2023

Duke Summer Research Showcase

July 28, 2023 | 10am - 12pm

Penn Pavilion, 107 Union Drive, Durham NC 27710

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Schedule

Times	Sessions
10:00 - 11:00 am	**Poster Presentations** *Light Refreshments Provided*
11:00 - 11:15 am	**Welcome Remarks** **Jessica Harrell** Director, Undergraduate Research Support Office **Candis Watts Smith** Vice Provost for Undergraduate Education **Edward Balleisen** Vice Provost for Interdisciplinary Studies
11:15 - 12:00 pm	**Poster Presentations**

Special Guest Biographies

Edward Balleisen

Vice Provost for Interdisciplinary Studies

Edward Balleisen is Professor of History and Public Policy. Arriving at Duke in 1997, Professor Balleisen's research explores the historical intersections among law, business, politics, and policy in the modern US, with a focus on the origins, evolution, and impacts of the modern regulatory state. He has pursued projects with historians and other social scientists who study regulatory governance in industrialized and industrializing societies. Balleisen's recent book, *Fraud: An American History from Barnum to Madoff* (Princeton University Press, 2017), emphasizes the connections between capitalist innovation and business fraud, as well as the efforts by private organizations and state agencies to curb the worst economic deceptions.

From 2010—2015, Balleisen directed the Rethinking Regulation Project, sponsored by Duke's Kenan Institute for Ethics. Since 2015, Prof. Balleisen has served as Duke's third Vice Provost for Interdisciplinary Studies, working with university-wide institutes and initiatives to foster collaborative, interdisciplinary research, teaching, and engagement.

Candis Watts Smith, PhD

Vice Provost for Undergraduate Education

Dr. Candis Watts-Smith currently serves as the Interim Vice Provost for Undergraduate Education at Duke, and she is the Faculty Director of the Duke Mellon Mays Fellowship Program. This program provides undergraduate students research funding, mentorship, and peer support in their junior and senior years in the areas of arts, humanities, and social sciences.

Smith's expertise highlights race and ethnicity's role in shaping the American political landscape. Her research agenda illuminates the ways in which demographic dynamics influence citizens' and denizens' of the U.S. understanding of their own identity, their political attitudes, and their policy preferences. Smith applies the knowledge gained from research to speak to issues that influence real people, including the effects racial attitudes on American politics, diversity issues, and access to resources that ought to be distributed equitably.

Prior to her appointment at Duke University, she was a member of the Departments of Political and African American Studies at Penn State. She is a co-host of the Democracy Works Podcast and a TEDx alumna.

The Duke Summer Research Showcase is Presented by:

Duke | UNDERGRADUATE RESEARCH SUPPORT OFFICE

Duke | OFFICE of UNDERGRADUATE EDUCATION

Participating Duke Organizations Include:

SURPH@Duke | Summer Undergraduate Research in PHarmacology & Cancer Biology

Summer Scholars Genome Sciences & Medicine

Duke Pratt School of Engineering

BSURF Biological Sciences Undergraduate Research Fellowship

Duke Experiential Education Office of Undergraduate Education

AMGEN Scholars Program

NCCU D-CARE Science Education Diversity Research

Duke Science & Society Huang Fellows

Duke Margolis Center for Health Policy

Duke Institute for Brain Sciences

Summer Neuroscience Program

Duke Evolutionary Anthropology

Summer Research Opportunity Program

About the Organizations

Duke Office of Undergraduate Education—Division of Experiential Education
The Office of Undergraduate Education (OUE) works to provide a transformative educational experience to all undergraduates at Duke by offering academic support, scholarly community, and experiential engagement opportunities.

OUE's Experiential Education (OUE-EE) Division offers students, faculty, and administrators opportunities and resources to engage in experiential programming. Our programs offer a unique and valuable opportunity for learners to gain real-world experience and develop important life skills that will serve them in their future endeavors. Duke programs and units affiliated with OUE-EE are: The Rubenstein-Bing Student-Athlete Civic Engagement Program (ACE), Duke Immerse, The Global Education Office, Duke Summer Experiences, and The Office of Global Health & Safety (OGHS).

Duke Undergraduate and Research Support Office
The Undergraduate Research Support Office (URS) promotes undergraduate research at Duke through hosting workshops and the annual Visible Thinking Symposium, funding independent research, assistantships and conferences, and by providing support for summer research programs. See the complete list of URS programs.

AMGEN Scholars Program at Duke
The Amgen Scholars Program (ASP) at Duke University is an intensive 10-week research experience for undergraduates interested in biotechnology and drug discovery. Scholars select a faculty mentor from 15+ departments including Pharmacology & Cancer Biology, Cell Biology, Biochemistry, Chemistry, and Biomedical Engineering, who conduct world-class drug discovery research. Funded by Amgen and multiple Duke departments.

