering our current climate crisis that threatens to alter environments and thus affect persistence and diversity of species. Future work will include a robust analysis of goatish feeding behavior through the inclusion of microCT scans and 3D kinematics data of feeding events to further investigate these ecomorphological relationships within the family.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Extracellular Vesicles from Patients with Sickle Cell Disease Disrupt Gap Junctions

Yifan **Mao,** 4th-Year, Biological Sciences & Neuroscience
Mentor(s): Dr. Eric Beyer, Department of Pediatric Hematology/Oncology, Knapp Center for Biomedical Discovery; Dr. Joanna Gemel, Department of Pediatric Hematology/Oncology, Knapp Center for Biomedical Discovery; Dr. Gabrielle Lapping-Carr, Department of Pediatric Hematology/Oncology, Knapp Center for Biomedical Discovery

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Aberrant cell-cell interactions involving the endothelium are central to the pathophysiology of sickle cell disease (SCD), including acute chest syndrome (ACS), a deadly and unpredictable complication. The current study was designed to examine the effects of extracellular vesicles (EVs) on cellular junctions including tight (zonula occludens 1, ZO-1) and gap junctions (connexin43, Cx43) and to test the hypothesis that the junctions would be more severely affected by EVs isolated from patients during an episode of ACS than by ones isolated from the same patient at baseline. We identified subjects with SCD in our biobank who had plasma isolated at baseline and at the beginning of an admission for ACS. EVs were isolated from platelet free plasma using established methodologies. To determine the effects on endothelium, cultures of human microvascular endothelial cells were treated with EVs for 48 hours and studied by immunofluorescence, immunoblotting, and RT-qPCR. Gap junction-mediated intercellular communication was assessed following microinjection of Lucifer yellow and neurobiotin. The distribution and abundance of ZO-1 at the plasma membrane were minimally affected by SCD EVs. While baseline EVs did not affect the distribution of Cx43, EVs isolated during an episode of ACS caused loss of Cx43 from the plasma membrane. The integrated intensity of Cx43 membrane staining was decreased by ~20% following treatment with ACS EVs. Cx43 protein decreased on average by 32%, Cx43 mRNA levels by 21% and neurobiotin transfer by 67-94% in cells treated with ACS EVs, compared to baseline EVs. Circulating EVs in SCD affect multiple components of endothelial junctions. Gap junctions composed of Cx43 are the most sensitive of the cell-cell junctions, since their abundance and function are reduced by ACS EVs even when the endothelial monolayer appears intact. Cx43- mediated intercellular communication may be an early and sensitive event in the endothelial disturbance caused by EVs in SCD patients.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Bioinformatic Analysis of the Connection between Gut Microbial Diversity and Patient Response to Anti-Pdl1 Immunotherapy

Malaika **Mathias**, 2nd-Year, Biological Sciences
Mentor(s): Dr. Thomas Gajewski, Pathology; Jessica Fessler, Pathology

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A computational analysis was carried out to determine the relationship between gut microbial diversity and response to checkpoint blockade treatment in patients with melanoma and other cancers. Prior research suggests correlations between greater bacterial diversity and a positive response to cancer therapies, including anti-PD-1 immunotherapy. This study analyzed metagenomic sequencing data from pre-treatment patient stool from a clinical study carried out at the University of Chicago, as well as from other research laboratories including the MD Anderson Cancer Center in Houston, Texas and the Gustave Roussy Cancer Center in France. The study incorporated data from the various laboratories and employed a bioinformatic and epidemiological approach to assess the relationship between bacterial, viral, and fungal diversity at different taxonomic levels and its correlation with response to treatment. The analysis pipeline Microbial Community Profiling (MiCoP) was used to detect viral and fungal reads in meta-genomic samples with high precision and sensitivity to low-abundance species. Our study found a statistically significant increase in the number of bacterial species from patients with progressive disease to those with a stable disease ($p=0.022$), as well as an increase in the number of fungal species between patients with stable disease and partial response to treatment ($p=0.04$), suggesting that increased microbial diversity may play an advantageous role in promoting patient response to treatment. This study may prove to be consequential when considering treatment for cancer patients as it may allow for manipulation of the gut microbiome in order to increase chances of patient response to certain immunotherapies. There is also potential for immunotherapies to show varied responses with different specific microbes, implying that specific treatments may be harnessed in response to a particular patient's existing microbial composition. Further research may identify and isolate specific bacterial, viral, or fungal strains in order to test their effects on patient response. It may also be valuable to compare the responses of different immunotherapies to microbial diversity and specific microbial strains.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Alternate Stable States in Temperate Intertidal Autotrophic Systems

