EMORY UNIVERSITY | Postdoctoral Association

The Postdoctoral Association Presents:

2022 *Virtual* Postdoctoral Research Symposium

Thursday, February 24th, 2022

Celebrate the accomplishments of your fellow Emory University Postdoctoral Scholars! Join us for two exciting research presentation sessions, and learn about the work of your colleagues!

Afterwards join a breakout room to explore different career paths pursued by *real* Emory University Postdoc Alumni!

Careers include: Medical Writing, Project Management, Government Forensic Psychologist, Data Science, and Clinical Translational Science.

Schedule of Events:

Morning Research Session:	9:30 AM – 12:00 PM (EST)
Afternoon Research Session:	1:00 PM – 3:30 PM (EST)
Careers After Postdoc'ing:	3:45 PM – 5:00 PM (EST)

Register For this Event!

2022 EU-PDA Research Symposium – Schedule

9:30 AM – 12:00 PM : Morning Presentation Session

- 9:35 AM – 9:55 AM : Alexandre Cammarata-Mouchtouris
- 10:00 AM – 10:20 AM : Sarah Curtis
- 10:25 AM – 10:45 AM : Cecilia Hinojosa
- 10:50 AM – 11:10 AM : Zachary McCann
- 11:15 AM – 11:35 AM : Christina Knippler
- 11:40 AM – 12:00 PM : Tiffany Terry

12:00 PM – 1:00 PM: Break

1:00 PM – 3:30 PM : Afternoon Presentation Session

- 1:05 PM – 1:25 PM : Robby Van Sciver
- 1:30 PM – 1:50 PM : Yun Hang
- 1:55 PM – 2:15 PM : Lorenzo Fernandes
- 2:20 PM – 2:40 PM : Saman Najmi
- 2:45 PM – 3:05 PM : Hala Zein-Sabatto
- 3:10 PM – 3:30 PM : Casey Schmidt

3:30 PM – 3:45 PM : Break

3:45 PM – 5:00 PM : Career Options Panel

- Breakout Room #1 : Amarallys Cintron, Ph.D. | Medical Writing
  Senior Medical Writer and Associate Medical Director, Arbor Scientia

- Breakout Room #2 : Nicole Azores-Gococo, M.S., Ph.D.| Government Science
  Forensic Psychologist, Georgia Department of Behavioral Health and Developmental Disabilities

- Breakout Room #3 : Yvonne Ogbonmwan, Ph.D. | Industry Science
  Associate Project Manager, Q^2 Solutions

- Breakout Room #4 : Andrew Brooks, Ph.D. | Data Science
  Head of Data Science, Torqata Data and Analytics

- Breakout Room #5 : Jithendra Kini Bailur, Ph.D. | Translational Science
  Clinical Translational Scientist, Takeda Oncology

Abstracts – Morning Session (9:30 AM – 12:00 PM)

9:35 AM – 9:55 AM : Alexandre Cammarata-Mouchtouris

Department, School or College: Pediatrics, School of Medicine

Title: Epigenetic Regulation of Lung-recruited Pathological Neutrophils in Cystic Fibrosis

Co-Authors: Diego Moncada, Brian Dobosh, Milagros Aldeco, Christopher Scharer, Rabindra Tirouvanziam

Rationale: Massive inflammation is a hallmark of cystic fibrosis (CF) lung disease. Despite the presence of neutrophils known for their antibacterial function, patients with CF suffer from crippling bacterial infections. Our laboratory discovered that CF lung neutrophils undergo a reprogramming process that represses their bacterial killing activity, in a fate we dubbed “GRIM”. We also established that GRIM neutrophils can be mass-produced in vitro by recruitment of blood neutrophils through a differentiated epithelial layer into sputum supernatant from CF patients.

Approach: Using our in vitro model, we are performing transcriptional and epigenetic techniques to identify the dynamic reprogramming events leading to the GRIM neutrophils fate. Methods used include RNA-Seq to track genes expression, and ATAC-Seq to determine changes in the chromatin structure. In addition, we are repurposing modulators to alter GRIM neutrophils phenotype and recover their bacterial killing function.