Biological Sciences Undergraduate Research Fellowship (BSURF)
The BSURF Program is an 8-week, immersive experience for undergraduates immediately following their first year at Duke. The Research Fellows receive intensive professional training and engage in research from all areas of the biological and biomedical sciences. The program is sponsored by the Undergraduate Research Support Office of the Trinity College of Arts & Sciences, with generous funding from Trinity College and the Pratt School of Engineering. BSURF is directed by Ron Grunwald, PhD, Department of Biology, with Jessica Harrell, PhD, Undergraduate Research Support Office, and Grace Hooks and Kehali Woldemichael, Graduate Assistants.

Abstracts

Department of Psychology & Neuroscience
Summer Neuroscience Program
The Summer Neuroscience Program is an eight-week research program that allows our undergraduate students to carry out a full-time research project, which can then be used toward the Graduation with Distinction senior thesis. During the program, students also attend professional development sessions aimed at enhancing their networking capabilities, developing science communication skills, and exploring diverse careers in science and medicine. The eight-week experience concludes with a poster session highlighting their research accomplishments and enabling them to interact with the research community in DIBS.

Duke Evolutionary Anthropology
The Evolutionary Anthropology Summer Research Internship seeks to provide talented undergraduate students with an immersive training experience through hands-on research and professional development opportunities to further enhance their career trajectory.

Duke Institute for Brain Sciences
The Duke Institute for Brain Sciences (DIBS) mission is to promote interdisciplinary brain science and translate discoveries into solutions for health and society. Each year, DIBS touches thousands of people, from our 190-member Faculty Network and hundreds of students and trainees to the many who benefit from campus, community, and outreach activities.

Duke-Margolis Center for Health Policy
Summer Experience Program
The mission of the Robert J. Margolis, MD, Center for Health Policy at Duke University is to improve health, health equity, and the value of health care through practical, innovative, and evidence-based policy solutions. The Duke Margolis Summer Experience is a collaborative and mentored 10 week program that students (undergraduate and graduate) contribute towards a variety of projects aimed at improving health and the value of health care through research and the development of innovative, practical, and evidence-based policy solutions.

Duke-NC Central Alcohol Research Education (D-CARE)
Duke-N.C. **C**entral **A**lcohol **R**esearch **E**xperience (**D-CARE**): The field of alcohol studies lacks racial and ethnic diversity, and few systematic efforts exist to engage undergraduate students in alcohol-related research or coursework. This program engages undergraduates from underrepresented minority groups in a coordinated program including didactic coursework, intensively mentored research experiences, and professional development activities related to alcohol studies and careers in alcohol-related fields. The goal is to broaden the diversity of the next generation of researchers in the field of alcohol studies.

Abstracts

Duke Pratt School of Engineering
The Pratt School of Engineering offers several Research Experience for Undergraduate (REU) programs: the REU for Meeting the Grand Challenges and the REU in Electrical and Computer Engineering. Through these programs, students work on research projects related to solving the Grand Challenges of Engineering for the 21st Century under the guidance of engineering faculty.

Duke Science and Society Huang Fellows
The Huang Fellows Program trains students to understand science in the context of and in service to society. Through their participation in the program, Fellows learn how to integrate ethics, policy, and social implications into their scientific research. This highly selective program fosters a community of accomplished undergraduate scholars who will be trained in the sciences and grounded firmly in the liberal arts–and who will be well prepared to serve as leaders in sciences and the biomedical professions. The program is supported by a grant to the Duke Initiative for Science & Society from Dr. Andrew Huang.

Duke Summer Research Opportunity Program (SROP)
The Duke University Summer Research Opportunity Program (SROP) is a 10-week training program designed to give motivated undergraduate students hands-on experience in graduate-level biomedical research. We welcome applicants from around the United States who are seriously considering joining a Ph.D. graduate program after completing their undergraduate degree.

Summer Scholars—Genome Sciences & Medicine
About the Summer Scholars Program in Genome Sciences & Medicine Program mission: Provides a high-quality mentored training experience for underrepresented underclassmen to gain the experience, knowledge and skills to pursue and successfully complete a major in a STEM field and prepare for a job or higher learning in a STEM-related field.

Summer Undergraduate Research Pharmacology & Cancer Biology (SURPH@Duke)
This ten-week summer research experience focuses on learning how scientific discovery at the bench can be translated to treatment of disease. Students will train with a faculty mentor and carry out an independent research project in Duke's Department of Pharmacology and Cancer Biology. Funded by ASPET and the Department of Pharmacology and Cancer Biology. Learn more about SURPH here.