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Mentor(s): Professor Cathy Pfister, Ecology and Evolution

This study examines marine primary production in a three-year time series of experimental plots in intertidal outer coast of the Pacific Northwest. We selected a site that was dominated by the marine *surfgrass Phyllospadix scouleri* and destructively sampled 4 1x1m plots to test for total biomass, elemental (C, N) and isotopic composition. In the subsequent year, we repeated the same sampling methodology in the same 4 removal plots and 4 control plots (which were unperturbed at t=0). We observed differences in species composition where a diverse assemblage of kelp colonized the surfgrass removal plots. Total biomass per unit area was the same across surfgrass dominated and kelp dominated assemblages but C:N ratios were significantly lower across all kelp assemblages. Kelp assemblages also exude Dissolved Organic Carbon at a greater rate than the surfgrass dominated system. This suggests that kelp dominated systems maintain a greater proportion of nitrogen per unit biomass than surfgrass. Kelp assemblages also have greater diversity (Shannon-Weiner) and richness, composed of species with varying temporal life history strategies. This is in comparison to surfgrass monocultures that are predominantly clonal and outcompete all other species in this substrate-limited ecosystem. The identity of autotrophic composition may shape higher trophic assemblages through the nutritional content made available through primary production as well as through the ecosystem engineering of the physical condition of the intertidal environment.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Is the Common Environment or Host Species the Major Driver of Microbiome Assembly?

Pranati **Movva**, 4th-Year, Neuroscience
Mentor(s): Dr. Elena Lopez Peredo, Marine Biological Laboratory

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The microbiome is key to the survival of the host species it inhabits, and it is integrated within the environment of its host. While there are many factors affecting the composition of microbial communities, two of the most important factors include the host species and the surrounding environmental location of the microbiome. This study explored the effects of host selection on microbiome composition. The purpose of my project was to determine how the microbial environment of the beach at Little Sippiwissett affects the microbial communities on the algal halobionts. This study took place at low tide in the beach region of Little Sippiwissett Marsh in Falmouth, MA. I collected water, sediment and two types of algae, *Sargassum* and *Codium*. *Sargassum* is a type of brown seaweed, and *Codium* is a dark green alga with cylindrical, multinucleated branches. While *Sargassum* and *Codium* have been used individually in studies, they have never been studied together. With my project, I looked to compare the microbiome associated with these two types of algae with the microbiome in the surrounding environment. The algal microbiome was collected by swabbing the algae in situ, at the beach. Microbes from the water column were collected by filtration and those in sediments were extracted from sand samples. DNA was extracted from all samples using the same extraction technique, followed by PCR amplification of the 16S ribosome gene and 16S rRNA amplicon analysis using Qiime2 to process the sequencing data. My hypothesis was that the common environment is a major factor driving microbial composition of the host species; the environment, and not the host, will more strongly affect the microbial communities. A main finding from this study did in fact show that there are many shared taxa between the environment and the algae studied, and this finding is important to further investigate the effects of the environment and climate change on the microbial composition of host species.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Microenvironmental Nutrient Stress Initiates the Integrated Stress Response through ATF4 in Pancreatic Cancer

Moses **Oh**, 3rd-Year, Biological Sciences
Mentor(s): Professor Alexander Muir, Ben May Department of Cancer Research

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Pancreatic ductal adenocarcinoma (PDAC) is a deadly cancer with an average survival time of 2-3 years after diagnosis. Current treatments are largely ineffective in delaying disease progression. A better understanding of essential PDAC cellular processes involving crucial genes and proteins is paramount for finding more effective treatments needed in this disease. The tumor microenvironment (TME) of PDAC is different than the microenvironment of healthy tissues with substantial desmoplasia and disorganized vasculature, resulting in a nutrient-deprived and hypoxic environment. These environmental pressures could alter the processes PDAC cells require for growth and survival. We have recently quantified the levels of all the metabolites present in the TME of mouse PDAC tumors defining the nutrient milieu of PDAC. From those results we have developed a cell culture system where mouse PDAC cells are grown in these TME nutrient levels. While immunoblotting to identify cellular processes essential to PDAC survival in TME, we found that cells cultured in this TME media had significantly higher levels of activating transcription factor (ATF4) expression compared to those cultured in standard culture. ATF4 is a major part of the integrated stress response (ISR), an adaptive cellular response to various types of stress including nutrient stress. The relevance of this observation to in vivo tumor biology and to human disease is supported by previous research showing upregulation of p-EIF2α in human PDAC tumors, a phosphorylation event critical for ATF4 activation. Given these preliminary results, we plan on investigating the role of ATF4 upregulation in PDAC. We want to first determine whether this upregulation is a necessary adaptation that PDAC cells must employ to survive in the TME. We intend to ask this question by using CRISPRi to knockdown ATF4 levels and observe cell growth. We also want to identify what mediates ATF4 upregulation. To approach this, we would like to use inhibitors for the four main kinases that are known to activate ATF4, then assay for ATF4 expression levels through immunoblotting. We believe that answering these questions will help us determine whether this stress responsive pathway is essential for growth in TME conditions.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Protein Palmitoylation via a Specific Palmitoyl Transferase Facilitates Golgi Dispersal Observed with Nicotine Exposure