Results: We observed that epigenetic-related proteins are significantly modulated over time in GRIM neutrophils. In a pilot ATAC-Seq assay, we probed the epigenetic remodeling of chromatin and observed broad derepression in lung-recruited cells compared to blood controls. We also showed that targeted inhibition of a histone deacetylase (HDAC11) and a methyltransferase (EZH2) using repurposed cancer drugs reverses the GRIM fate in neutrophils, restoring their bacterial killing activity.

Conclusion: Dynamic adaptation of lung-recruited neutrophils associated with human lung inflammation is regulated by epigenetic and transcriptional modulators, which is unexpected in these cells owing to the hypercondensed chromatin they display while in blood. Further experiments using CUT&RUN-Seq and DNA methylation profiling will bring further understanding into these processes and help identify novel epigenetic and transcriptional targets for treatment of CF and other intractable lung diseases via fate modulation of tissue neutrophils.
Funding: Cystic Fibrosis Foundation (TIROUV19G0, CAMMAR21F0), Emory I3 Team Award.

10:00 AM – 10:20 AM : Sarah Curtis

Department, School or College: Human Genetics, School of Medicine

Title: Functional annotation of de novo mutations found near GWAS loci associated with cleft lip with or without cleft palate

Co-Authors: Axel Visel, Robert A. Cornell, Justin L. Cotney, Jeffrey C. Murray, Terri H. Beaty, Mary L. Marazita, Jenna C. Carlson, and Elizabeth J. Leslie

Orofacial clefts (OFCs) are the most common craniofacial birth defects, affecting 1 in 700 births, and have a strong genetic basis with a high recurrence risk within families. While many of the previous studies have associated common, noncoding genetic loci with OFCs, previous studies on de novo mutations (DNMs) in OFC cases have focused on coding mutations that could have a functional impact on protein structure, and the contribution of noncoding DNMs to the formation of OFCs has largely been ignored and is not well understood. Therefore, we reanalyzed an existing dataset of DNMs from 1,409 trios with OFCs that had undergone targeted sequencing of known OFC-associated loci. We then annotated these DNMs with information from datasets of predicted epigenetic function during human craniofacial development. Of the 66 DNMs in this cohort, 17 (25.7%) were within a predicted enhancer or promotor region. Two DNMs fell within the same enhancer region (hs1617), which is more than expected by chance ($p = 0.0038$). The sequence change caused by these DNMs are predicted to lead to binding sites for PAX6 and ZBTB7A transcription factors (not seen in the reference sequence) and to disrupt binding sites for STAT1 and STAT3. This region is also within the same topologically-associated domain as HHAT, SERTAD4, and IRF6, all of which are involved in craniofacial development. All three genes are highly expressed in human neural crest cells, and HHAT knockout mice have abnormal embryonic development including a cleft palate, and mutations in IRF6 are associated with both nonsyndromic and syndromic forms of OFCs. Taken together, this suggests that noncoding

DNMs contribute to the genetic architecture of OFCs, with a burden of DNMs in OFC trios in enhancer regions near known OFC-associated genes, and overall, this adds to our understanding of the genetic mechanisms that underly OFC formation.

10:25 – 10:45 AM : Cecilia Hinojosa

Department, School or College: Psychiatry and Behavioral Science, School of Medicine

Title: Does hippocampal volume in patients with posttraumatic stress disorder vary by trauma type?

Co-Authors: N/A

Posttraumatic stress disorder (PTSD) is a debilitating disorder that can develop after experiencing a traumatic event and is, in part, characterized by memory disturbances. Given its important role in learning and memory, the hippocampus has been studied extensively in PTSD using volumetric neuroimaging techniques. However, the results of these studies are mixed. The variability in findings across studies could arise from differences in samples with regard to trauma type, but this has not yet been formally assessed. To assess this question, we conducted (1) mixed-effects meta-analyses to replicate previous meta-analytic findings of significant differences in hippocampal volumes in PTSD groups versus two different types of control groups (trauma-exposed and unexposed groups); (2) mixed-effects subgroup and meta-regression analyses were conducted to determine whether trauma type moderated these hippocampal volume differences. Overall, the PTSD groups showed significantly smaller right hippocampal volumes compared to both control groups, and significantly smaller left hippocampal volumes compared to trauma-unexposed control groups. Subgroup and meta-regression analyses revealed that trauma type did not moderate the effect seen between PTSD and trauma-exposed non-PTSD groups but did moderate the effect between the PTSD and trauma-unexposed control groups: studies that contained participants with PTSD related to combat trauma exhibited significantly smaller effect sizes for right hippocampal volumes compared to the interpersonal violence and 'other' trauma type groups with PTSD. These findings suggest that trauma type may moderate hippocampal volume in trauma-exposed individuals but not in those with PTSD.