Abstract Book

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Abstracts

UNDERGRADUATE RESEARCH SUPPORT OFFICE

ABSTRACT NO. 1

A NOVEL ACOUSTOFLUIDIC PLATFORM FOR MICROFLUIDIC DROPLET PICOINJECTION

S Jain, T Naquin, T Huang
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Droplet microfluidics has risen in importance due to its ability to create test tube-like organization efficiently on a micro-scale. Injection of materials into each droplet precisely enables a wide range of lab-on-a-chip and biomedical applications, yet currently injection can only be done through manipulation of an electric field at high voltage. Here, we present an alternative method for particle injection into microfluidic droplets: an acoustofluidic platform that enables on-demand, energy-efficient, and biocompatible injection at the picoliter volume specificity. We use the acoustic radiation force via traveling surface acoustic waves to inject a controllable amount of fluid into each droplet. The injection rate is set in phase with droplet flow rate to allow for precise and regular injection. The picoliter injector can use input voltage as little as 20 V to increase droplet volume by as much as 20%. We applied the acoustic injector to increase the efficiency of droplet digital polymerase chain reaction (ddPCR), directly injecting reagents droplet-wise to ensure viability of each droplet during testing. This acoustofluidic picoliter injector broadens the utility of droplet microfluidics with both high efficiency and high throughput, enabling more seamless integration into multiplexed biocompatible systems.

DUKE-MARGOLIS SUMMER EXPERIENCE

ABSTRACT NO. 2

HOW SPIRITUALITY AFFECTS SHARED DECISION MAKING BY BLACK AND WHITE CAREGIVERS OF CRITICALLY ILL PATIENTS IN THE INTENSIVE CARE UNIT

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Health Policy and Management, UNC Gillings School of Global Public Health, Chapel Hill, NC 27599.

Background: Almost 600,000 Black Americans have critical illnesses each year, with about 20% dying in the intensive care unit (ICU). For Black caregivers, spirituality plays a major role in their personal lives and during shared decision making; however, Black families do not receive adequate spiritual support from ICU clinicians and ways to improve such support remain unknown. The aim of this study was to gain a better insight into ways to support such caregivers spiritually in the ICU.

Methods: 23 semi-structured interviews lasting between 45-60 minutes were conducted with white or Black caregivers of ICU patients at Duke Hospital. We asked participants open-ended questions about the role of their religion or spirituality (R/S) in their personal lives and during medical decision making. The interviews were recorded, transcribed and analyzed using NVivo 12 Pro and through a consensus-based coding process with the research team.

Results: The first theme observed was that many caregivers reported that they believed a higher power was in control of their loved one's outcome, whilst others reported the clinicians alone, or a mixture of both (e.g. the higher power working through the clinicians). R/S also affects caregivers in varying ways. For some, it provides hope, acceptance, comfort and resilience, and for others, it leads to disagreements with family

members during decision-making, or triggers hopelessness and fear for loved ones. The main suggestions raised by caregivers on ways to improve the spiritual support provided were to make such resources more accessible and to encourage ICU staff to offer up the resources to family members.

Implications: Our current findings highlight the importance of R/S for caregivers of critically ill patients. As a result, health policy efforts aimed at improving care for critically ill patients should prioritize training hospitals and clinicians on how to spiritually support caregivers in the ICU.

ABSTRACT NO. 3

POLICY STRATEGIES FOR CHILD MALTREATMENT PREVENTION

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*authors contributed equally

In 2021, there were 4 million reports of child maltreatment in the United States. Child abuse and neglect are adverse childhood experiences (ACEs), which have been linked to physical and mental health risk factors in adulthood. Given the long-term health consequences of ACEs, our Bass Connections project focuses on policy interventions for child maltreatment prevention. To better understand the existing landscape, we researched the Family First Prevention Services Act, Medicaid, and Child Protective Services. We created a research design focused on three contributory factors related to child maltreatment—(1) parental substance use, (2) parental mental health, and (3) parenting skills. In the upcoming school year, our team will evaluate the efficacy and utilization of risk-based interventions across multiple states in these three areas.

ABSTRACT NO. 4

THE COLLECTION AND UTILIZATION OF RACE, ETHNICITY AND LANGUAGE DATA ACROSS COMMERCIAL PAYERS IN NORTH CAROLINA

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Complete and accurate Race, Ethnicity, and Language (REL) data is critical for healthcare entities to effectively identify and address health disparities and direct their efforts to advance health equity. While North Carolina Medicaid has relatively complete REL data, less is known about practices among commercial payers in the state. This research explores the current landscape of REL data collection and utilization practices across the four largest commercial payers in NC. A review of the available literature, findings from previous Healthcare Transformation Workgroup convenings, and learning calls revealed there is limited REL data among commercial payers, yet a general understanding of its importance, and continued efforts to increase the collection of such data from members. There is also increased interest in understanding the role of social drivers of health in healthcare access and clinical outcomes. Looking forward, commercial payers can continue to learn from best practices exhibited across health systems and state Medicaid programs. Practices such as training healthcare staff on how to collect REL data from patients, increasing transparency with members about the use of the data, and aligning data granularity to follow minimum OMB standards are examples of effective practices in increasing self-reported REL data. Finally, increasing multi-stakeholder engagement in the alignment of REL data collection and utilization can allow an apples-to-apples comparison of health access and outcomes by REL across payer and provider organizations. Taken together, these efforts to collect and use REL data can work to advance health equity in NC.