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Mentor(s): Professor William N. Green, Neurobiology; Okunola Jeyifous, Neurobiology; Anitha Govind, Neurobiology

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Our lab has observed dispersal occurring in nicotine treated neurons and human embryonic kidney cells (HEK) expressing α4β2-type nicotinic acetylcholine receptors (α4β2Rs). α4β2Rs bind nicotine with high affinity and initiate the additive process with nicotine binding. Typical GA morphology is observed as a set of membrane stacks in the soma of neurons. During nicotine-induced dispersal we find that the stacks disperse into mobile membranes throughout dendrites and axons. Preliminary data from our lab has implicated the palmitoyl transferase, DHHC2, in the downstream events after nicotine binding to α4β2Rs causing GA dispersal. The identification of DHHC2 as being involved in Golgi dispersal is also consistent with additional evidence from our lab that the posttranslational modification, palmitoylation, is part of the signaling that leads to GA dispersal. To further test whether DHHC is involved, we overexpressed DHHC2 in HEK cells and imaged for changes in GA morphology. Fluorescently tagged sialyltransferase 3 (eGFP-ST3) and DHHC2 (myc-DHHC2) were assayed on the Zeiss spinning disk confocal system with or without the expression of tagged α4β2Rs (HA-α4β2Rs). Preliminary results suggest that DHHC2 overexpression does facilitate GA dispersal and that the GA dispersal induced by DHHC expression occurs most prominently in cells with α4β2R expression.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Evaluating Racial Population (Pop)-Specific Risk for Clinically Actionable Pharmacogenomic (PGx) Guidance

Adam **Rizk**, 4th-Year, Biological Sciences
Mentor(s): Dr. Peter H. O'Donnell, Medicine; Dr. Mark J. Ratain, Medicine; Professor David O. Meltzer, Medicine; Professor Minoli Perera, Pharmacology, Northwestern University; Emily Schierer, Center for Personalized Therapeutics; Keith Danahey, Center for Personalized Therapeutics

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Pharmacogenomics seeks to predict a person's response to medications based on their genetics. Despite PGx information increasingly being considered, the evidence supporting guidance is mostly based on studies of Europeans. Race-specific evidence might better inform clinical decision support (CDS) for some medications (e.g., warfarin). Actionable medications have clinically actionable PGx like changes in efficacy, dosage, metabolism, or toxicity due to gene/protein/chromosomal variants or phenotypes. We sought to identify variants with divergent minor allele frequencies (MAF) in racial sub-populations to determine population-specific PGx risk. We hypothesized that PGx single nucleotide polymorphisms can have different allele frequencies in distinct racial populations which might be helpful for determining population-specific risk when PGx CDS is delivered to diverse cohorts. We analyzed germline variants underlying CDS guidance for 47 medications (meds) within our institutional PGx results system. Racially divergent variants (RDV; defined as polymorphic [>1%] in one pop but rare [<1%] or absent in another; or those having 25% absolute difference in MAF [2 x avg FST for pop-based differences]) were ascertained from YRI (Yoruba in Ibadan, Nigeria population) versus CEU (Utah Residents with Northern and Western European Ancestry population) comparisons using 1000 Genomes Project data. For each RDV, we examined whether supporting PGx evidence was studied in racial sub-pops or only in Europeans. The aim was to identify meds that may require race-specific guidance. Of 118 variants linked to 47 actionable meds, 33 RDVs were identified (avg MAF difference 43.4 [±13.8]%), comprising 29 meds. Variants with greatest divergence included 11 for which the minor allele was opposite between YRI/CEU including rs776746/clopidogrel, rs1024323/metoprolol, rs2239050/amlodipine. Four variants were rare in CEU but common in YRI (impacting warfarin, Ca channel blockers); 9 were rare in YRI but common in CEU (affecting CYP2C19, SLC22A1, TPMT, CYP2C9). Of 29 meds with RDVs, 18 were only studied in Europeans and not in populations of African descent. Numerous RDVs associated with clinically actionable meds have not been studied in non-white racial sub-populations, raising the potential for unintended consequences if standard PGx CDS is delivered to diverse cohorts.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