10:50 AM – 11:10 AM : Zachary McCann

Department, School or College: Environmental Health, Rollins School of Public Health

Title: The Effects of Social Capital on Cardiovascular Mortality in Counties Affected by Hurricane Matthew

Co-Authors: Magdalena Szaflarksi

Social capital refers to the social relationships and structures that provide individuals with material, financial, and emotional resources throughout their lives. Previous research has found an association between high levels of social capital and lower rates of cardiovascular disease (CVD) mortality. Severe disasters have been linked to higher rates of CVD mortality for an extended period of time after the disaster. In post-disaster settings social capital may be a valuable resource for protecting against CVD mortality by improving access to resources, such as food, water, and medical supplies. Using previous research on social capital, disasters, and cardiovascular disease as a guide, the aim of this research is to understand the protective effect of social capital against CVD mortality 18 months after hurricane Matthew. Specifically, we hypothesized that counties that experiences high levels of hurricane damage will experience higher levels of CVD mortality, and that social capital reduce CVD mortality rates in highly damage counties affected by hurricane Matthew. To test this hypothesis, we compiled county-level data from several federal surveys before and after hurricane Matthew to create a novel social capital index. We then examined the relationship between hurricane damage and CVD mortality rates and the relationship between social capital and CVD mortality in highly damage counties. We found that Hurricane damage is associated with an increased trajectory of CVD mortality rates. Collective efficacy reduced the immediate hurricane damage on CVD mortality in highly damaged counties, but the overall effects of social capital are largely insignificant. Findings suggest that hurricane damage is associated with increased CVD mortality for an extended period of time after hurricanes. Future research should focus on improving measurements of social capital so that researchers and policymakers can better understand the role of social capital in post-disaster scenarios.

11:15 AM – 11:35 AM : Christina Knippler

Department, School or College: Hematology and Medical Oncology, School of Medicine

Title: Decoupling metabolic heterogeneity in metastatic lung cancer

Co-Authors: Janna Mouw, Jamie Arnst, Mala Shanmugam, Adam Marcus

Approximately 80% of lung cancer patients present with cancer that has spread from the lungs to other organs (metastasis) and have a poor prognosis. These metastases are often formed by groups of cancer cells with diverse subpopulations that move together in packs; however, most research focuses on the bulk cellular population and, therefore, rare subpopulations that drive metastasis and therapeutic resistance are masked. To identify and characterize subpopulations, our lab developed a method to isolate subpopulations of collectively moving lung cancer cells. Cells leading the group are called “leaders” and those behind are “followers”. We identified phenotypic, genetic, and epigenetic differences, highlighting the complexity and heterogeneity of these cells. Importantly, we determined metabolic heterogeneity, in which leaders utilize their mitochondria to generate energy more than followers. Therefore, we hypothesized that leaders would be preferentially sensitive to mitochondrial stress. Using a probe with affinity to polarized (healthy) mitochondria, we observed that leaders have more polarized mitochondria than followers. When grown together in the original “parental” population, leaders and followers have higher mitochondrial polarization than when cultured alone, suggesting cooperation to enhance functional mitochondria. We used an antibiotic, alexidine, to depolarize mitochondria. Interestingly, leaders maintained higher amounts of polarized mitochondria than followers after alexidine treatment, with no loss of mitochondrial amount. Cells can recycle damaged proteins or organelles via autophagy and mitophagy. By probing for markers indicative of these, we found that leaders have higher baseline autophagy than followers and upregulate autophagy earlier after alexidine treatment. Taken together, our data indicate that lung cancer subpopulations within the “bulk” exhibit different degrees of mitochondrial function and clear damaged mitochondria via different mechanisms. This suggests a model whereby a lung cancer tumor has subpopulations with different but complementary mechanisms of metabolism and mitochondrial damage repair to better strengthen the tumor during the metastatic process.