ABSTRACT NO. 5

BARRIERS FACED BY RURAL PROVIDERS IN MACRA PARTICIPATION

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Rural healthcare providers face unique challenges in caring for populations that are often elderly, uninsured, suffering from multiple chronic diseases, and living in areas with poor social determinants of health. Without the support of sub-specialists and with limited providers, they treat a wide range of conditions with limited access to sophisticated technology. Rural providers have also encountered these challenges in meeting the requirements of MACRA, the Medicare Access and CHIP Reauthorization Act of 2015, which sought to generate smarter spending and positive health outcomes by concentrating on incentives, quality care delivery, and information sharing. I conducted a qualitative literature review that examined the struggles that rural providers face in meeting the demands of the Quality Payment Program and the efficacy of the programs and services implemented to support these practices. Challenges faced by rural practices in meeting MIPS requirements as well as transition to Advanced Alternative Payment Models (AAPMs) include a lack of capital to finance the upfront transitional and subsequent ongoing costs as well as challenges in conducting the data analysis necessary for participation. Solutions to these challenges include the CMS Accountable Care Organization (ACO) Investment Model (AIM), which encouraged the growth of Medicare Shared Savings Program (MSSP) ACOs in rural and underserved areas by providing financial support to eligible MSSP ACOs by means of prepayment of shared savings, CMS's Small, Underserved, and Rural support program, which provided clinicians with in-person and virtual training and education on all aspects of the program, and the provision of upfront funding and global payments for providers transitioning to AAPMs. These programs have helped to alleviate burdens for rural providers to participate in MACRA programs and increased and ongoing support from CMS to assist in care coordination, data analysis, and funding to adapt to changing program requirements will be crucial to ensure that the gap between rural and non-rural providers in MACRA participation is bridged.

ABSTRACT NO. 6

ADDRESSING HOUSING-RELATED SOCIAL NEEDS THROUGH MEDICAID: LESSONS FROM NORTH CAROLINA'S HEALTHY OPPORTUNITIES PILOTS

V. Nandagiri, K. Huber, R. Nohria, N. Pylypiw, M. Dennison, Y. Pokam, B. Van Stekelenburg, R. Whitaker, A. Van Vleet, A. Thoumi, M. Lyn, R. Saunders, W. Bleser
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The impact of stable, safe, and affordable housing on health costs and outcomes is well-documented. North Carolina Healthy Opportunities Pilots ("Pilots") is an experimental Medicaid Section 1115 Waiver Demonstration Program assessing the impact of providing services for four domains of health-related social needs (HRSNs), one of which is housing, in three regions of the state. Housing services are provided by local community-based organizations and are reimbursed based on a novel social service fee schedule.

In our mixed-methods study, we explored the design and implementation of Pilots housing services. Quantitatively, we analyzed census tract-level data to visualize the housing-health relationship across the Pilots regions. Qualitatively, from 2021 through mid-2023, we conducted 20 key informant interviews focused on Pilots housing services while also discussing housing as part of 2 focus groups and 1 expert stakeholder convening. Consensual, team-based qualitative research methods were used to synthesize major themes and policy implications.

We identified four key implementation and policy themes addressing 1) the geographic variability of the housing-health relationship within the Pilots; 2) the intricacies of designing an appropriate fee schedule for housing services in Medicaid; 3) financial models to support community-based organizations in sustaining housing service delivery; 4) strategies for cross-sectoral collaboration to provide high-quality housing services. These themes touched on challenges, but also successes and innovations in Pilots housing services.

We built on interview themes by discussing policy implications in several areas: balancing expanding service delivery with ensuring efficiency and return on investment; expanding current housing services by altering the Pilots fee schedule or bundling services together; exploring potential future financial models to support housing services such as capitated models and value-based payment arrangements. These implications were considered in the context of North Carolina's rapidly changing Medicaid landscape with the upcoming expansion of Medicaid and the potential next phase of the Pilots.