C-Reactive Protein is Associated with Depression and Anxiety in Patients with Inflammatory Bowel Disease

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Jordan **Karpin**, 4th-Year, Psychology, Creative Writing
Mentor(s): Dr. David T. Rubin, Gastroenterology, Hepatology, and Nutrition

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Depression and anxiety are comorbidities of inflammatory bowel disease (IBD). Though previous studies have proposed a relationship between anxiety, depression and IBD, causality and directionality are unknown. We used a novel computerized adaptive testing technology to screen IBD patients for depression and anxiety and compared the screening results to recent measures of C-reactive protein (CRP). Consecutive patients at our tertiary IBD clinic were asked to complete the validated CAT-MH™ survey from Adaptive Testing Technologies (Chicago, IL); we then reviewed disease and patient characteristics. CRP measures from within 6 months of survey administration were used and levels ≥5 mg/L were considered positive. Patients who are CRP non-reactive were excluded. Pearson Chi-Square test was used to assess correlation. 134 patients (75 women, 112 Caucasian, 84 Crohn's disease) participated in the study, 85 of whom had no prior history of psychiatric disorders. We identified 51 patients with depression (46 mild, 3 moderate, 2 severe) and 36 subjects with anxiety (24 mild, 10 moderate, 2 severe). Of the 134 patients recruited for this study, 57 had CRP reported. Median time between CRP measurement and CAT-MH™ administration was 2 days (IQR=70). Categorical analysis stratified patients with positive and negative CRP who are also positive for depression and/or anxiety. Compared to patients with negative CRP values, patients with positive CRP were more likely to also test positive for depression and anxiety. These results were statistically significant for depression (p-value = 0.008) and nearly significant for anxiety (p-value= 0.058). Quartile analysis of the 21 patients with elevated CRP levels revealed an increasing trend of average depression and anxiety severity scores. However, this correlation was lost when CRP >21 mg/L. We illustrate the significant association between CRP and depression and anxiety severity scores on the CAT-MH™ survey. These findings suggest a positive relationship between inflammation and depression and anxiety in IBD patients. Physicians should consider patients with elevated CRP levels at risk for these mental health conditions.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Characterizing Secreted Effector Network Interactions within *Pseudomonas syringae (Psy)*

Misra **Sengeldi,** 3rd-Year**,** Biological Sciences & Neuroscience
Mentor(s): Professor Jean Greenberg, Molecular Genetics and Cell Biology

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Bacterial effector proteins are involved in suppressing host immunity and promoting bacterial growth. Analyzing the pathogen effector network is crucial for understanding pathogen-host interactions and predicting the infection outcomes. The bacterial pathogen *Pseudomonas syringae (Psy)* is known to use a type III secretion system to inject effector proteins into host plant cells. We are investigating possible effector network complexes formed through effector protein interactions to help determine their roles in plant infections. In this project, the effector network of HopZ3 was chosen. HopZ3 is an acetyltransferase that creates post-translational modifications in effectors AvrRpm1, AvrPto1 and AvrB3. The roles of the chosen effectors were previously analyzed in planta and we aim to further investigate their roles before they are injected into the host cells by studying their ability to form higher order complexes. Towards this end, we made recombinant proteins using Escherichia coli and used nickel affinity chromatography and size exclusion chromatography via FPLC to purify them. The next steps involve using various interaction assays to understand the structure and functions of possible complexes the effector proteins form within the network. At this point in the project, HopZ3, HopAB1and HopI1 (negative control) effector proteins were successfully purified, while AvrRpm1 was successfully solubilized. In order to genetically assess the effect of acetylation on immune responses, we aimed to prepare constructs using *Psy* strains that are double mutants for HopZ3 and AvrRpm1 or AvrB3. To these constructs, HopZ3 or HopZ3CA, a catalytic mutant that lost its ability to acetylate the effector proteins were added back as well as the effectors of interest using plasmid vectors with different molecular tags, such as HA and MBP. The double mutant constructs were prepared in order to analyze possible interactions as well as the effects of acetylation on immune response, with the help of different molecular tags. In the future, the interactions of these effector proteins will be analyzed genetically and biochemically to understand the possible complexes better, potentially helping to see their role in plant infections.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Motivations for Participation in and Implementation of Diabetes Group Visits from Different Perspectives: Patients, Providers, Staff and Leadership

Sara **Siddiqui**, 3rd-Year, Comparative Race & Ethnic Studies
Mentor(s): Professor Arshiya Baig, Medicine; Ms. Erin Staab, Medicine; Dr. Michael Quinn, Medicine