11:40 – 12:00 PM : Tiffany Terry

Department, School or College: Human Genetics, School of Medicine

Title: The critical role of ciliary ARL13B in energy homeostasis and obesity

Co-Authors: Eduardo Gigante and Tamara Caspary

Obesity, a disorder of energy imbalance, is a significant public health concern. Disruption to the cilia, a small cell protrusion, in the feeding center of the brain causes obesity. However, we do not understand how ciliary signaling proteins function to maintain normal energy homeostasis. Arl13b encodes a GTPase highly enriched in cilia. In mice, Arl13b null mutations are embryonic lethal with abnormal Sonic hedgehog (Shh) signaling. To investigate the ciliary role of ARL13B, we generated a mouse line expressing a cilia-excluded ARL13B variant, ARL13BV358A. We found Arl13bV358A/V358A mice are viable, fertile, and display normal responses to Shh signals. Interestingly, we found that Arl13bV358A/V358A mice are hyperphagic and become markedly obese, showing that ciliary ARL13B regulates pathways that control energy homeostasis. The weight increases in Arl13b V358A/V358A mice began at five weeks of age, and by ten weeks of age, the mice were 33% heavier than controls. Since diabetes is often comorbidity for obesity, we measured blood glucose changes in response to a single glucose or insulin dose. We found that Arl13bV358A/V358A mice display impaired glucose and insulin tolerance compared to littermate controls. These data implicate ciliary ARL13B as a critical regulator of energy homeostasis. Importantly, our cilia-excluded ARL13B mouse model allows us to dissect the cilia-specific role of ARL13B in energy homeostasis. A better understanding of the ciliary pathways that regulate energy homeostasis will uncover new therapeutic targets and strategies to combat obesity.

Abstracts – Afternoon Session (1:00 PM – 3:30 PM)

1:05 PM – 1:25 PM : Robby Van Sciver

Department, School or College: Department of Human Genetics, School of Medicine

Title: ARL13B negatively regulates kidney cysts from within cilia

Co-Authors: Eduardo Gigante, Tamara Caspary

Polycystic kidney disease (PKD) is a chronic, progressive disease in which the kidneys develop fluid filled sacs or cysts that lead to loss of kidney function, end stage renal disease, and even death. PKD affects 140,000 Americans and has an economic burden exceeding $7 billion annually. PKD is intricately linked to the primary cilium, a small microtubule-based organelle that protrudes from the cell. Polycystins are proteins that localize to cilia. In mouse models, loss of these proteins or loss of cilia leads to kidney cysts. While we know that the polycystins are necessary to stop cysts from forming, we don't know what molecules cause cysts to form in the first place. PKD mouse models often disrupt ciliary genes, removing both ciliary and cellular pools of these gene products and making it challenging to isolate ciliary signaling from cilia localization. Using CRISPR/Cas9, we engineered a mouse mutant in which an integral cilia signaling molecule, ARL13B, is mutated, preventing it from localizing to the cilium. These mice are developmentally normal and fertile but develop polycystic kidneys. These cysts are detected in all nephron segments, and the kidney cells of these mice have normal length cilia. Our findings indicate that ARL13B plays a critical role within the cilium in regulating kidney cystogenesis. These results suggest that ARL13B functions as a negative regulator of kidney cysts, specifically from within the cilium. Further studies are ongoing to dissect the mechanism(s) by which ciliary ARL13B regulates kidney cystogenesis.

1:30 PM – 1:50 PM : Yun Hang

Department, School or College: Environmental Health, Rolling School of Public Health

Title: Particulate nitrate air pollution in China remains a considerable health problem