ABSTRACT NO. 7

FACTORS CONTRIBUTING TO PERSISTENTLY ELEVATED A1C AND POOR GLYCEMIC CONTROL IN PATIENTS WITH DIABETIC RETINOPATHY

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Hyperglycemia, as evidenced by elevated hemoglobin A1C, is associated with greater incidence and worsened disease progression of diabetic retinopathy which is the leading cause of blindness in American adults. It has been demonstrated that proper treatment of hyperglycemia reduces both the prevalence and progression of diabetic retinopathy. This study aims to elucidate which factors largely contribute to persistently elevated hemoglobin A1C levels in Duke Health System patients with Type 1 or Type 2 diabetes and diabetic retinopathy. A chart review of 87 patients with both diabetes and diabetic retinopathy was performed to determine if their medication regimen was optimal, and if there were issues with medication costs, intolerance, or adherence. Subsequently, medication recommendations were made to primary care providers. Patient-reported social determinants of health (SDOH) and history of diabetes education were also recorded. Hemoglobin A1C values as well as age, race, and ethnicity data were retrieved on 11,446 patients with diabetic retinopathy and compared to the subgroup of 87 rounded patients with diabetic retinopathy to ensure a representative sample was retrieved. It was found that medication adherence and lack of diabetes self-management education and support (DSMES) had the highest prevalence in the subgroup where 41.3% and 40.2% reported these issues, respectively. Despite these results, the highest average A1C values were correlated with SDOH not on file (avg. A1C = 10.1%), physical inactivity (avg. A1C = 9.9%), and medication cost/underinsurance issues (avg. A1C = 9.9%). These findings suggest that more referrals to care management and/or DSMES services should be facilitated to improve glycemic control in patients with diabetic retinopathy. Furthermore, policy changes to address financial factors like the cost of medication and food insecurity should be developed and employed to help control patients' hyperglycemia and decrease the incidence or progression of diabetic retinopathy nationwide.

ABSTRACT NO. 8

UNDERSTANDING THE NETWORK OF DEVELOPMENT ASSISTANCE FOR HEALTH (DAH): UNVEILING THE DYNAMICS OF HEALTH AID FLOWS

A. Owens, O. Ogbuoji
Sanford School of Public Policy; Margolis Center for Health Policy; Duke University; Durham, NC, 27701

The Network DAH project aims to investigate the dynamics of Development Assistance for Health (DAH) flows and analyze the network properties of the global DAH system. The study focuses on understanding the central nodes, the distribution of aid, and the network's robustness.

Using R Studio, the project involves data formatting and manipulation to create a comprehensive dataset of DAH flows from 1990 to 2021. The data is then visualized in Gephi, enabling the exploration and analysis of the network structure.

Preliminary findings reveal a hierarchical pattern in the DAH network, with a small number of donor nodes exhibiting high centrality, while numerous recipient nodes rely on them for aid. The Eigenvector Centrality algorithm identifies prominent nodes such as the United States, Bill & Melinda Gates Foundation (BMGF), and the United Kingdom as key players in the network. Additionally, network analysis reveals that the DAH network exhibits limited robustness, indicating vulnerability to disruptions in connectivity. Removal of highly central nodes may lead to significant network failures.

Understanding the network dynamics and central nodes in DAH can inform aid allocation strategies and provide insights into the resiliency of the global health aid system. Further analysis and exploration of the DAH network are ongoing to gain a comprehensive understanding of its structure and implications for global health assistance.

ABSTRACT NO. 9

THE EFFICACY OF PATIENT INSURANCE DECISION AIDS

A Sai Harshith Rachakonda, B Anna Hung, PharmD, PhD
Duke University Trinity College of Arts and Sciences, Duke-Margolis Center for Health Policy

Many patients find selecting a health insurance plan an arduous and confusing process due to many factors, such as system complexity, potentially having competing options, and a dearth of decision support. Patient Insurance Decision Aids (PtDAs) can equip patients with better tools to assist their insurance selection process, tailor relevant information, and offer further support in understanding costs. This systematic literature review aimed to survey the current research landscape of PtDAs to 1) evaluate PtDA efficacy as measured by patient satisfaction and 2) examine the best aspects of PtDA design that may contribute to their success. This study screened 168 studies via Covidence under PRISMA review guidelines and found 16 RCTs relevant to the research aims. The literature review was performed alongside two stakeholder interview panels providing input into what patients would like to see reflected in PtDAs. This review found that deployed PtDAs have augmented patients' insurance selection process, making it more transparent. However, effects on insurance-related financial toxicity were mixed, with no conclusive effect elucidated. The most efficacious PtDA designs included smaller choice sets, open designs, less numeracy, and more symbolism. Future PtDA studies and implementations should consider these results to supplement their development process. We hope this can increase patient satisfaction with the insurance selection process, ameliorate potential financial toxicity, and eventually lead to more widespread PtDA use.