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As a complex chronic disease, diabetes requires adherence to self-management. Diabetes group visits (GVs) are shared medical appointments that combine diabetes group education and support with individual primary care provider (PCP) visits. While several studies have examined the impact of diabetes GVs on clinical outcomes, no study has examined the motivators for involvement in diabetes GVs from patient, PCP, staff and leadership perspectives, especially in the health care setting. This study identified motivators for involvement in diabetes GVs at six Midwestern federally qualified community health centers (CHC) from patient, PCP, staff and leadership perspectives. We administered surveys to CHC patients, PCPs, staff and leadership prior to the start of a 6-month GV program. The surveys asked respondents why they engaged in the program. We conducted descriptive analysis of the survey responses with SAS and used a modified template approach to analyze free response answers through NVivo. Primary motivators for patients (N=58) participating in GVs were learning about diabetes, improving glycemic control, and gaining support and accountability. Healthcare providers and staff (N=55) were interested in implementing successful and sustainable programs and improving patient care. Leadership (N=13) saw GVs as an opportunity to achieve better population-level diabetes control, to try out a new model of care and to improve quality of care. Identifying motivators for involvement in diabetes GVs at the patient, PCP, staff and leadership level can help guide best practices for recruitment, retention and engagement in the program, ultimately to aid in the adoption of this care model.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Oral Somatosensation of Touch Events during Feeding

Derrick **Tang**, 4th-Year, Neuroscience, Philosophy
Mentor(s): Professor Fritzie Arce-McShane, Organismal Biology and Anatomy

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The orofacial cortex plays an important role in the sensorimotor control of vital and complex behavior, such as feeding and speech. Yet, the cortical representation of oral somatosensation remains largely unexplored. This is primarily due to the difficulties of dissociating tactile from proprioceptive feedback and of quantifying tongue movements inside the oral cavity. Here we investigate how neurons in orofacial primary motor cortex (M1) and primary somatosensory cortex (S1) of non-human primates represent tactile sensation when the tongue is in contact with other oral structures such as the teeth and palate, i.e. *touch events*. To dissociate tactile from proprioceptive inputs, we applied local anesthetics to specific sensory branches of the trigeminal nerve. We recorded neuronal activity from chronically-implanted microelectrode arrays in M1 and S1 simultaneous with 3D tracking of tongue kinematics using high-resolution bilateral video radiography and the X-Ray Reconstruction of Moving Morphology (XROMM) workflow while monkeys engaged in a natural feeding behavior. We anticipate finding changes in spiking activity as a function of the oral structure with which the tongue comes in contact and that encoding of touch events will differ between M1 and S1. Understanding the neural basis of oral somatosensation leads to a better understanding of the interplay between motor and somatosensory cortex. This also impacts the development of evaluation and treatments for orofacial pain and sensorimotor disorders such as dysarthria and dysphagia.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Probing Cell-Extracellular Cell Matrix Interactions with RGD Inhibitory Peptides

Yodit **Tesfu**, 3rd-Year, Neuroscience, Health and Society
Mentor(s): Professor Jocelyn Malamy, Biological Sciences; Elizabeth L. Lee, Biological Sciences

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Epithelial cell layers cover the outside of organisms and line organisms' internal spaces. These layers provide protection by acting as a barrier to pathogens and other insults in the external environment. Underneath the epithelial layers is an extracellular matrix (ECM). The ECM is a non-cellular structure that is made of water, proteins and polysaccharides. The ECM is responsible for physical scaffolding and signaling that regulates cell morphogenesis, differentiation, and homeostasis. Integrins are the primary group of receptor proteins responsible for communication between the cell and the ECM. Integrins bind ECM molecules like collagens, fibronectin, and laminins to adhere the ECM to the cytoskeleton. Since adhesion is weak, adjusting integrin attachment can modulate cell migration, an essential process to epithelial wound healing. Although the importance of the cell-ECM interactions is widely acknowledged, it is not well understood. Part of this disparity exists due to the difficulty in accessing the ECM of model organisms. The Cnidarian model organism Clytia Hemispherica, on the other hand, has just one layer of epithelial cells over a large ECM, rendering the matrix easily imaged and accessible. The ease of imaging in Clytia has allowed the Malamy lab to extensively characterize epithelial wound healing, providing a basis from which to analyze the role of the ECM. Here I describe experiments that investigate the effect of the integrin inhibitor peptide, RGD, on the wound healing process in Clytia. Since RGD inhibits protein binding to integrins, we predict this peptide will modulate cell migration, and therefore impact wound healing. To test this hypothesis, we are injecting the peptide into the ECM and studying whether there is a deviation from the normal wound healing process.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Sensory and Cognitive Encoding in Middle Temporal Area during Categorical Decision Making