Co-Authors: Yang Liu

Air pollution is a major environmental issue in China and has posed a threat to Chinese public health. To improve air quality, the Chinese government has implemented a series of strict policies such as the toughest-ever Air Pollution Prevention and Control Action Plan (APPCAP) issued in 2013. However, NO3- concentrations remain high or even increase at monitoring sites despite total PM2.5 concentrations are decreasing. Unfortunately, it has been difficult to estimate NO3- concentrations across China due to the lack of a PM2.5 speciation monitoring network. Here, we use a machine learning model incorporating ground measurements and satellite data to characterize the spatiotemporal patterns of NO3-, thereby understanding the disease burden associated with long-term NO3- exposure in China. Our results show that existing air pollution control policies effectively reduce ambient NO3- levels in areas with many coal-fired power plants and extensive industry facilities. Estimated national mean NO3- decreased by 25.8% from 2006 to 2016, translating to 0.53 million reductions in adult premature deaths. But the decreasing trend stagnated in 2017 following an increase of NO3- in civilian vehicle fleets, as well as cities with dense road networks. In 2018, the national mean mortality burden of NO3- increased to 0.67 million, indicating targeted regulations on vehicle emissions are needed to control NO3- pollution.

1:55 PM – 2:15 PM : Lorenzo Fernandes

Department, School or College: Department of Orthopedics, School of Medicine

Title: Early Players in Cartilage Repair Microenvironments.

Co-Authors: Maddie Hasson, Jay M. Patel

Microfracture (MFx) is a common cartilage repair procedure that recruits marrow to the chondral defect site. This marrow clot is relatively rich in mesenchymal stromal cells (MSC's) and stabilizes the chondral defect, providing short-term symptomatic relief. However, in many cases, the clot is remodeled into an inferior fibrocartilaginous tissue rather than high-quality hyaline cartilage, leaving the tissue susceptible to further degradation. Here, we sought to understand the molecular changes that drive early MFx remodeling and fibrocartilage formation, with the long-term goal of enhancing neo-cartilage

formation. In this study, we combined fibrinogen, thrombin, and bMSC's to simulate the early MFx clot environment and explored the role of cell contractility and fibrinolysis on macro-scale clot contraction and chondrogenic potential.

To ascertain the role of cell contractility, we manipulated the Rho/Rho-associated kinase pathway (ROCK) by adding Fasudil (ROCK inhibitor) to clot cultures. After four weeks of culture, Fasudil-treated clots were significantly larger than clots in control media, suggesting a link between cell contractility and clot remodeling. Interestingly, bMSC's in Fasudil-treated clots showed an inclination towards cartilage matrix production, with several-fold increases in type II collagen and aggrecan (two of the major components of hyaline cartilage matrix). Finally, Fasudil treatment significantly enhanced the chondrogenic potential of clots subjected to TGF-B supplementation (a known chondrogenic agent).

Next, we explored the role played by fibrinolysis in this process by treating clots with aprotinin, an inhibitor of fibrinolysis. Aprotinin rescued clot contraction, attributing clot remodeling to fibrinolytic factors produced by bMSC's. We are currently investigating the role of fibrinolysis in chondrogenic differentiation of bMSC'S.

Our findings implicate both the Rho-ROCK pathway and bMSC's in mediating clot remodeling and matrix deposition. Therefore, modulating these factors represents a novel and impactful means for directing the early MFx environment towards forming new cartilage tissue.

2:20 PM – 2:40 PM : Saman Najmi

Department, School or College: Biochemistry, School of Medicine

Title: The role of the AAA+ ATPase Rvb1/2 in snoRNP assembly

Co-Authors: Jacob Ball, Sohail Khoshnevis, Homa Ghalei

Ribosomes are essential RNA-protein machines responsible for catalysis of protein synthesis in all cells. Ribosomal RNAs (rRNAs), which account for a large portion of the ribosomal mass, are chemically modified at over 100 positions in yeast (>200 in human cells). These modifications are required for ribosome biogenesis and protein production, and their dysregulation is linked to several human diseases including cancer and neurodevelopmental disorders. A prominent rRNA modification is 2'-O-methylation which is guided by the C/D class of small nucleolar RNAs (snoRNAs). These snoRNAs interact with a set of four evolutionarily conserved proteins to form functional ribonucleoproteins complexes (snoRNPs). Formation of snoRNPs requires the action of several assembly factors including the AAA+ ATPases Rvb1 and Rvb2, which together form a heterohexameric complex (Rvb1/2). Although the ATPase activity of Rvb1/2 is essential for cell viability and required for biogenesis of snoRNPs, the mechanism of action of Rvb1/2 and the functional consequence of ATP hydrolysis by this complex for snoRNP assembly are not understood. Using budding yeast as a model organism, we have shown that mutation of each of the highly conserved arginine fingers of Rvb1 and Rvb2 to alanine (Rvb1-R366A, Rvb2-R350A) confers distinct growth phenotypes and ATPase activities. A targeted genetic screen suggested that the ATPase activity of Rvb2 may be necessary for the interaction of the protein with the core snoRNP protein, Nop58. This finding is supported by our comparative preliminary proteomics analysis of the composition of precursor snoRNP complexes from yeast cells expressing wildtype and mutant Rvb2. Currently, we are building on these findings with further experiments including co-immunoprecipitation and in vitro ATPase assays, and a yeast suppressor screen.