ABSTRACT NO. 10

LEVERAGING REAL-WORLD EVIDENCE (RWE) IN SHORTENING RARE DISEASE DIAGNOSTIC DELAYS

N Shaw
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Delay at each stage of receiving a rare disease diagnosis presents one of the primary barriers to treatment, mainly due to a lack of sufficient research and lags in referrals to specialty care. Real-world data (RWD) provide a powerful source of support at multiple points of delay by bolstering patient registries, catalyzing synthetic data genesis, and increasing accessibility of contribution through wearable biometric monitoring devices. The primary aims of this project are to establish the feasibility of incorporating RWD and synthetic data into rare disease patient registry generation and identify a model by which patient-generated health data (PGHD) can effectively accelerate rare disease detection, diagnosis, and treatment for patients. A literature review conducted through a PubMed search of "'rare disease' AND (wearables OR 'patient-generated health data') AND diagnosis" yielded eleven articles for analysis. Myriad multinational patient registries set a precedent for using RWD to catalogue rare disease symptom progression and treatment outcomes as well as specialty referral networks, and machine learning methods provide an avenue for efficient, accurate decision support and dataset augmentation. Furthermore, several wearable biometric monitoring devices have emerged to monitor rare disease progress and produce PGHD to contribute to registries and inform diagnosis. Consequently, the proposed model leverages wearables to use multimodal sensing to gather data on symptoms, compare these data to existing registries and RWD, and alert and refer the user to specialty care. Understanding how to strengthen patient registries with more prospective RWD and natural history data and then implementing these methods could provide a foundation for and catalyze this method of bridging rare disease diagnostic delays.

ABSTRACT NO. 11

IDENTIFYING BARRIERS TO THE DEVELOPMENT OF PRETERM BIRTH THERAPEUTICS AND A PATH FORWARD

R. Shendell, & D. Kim
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One in ten babies in the United States is born preterm and preterm birth is a leading cause of infant mortality. Although preterm birth poses a significant medical and economic burden on the individuals, families, and communities it affects, there are currently no FDA-approved therapeutics for preterm birth. Treatments used off-label to prevent and mitigate preterm birth are limited and their effectiveness is debated by clinical researchers, doctors, medical organizations, and regulatory bodies. Through a partial literature review, this project investigated the evidence and use of current treatments for preterm birth and explains the factors shaping the availability of effective preterm birth therapeutics. The poster presents key barriers that regulators, industry sponsors, and researchers face during drug development, clinical trials, and drug approval for preterm birth therapeutics. The project concludes with initiatives and policies that should be prioritized to incentivize drug development and improve clinical evidence for treatments to prevent preterm birth.

ABSTRACT NO. 12

DEVELOPING A DATA COLLECTION AND EVALUATION APPROACH FOR NCINCK REFERRALS

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The North Carolina Integrated Care for Kids (NCInCK) Program is a pilot model sponsored by the Centers for Medicare and Medicaid Services (CMS) dedicated to connecting children insured by Medicaid in a 5-county region with intensive care management. Children are identified for the model based on an innovative risk-stratification algorithm that merges data on social, educational, behavioral, and physical health factors that contribute to the overall well-being of children. However, data updates to NCInCK's algorithm experience lags, which can delay children's ability to access care management services in a timely manner, possibly leading to worsened health outcomes. The algorithm may also miss some children who have needs not captured by the data utilized. To mitigate this challenge, NCInCK implemented a referral process where community partners can directly refer children to NCInCK care management services. The goal of the following project is to evaluate the NCInCK referral process and to develop a more streamlined approach to track engagement and model completion progress among children in the NCInCK model using RedCap. We based our guiding principles on the Implementation Research Logic Model (IRLM) and developed a data mapping tool to guide us in considering the factors, strategies, and mechanisms we are encapsulating in the referral tracker. In sum, we developed a RedCap instrument that streamlines the tracking of referred children through the NCInCK care model. The data from the new tracking system will be used by NCInCK to evaluate the impact of opening InCK to community referrals and aid the team in improving equity in access and decreasing health disparities among children in the model. Our instrument should support decision-making processes for NCInCK and promote transparency in health outcomes for children in the model.

ABSTRACT NO. 13

BARRIERS TO DIABETES EDUCATION

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Diabetes Self-Management Education and Support (DSMES) is a program that provides an evidence-based foundation to empower people with diabetes to navigate self-management decisions and activities. Despite large success for patients that completed DSMES, there are low referral and engagement rates that have limited the expansive effect that DSMES could have on diabetes patients. In a review of 26,970 patients with diabetes receiving care at Duke Health who had over 84,889 visits where diabetes control was not at goal (A1c over 8%), only 7.1% of patients received a referral to DSMES. There was a significant racial difference, where even when controlled for demographic, clinical, and service factors, Black patients were 1.49 times more likely to get a referral to diabetes education than their White counterparts ($p < 0.001$). We investigated barriers to diabetes education within Duke Clinics, where provider, patient, and health system factors were identified. To better address the complicated referral process, we recommend that restrictions whereby only providers can refer be removed, giving nurses and patients the ability to refer themselves. In addition, the ability to self-schedule is a known improvement in patient-keeping appointments and patient satisfaction. Providing flexible venues (zoom, in-person, class-based, one on one) and times for appointments are also key. Lastly, overall spending for DSMES services needs to increase. We hope to further investigate factors related to a lack of participation and work to develop a "How Much Do You Know about Diabetes Education"

test for patients to improve motivation, understanding, and attendance at DSMES services.