Stephanie **Tetrick,** AB '19, Biological Sciences
Mentor(s): Professor David Freedman, Neurobiology; Barbara Peysakhovich, Neurobiology

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Categorization is a cognitive process that helps the brain assign meaning to sensory stimuli. We associate lemons and grapes together as 'fruit' although they are quite visually dissimilar, whereas perceptually similar stimuli sometimes belong to different categories (e.g. lemons and tennis balls, similarly round and yellow). Here, we focus on the transition between sensory and category information in the primate visual system. In particular, the middle temporal area (MT) is thought to primarily represent sensory information about motion direction. However, previous neurophysiological work has identified encoding of learned motion categories in the lateral intraparietal (LIP) and middle superior temporal (MST) areas, both of which receive direct input from MT. Thus, MT is on the cusp of a transition between sensory and categorical representations. To study this transition, we recorded from 54 single neurons in MT in a macaque trained to perform a task that required assigning 360° of visual motion directions into two categories. In this study, we used a complex category boundary that created four 90° quadrants in which opposite quadrants belong to the same category while adjacent quadrants belong to opposite categories. In this task, directions in the same category are from dissimilar directions, dissociating sensory and category signals. The monkey reported his categorical judgments by indicating (via lever release) whether a test motion stimulus matched the category of a previously shown sample stimulus. We show that MT neurons, via firing rate modulation, encode both directional and categorical information, evident at the single-cell and population levels. As expected, many MT neurons were strongly direction-selective for sample motion stimuli, with little evidence of categorical signals in sample or delay. Interestingly, during the test period, where the animal must recall the category identity of the sample stimulus, MT shows encoding of the remembered sample category. These category signals emerge, however, with greater latency relative to MST and LIP. Hence, we hypothesize that these test-period category signals in MT arise via feedback from higher processing stages. This suggests that through training, cognitive processes may affect representations of task-relevant information in areas traditionally considered to be purely sensory.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

The Role of EGF and Caveolin-1 in the Pathophysiology of Lung Fibrosis

DeShawn **Thompson**, 3rd-Year, Biological Sciences & Psychology
Mentor(s): Professor Stephen Kron, Biological Sciences; Dr. Tamica Collins, Molecular Genetics and Cell Biology

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Idiopathic Pulmonary Fibrosis (IPF) is a fatal age-related disease with poor prognosis and an increasing rate of hospital admissions and deaths. Fibrosis has been shown to not only become more common with age but to also be induced by exposure to environmental factors that cause oxidative stress such as smoking. Senescence of alveolar epithelial cells and fibroblasts appears to be a central phenotype that promotes lung fibrosis; however, many aspects of the mechanisms associated with the pathophysiology of IPF remain unknown. Using primary mouse lung fibroblasts, we have shown that the inhibition of the epidermal growth factor receptor (EGFR) by the tyrosine kinase inhibitor, erlotinib, leads to an increase in senescence-associated-β- galactosidase activity. We have also demonstrated increased proliferation and migration of cells treated with EGF. These data suggest that the EGFR pathway plays a role in the proliferation and senescence of lung fibroblasts. In addition, previous data from others have shown that caveolin-1 (Cav-1) is overexpressed in senescent cells induced by oxidative stress. It has also been shown that EGF promotes the interaction between EGFR and Cav-1. Here we wish to examine whether the interaction of Cav-1 and EGF promotes senescence and contributes to the pathophysiology of lung fibrosis. We will employ biochemical methods to observe the interaction of EGF and Cav-1 in alveolar epithelial cells and lung fibroblasts after exposure to bleomycin and other inducers of cellular senescence. To accompany these in vitro data, we will use the previously identified bleomycin-induced lung fibrosis mouse model and observe levels of EGFR, Cav-1, and senescence biomarkers. These studies aim to reveal how the interaction between Cav-1 and EGF could promote cellular senescence and provide insight into one of the main mechanisms associated with the pathophysiology of IPF.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

The Contribution of Endolysosomal Trafficking Complexes to Bacterial Feeding and Digestion Efficiency in *Tetrahymena thermophila*

Maya **Waarts**, 3rd-Year, Biological Sciences, Biochemistry
Mentor(s): Professor Aaron Turkewitz, Molecular Genetics and Cell Biology