2:45 PM – 3:05 PM : Hala Zein-Sabatto

Department, School or College: Cell Biology, School of Medicine

Title: Exploring the role of dynein in transporting *cen* mRNA to the centrosome

Co-Authors: Li Jin, Simon Bullock, and Dorothy A. Lerit

The centrosome is a multi-functional organelle that plays a key role in nucleating and organizing microtubules, facilitating ciliogenesis, and organizing the bipolar mitotic spindle during cell division. A protein matrix known as the pericentriolar material (PCM) surrounds the centrosome and regulates centrosomal function. Various mRNAs also concentrate around the centrosome, but their functional significance is not yet fully understood. Our lab and others have identified centrocotin (cen) mRNA as forming micron-scale RNA granules near the centrosome in a cell cycle-dependent manner. We also showed localization of cen mRNA at the centrosomes is needed for error-free mitosis. However, how cen mRNA localizes to the centrosome is still unknown. Preliminary data from immunofluorescent imaging combined with smFISH reveals cen

mRNA decorates astral microtubules. Further, biochemical studies show that Cen protein, a component of the cen mRNA granule, interacts with the dynein motor complex. Taken together, these data suggest that cen mRNA is transported to the centrosome via dynein-directed trafficking along microtubules. To test this hypothesis, cen mRNA localization was quantified in CRISPR-edited Drosophila embryos designed to disrupt a predicted dynein light intermediate chain binding site within the cen sequence. Moreover, the effect of destabilizing the microtubule network on cen granule localization to the centrosome was analyzed. Inhibiting the interaction of cen mRNA with dynein and microtubules resulted in a decrease in cen mRNA granules localized to the centrosome, consistent with a role for dynein in RNA trafficking to the centrosome. Furthermore, fly lines harboring N- and C-terminal truncations of the cen transcript were made to identify the minimal sequence required for cen mRNA localization to the centrosome. This work provides insight into the dynamic localization of cen mRNA through active intracellular transport.

3:10 PM – 3:30 PM Casey Schmidt

Department, School or College: Biology, College of Arts and Sciences

Title: Remote research: A bioinformatics adventure for undergraduates

Co-Authors: Lauren Hodkinson, Skye Comstra, and Leila Rieder

Numerous studies have demonstrated the value of involving undergraduates in laboratory research. However, access to research labs is often limited by available space and time. To reach a larger population of students, many faculty have incorporated portions of their research into Course-based Undergraduate Research Experiences (CUREs). CUREs provide authentic research experiences to a much larger number of students than traditional apprenticeship models, and their inclusion in biology curricula is becoming much more widespread. We took advantage of the COVID-19 pandemic to pilot a bioinformatics CURE with undergraduates who were unable to physically work in laboratories. The Rieder lab is interested in the regulation of the Drosophila histone genes, and our goal was to identify novel histone gene regulators using publicly available high-throughput datasets. We first engaged students in background discussions and literature searches, and they formed hypotheses and chose candidate proteins. Next, the students found ChIP-seq datasets in public databases and mapped reads to the histone gene array using Galaxy, a free web-based platform that integrates many bioinformatics tools. Students visualized their data using the open-source Integrative Genomics Viewer (IGV) software and presented their results to the group. We repeated this workflow with additional students who examined histone post-translational modifications at the histone gene array. Our approach solved the accessibility issue exacerbated by the COVID-19 pandemic, is completely free, and presents an opportunity for more accessible and inclusive access to undergraduate research.