ABSTRACT NO. 14

ENGAGING COMMUNITY STAKEHOLDERS IN STATE MEDICAID PROGRAMS TO ADVANCE HEALTH EQUITY: A LANDSCAPE REVIEW AND ANALYSIS

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A growing number of Medicaid programs are implementing policies to improve population health and address barriers to accessing health care. As state Medicaid Agencies adopt new policies to reform health systems, public input in policy solutions is important for shaping how health care is managed and delivered. By engaging diverse community stakeholders, especially in health care payment and delivery policies, state Medicaid programs can create person-centered initiatives to address people's needs and support communities. Despite significant literature on the benefits of community partnerships in health care planning, there is limited evidence on state efforts for engaging consumers in the design and implementation of Medicaid policies. To investigate state Medicaid strategies for engaging consumers in health policy and programmatic decision making, this landscape review synthesizes available information on Medicaid community engagement approaches and highlights motivations, barriers, and benefits of engagement activities. An assessment of state Medicaid programs identified large variations in consumer engagement efforts with a range of specialized and multi-faceted strategies to engage different Medicaid populations. Additionally, common motivators for engaging community stakeholders in policy design included regulatory obligations and the need to identify community issues, needs, and priorities in advancing health equity efforts.

ABSTRACT NO. 15

A REVIEW OF COMMUNITY-BASED PARTICIPATORY RESEARCH INVOLVING DIVERSE COMMUNITY PARTNERS

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Community-based participatory research (CBPR) is a collaborative approach to equitably involve partners from both academia and community in the research process and integrate the unique perspectives of diverse members. Although many studies have documented the differences between academic scholars and community partners and their influence on CBPR, few have examined the diversity among community partners. This review looks at the literature on CBPR with community partners from different demographic backgrounds and regions with respect to reasons for, benefits and challenges of this diversity, and strategies used to address diversity. Through database search (PubMed, Web of Science, Scopus, and Global Health) and bibliographical information, we identified and included 64 articles in our analysis. Our analysis showed that current CBPR involves community partners that differ in race/ethnicity, socioeconomic status, region, sexual orientation, and age. Despite varied demographic backgrounds, only a few of the studies represented in the literature paid attention to the differences between community partners. Those that did indicated that the diversity across partner communities brought both benefits and challenges. While this diversity brought different perspectives and unique expertise from each partner and facilitated connections to communities, tensions from bias, stereotypes, and distrust among community partners also posed new challenges. To resolve potential conflicts, the literature cites acknowledging the differences, developing a shared vision, and allowing flexible project management as potential hopeful solutions. Through this review, we identified a research gap in CBPR partnership

and called for more attention to diversity among community partners.

ABSTRACT NO. 16

REIMAGINING GLOBAL HEALTH MULTILATERALISM: A QUALITATIVE STUDY ON IMPROVING PANDEMIC VACCINE EQUITY

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The focus of this project, funded by the Carnegie Corporation of New York, is to reconceptualize the global response to pandemics and other global public goods for health, with the development of a novel pandemic vaccine finance facility called “PANVAX.” The idea behind this project is to design a pandemic vaccine finance facility that has incentives so strong, every country and multilateral organization would feel compelled to become an active participant. In creating a unified response to future pandemics, we will be better prepared to tackle global health crises in a timely manner, ultimately saving lives and mitigating financial loss. This 24-month project will primarily use interviews with key informants involved in pandemic preparedness, the application of game theory, qualitative analysis, and policy analysis to help guide a design for PANVAX.

Thus far, I have analyzed the transcripts of the first ten interviews. Three key themes have emerged: focusing on regional cooperation may be more realistic to develop than a global unified response, decentralizing production and manufacturing is an imperative next step to increase global supply of medical countermeasures, and public funding put towards R&D should lay out specific rules regarding sharing of intellectual property and findings. With the culmination of this project in September 2024, representatives from multilateral health agencies, ministries of health and finance from certain low-income and middle-income countries, and other individuals in the space of global health will be brought together for a policy workshop to discuss next steps and policy implications.