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Ciliates, including the genus Tetrahymena, are a group of unicellular protozoa that serve as key bacterivores in many ecosystems. Many are filter feeders and feed using a specialized ring of cilia around their oral apparatus to generate water currents shuttling bacterial prey toward the oral apparatus where it is ingested. Although this pathway is well established, mechanisms influencing feeding efficiency remain unknown. We hypothesized that bacterial uptake and/or digestion efficiency could be linked to endolysosomal trafficking. In Tetrahymena thermophila, the CORVET complexes are six distinct complexes (named 8A-CC to 8F-CC, each for the unique Vps8 subunit that it includes) that act as tethers in vesicular fusion events in the endolysosomal pathway. Some subunits (Vps8b, Vps8e, and Vps8f) are seen to localize to phagosomes in which bacteria are taken up and subsequently digested. We used a flow cytometry-based assay to quantify bacterial uptake and digestion in strains with individual knockouts of the *VPS8A, B, E,* and *F* genes. Surprisingly, although Vps8a is not seen to localize to the oral apparatus or to phagosomes, Δ*vps8a* cells showed higher rates of uptake and lower rates of digestion when compared to wild type cells. To further investigate the potential involvement of Vps8a we tested Δ*stx7l1* strains for uptake and digestion phenotypes. Stx7l1 is a SNARE protein thought to function in the same stage of the endolysosomal trafficking as Vps8a. We found that Δ*stx7l1* cells were near phenocopies of Δ*vps8a* cells when tested under starvation conditions, but not when tested under growing conditions. Previously, Vps8a was shown to be required for the formation of lysosome-related secretory organelles known as mucocysts. We therefore considered the possibility that mucocyst formation or release contributes to feeding and/or digestion efficiency. To this end we measured the bacterial uptake and digestion rates of a number of independent mucocyst-deficient strains, where each strain was defective at a different stage of mucocyst maturation or release. These mucocyst-deficient strains did not show any defect in bacterial uptake or digestion. This suggests that the bacterial uptake and digestion phenotypes in Δ*vps8a* are not linked to the mucocyst defects, and potentially indicate other activities of Vps8a and Stx7L1.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Education-Labor Mismatch and Health Outcomes among Immigrants in the U.S.

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Mentor(s): Dr. Aresha Martinez-Cardoso, Public Health Sciences

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In the U.S. labor market, foreign-born workers are disproportionately overeducated for their labor occupations, a phenomenon known as education-labor overmatch. While prior literature has explored the role of education-labor mismatch on the social and economic integration of immigrants, few studies have examined the role of education-labor mismatch on health. In an increasingly globalized society, the relationship between migration and health is being recognized as a global health priority as migration becomes increasingly understood as a determinant of health. However, because of complexity in the mixed flow of economics, education and income, the mechanisms behind how migration affects health remains poorly understood. In this project, we aim to investigate how education-labor mismatch shapes the integration and health of immigrants in the U.S. We analyze work trajectories, education, and health among a representative sample of U.S. and foreign-born older adults using data from the Health and Retirement Study. We will examine the patterns of education-labor mismatch by nativity, and the correlations between such mismatch and health outcomes associated with stress-response, including waist circumference, blood pressure, c-reactive protein (CRP), glycosylated hemoglobin A1c (HbA1c), and total and high-density lipoprotein cholesterol (HDL-C), and self-reported health. We assessed mismatch and health using the realized matches-technique developed by Chiswick et. al. (Chiswick & Miller, 2010). Preliminary analysis has shown that immigrants are more likely to be mismatched, as they are overrepresented among overmatch and undermatch workers. Bivariate analysis showed that being overmatched is protective of stress-related health outcomes among US-born, but no significant association between education-labor mismatch and health outcome among immigrants was found. Further analysis will be conducted by using logistical regression models to assess whether education-labor mismatch is associated with each health outcome of interest, while controlling for specific occupation categories. This work advances inquiries of how social environments shape the incorporation and health trajectories of immigrants who play an important role in the U.S. labor market and healthcare landscape. Particularly, we contribute to the immigrant integration literature by exploring how a unique manifestation of social inequality in the U.S., labor-education mismatch, may be consequential for the health and wellbeing of immigrants.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Characterization of Splicing Factor Mutations associated with Different Cancer Subtypes

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Genetic information in our DNA is translated into proteins by way of an RNA intermediate called pre-mRNA. Before translation, pre-mRNA must be modified by a process called splicing in which non-coding parts of the pre-mRNA molecule ("introns") are removed to generate a translatable mRNA molecule. This process allows for many different forms of mRNA to result from a single gene and is an essential process by which genes can be regulated. Genes encoding the cellular machinery that catalyzes splicing (the "spliceosome") are commonly mutated in hematopoietic cancers. Spliceosome mutations can result in mis-splicing and altered mRNA forms, the result of which can deregulate normal cell process and contribute to cancer progression. One of the most commonly mutated spliceosome genes, SF3B1, is mutated in ~5-20% of acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL) cases. Under normal conditions the SF3B1 component of the spliceosome is responsible for recognizing particular pre-mRNA sequences that define the 3' edge of an intron. Though there are many different mutations in SF3B1that may occur, the cancer-associated tend to appear in a "hotspot" region of the protein and result in altered 3' splice sites. Interestingly, some hotspot mutations occur more frequently in different leukemia subtypes. For example, the K700E mutation is common in AML and rare in CLL, while the G742D mutation is common in CLL and rare in AML. I hypothesize that the molecular phenotypes of these mutations are distinct and may drive hematopoietic cells into a distinct cancer subtype. Characterization of these distinct molecular phenotypes may yield insight into the disease's pathology. Here I present a model for studying these disease specific hotspot mutations in order to characterize their molecular difference. Using a hematopoietic progenitor cell line, I measure the effects of different cancer associated SF3B1 mutations on splicing in cell culture. Further points of inquiry involve investigating how the mutations affect the spliceosome's function at the molecular level. Insights gained from this will yield a deeper molecular understanding of SF3B1 mutations and reveal how different genes get mis-spliced to affect hematopoiesis during cancer progression.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Similarities and Differences between *Ulva* sp., *Gracilaria* sp., and Seawater's Microbiome Structure in Little Sippewissett Marsh

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Microbial communities are diverse and dynamic forces within ecosystems, and microbial composition differs based on its host organism and environment. As such, this project seeks to further understand the microbiome of seawater, *Gracilaria sp*., and *Ulva sp*. from the marsh in Little Sippewissett Marsh in Falmouth, Massachusetts. I hypothesized that seawater will have more richness and phylogenetic diversity than both genera of algae because of the seawater's flow and freestanding environment, and that *Ulva sp*. and *Gracilaria sp.* will be more even than the seawater because of its rooted environment. However, using 16S sequencing and data analysis in Qiime2, I found that microbial community composition between seawater, *Gracilaria sp.,* and *Ulva sp.* might be more similar than originally thought. Specifically, there was no significant difference in the richness, phylogenetic diversity, and evenness between Ulva sp. and *Gracilaria sp*., and only marginally-significant differences between the seawater and both genera of algae. This project provides a glimpse into the microbial community in Little Sippewissett Marsh and its interactions with seawater, *Ulva sp.,* and *Gracilaria sp*. Although it is a mere drop in the ocean of microbial research and how the microbiome exists in an ecosystem as a whole, the results from this study present the opportunity to learn more about how changes in certain metrics—such as species composition—can impact microbial functioning.

The 2020 University of Chicago Undergraduate Research Symposium Proceedings: Abstract

Do Human Gut Plasmids Exclusively Control Their Own Replication?

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Mentor(s): Professor A. Murat Eren, Medicine; Emily Fogarty, Committee on Microbiology

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Microbes are able to adapt to rapidly changing conditions in the human gut through a process called horizontal gene transfer (HGT), where genetic material is transferred from one bacterial cell to another via plasmids. Plasmids, extrachromosomal DNA that may carry accessory genes, can have dramatic impacts on bacterial fitness. By examining 2,137 globally distributed human samples, we show that pBI143 is abundant in individual gut metagenomes, and present in over 75% of humans in industrialized countries. Additionally, we identified three versions of the plasmid that differ only in a gene that controls replication, *repA*. pBI143 is found predominantly in bacterial hosts from the genus *Bacteroides*. Unlike other plasmids which carry clear fitness determinants, such as antibiotic resistance or bile acid tolerance, pBI143 only contains two genes, *repA* and *mobA*, which are predicted to facilitate its replication and transfer, respectively. Despite the apparent lack of beneficial genes, the conservation of pBI143 across human populations and its dynamics with its *Bacteroides* hosts suggests that it may play an important role in the fitness of *Bacteroides* in the human gut ecosystem. My research will determine if the different versions of pBI143 are present in differing relative abundances in globally distributed human populations, suggesting that the regulation of plasmids replication differs between plasmid versions. This will be followed by experimental validation of the trends we see in our metagenomic sequencing data. The experimental validation will investigate whether different versions of *repA* cause the copy number of pBI143 to vary. Copy number variation is significant as pBI143 may affect the fitness of its host bacterium and will be determined in the future via qPCR. Through my research, I hope to gain a better understanding of how pBI143 may impact *Bacteroides* fitness, which may serve to elucidate new factors that regulate plasmid replication in bacteria.