SUMMER SCHOLARS PROGRAM IN GENOME SCIENCES AND MEDICINE

ABSTRACT NO. 17

IN VIVO VALIDATION OF AN α-SYNUCLEIN-TARGETED EPIGENOME THERAPY FOR PARKINSON'S DISEASE

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Parkinson's disease (PD) is a prevalent neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia night (SN). Elevated α-synuclein (SNCA) levels in the SN are causative in the pathogenesis of PD. Current treatments for PD manage symptoms, but do not address the underlying causes of the disease. Our study aims to explore an innovative approach, SNCA-targeted epigenome therapy, as a potential treatment strategy for PD.

We employed an all-in-one lentiviral vector (LV) carrying deactivated CRISPR/(d)Cas9 fused with the catalytic domain of DNA-methyltransferase 3A (DNMT3A). We have previously shown in vitro that this LV-dCas9-repressor system effectively reduces SNCA expression in dopaminergic neurons derived from human induced pluripotent stem cells . We now progress to in vivo validation with a PD mouse model, using AAV-A53T-SNCA to induce overexpression of human SNCA in the SN. We performed bilateral stereotactic injection of the AAV-A53T-human SNCA vector into the mouse SN, the right SN was co-injected with the therapeutic LV-dCas9-repressor and the left SN was co-injected with the control inactive LV-dCas9 vector.

Using immunofluorescence techniques we measured levels of SNCA protein in the SN.

Specifically, we quantified the levels of total, phosphorylated, and aggregated human SNCA. Additionally, we examined the levels of tyrosine hydroxylase (TH), a marker of dopaminergic neurons, in both the SN and the striatum to evaluate the loss of dopaminergic neurons. qPCR analysis targeted SNCA and TH gene expression specifically in the SN, allowing us to further understand the molecular changes resulting from our therapeutic intervention. This integrative approach provides crucial data on SNCA pathology and dopaminergic neuron preservation.

The goal of our study is to reduce SNCA expression in a mouse model of PD, leading to a reversal of PD pathological hallmarks. Achieving these outcomes would provide in vivo validation for our innovative therapeutic strategy for PD treatment.

ABSTRACT NO. 18

EXPANDING REFERENCE DATABASE FOR DNA METABARCODING

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To study how diet affects the gut microbiome, it is important to have accurate information about what individuals consumed. Due to various reporting biases and human error, this is difficult to determine from self-reported surveys. trnL DNA metabarcoding uses primers designed to target highly conserved regions of DNA that flank variable regions of DNA in the chloroplasts of plants. These variable regions are “barcodes” unique to each plant species. We can cross-reference the barcodes found in stool samples with known crop DNA to determine the crops present in the stool samples. DNA metabarcoding was commonly used to determine what animals consumed from their stool samples to overcome the limitations of field studies. The technique has been further developed for use on human stool samples to precisely determine food consumed without the inaccuracies that arise from self-reporting. This project involves expanding a reference database of crop DNA by extracting and sequencing the DNA from 22 major crops. The 22 major crops include mamey, pearl millet, and pili nuts, and are commonly eaten in parts of the world other than North America. These crops are important to sequence to develop an accurate perception of global eating patterns. By using DNA metabarcoding to determine what people consumed, we hope to both track dietary patterns across global populations and give individuals meaningful feedback about their diets.

ABSTRACT NO. 19

DALBAVANCIN AS AN OPTION FOR TREATMENT OF *Staphylococcus aureus* BACTEREMIA

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Staphylococcus aureus bacteremia is a bloodstream infection caused by the bacteria *Staphylococcus aureus* which can cause serious complications, such as endocarditis, bloodstream infections, pneumonia, or bone and joint infections. It is the leading cause of skin and soft tissue infections such as abscesses (boils), furuncles, and cellulitis. Current treatment for *Staphylococcus aureus* typically involves the use of intravenous delivery of antibiotics for a prolonged period of time, usually around 4 weeks. This method poses a risk of catheter-related complications. Dalbavancin is an appealing treatment for *Staphylococcus* due to its potent activity against the bacteria and long half-life, without the need for vein access. “DOTS,” which stands for Dalbavancin as an Option for the Treatment of Staphylococcus Aureus Bacteremia, is an ongoing clinical trial to determine the many potential cost benefits of this alternative treatment. For IV drug users who have to be monitored for the entirety of their time on the

catheter, Dalbavancin introduces an alternative to avoid the high hospital bills they would normally face. Dalbavancin is also more economical for hospitals, as two doses of the drug are cheaper to administer than 4 weeks on a catheter.

In Dr. Wahid's clinical research group at Duke University, this study was performed among 37 patients. Eligible and consenting patients were randomized into either a treatment or a standard-of-care group. 24 patients received standard of care while the other 13 received Dalbavancin. The study is ongoing, and conclusive results cannot be provided at this time. The primary objective of this study is to compare the Desirability of Outcome Ranking (DOOR) of Dalbavancin to that of the standard of care. We hope to provide a more affordable and less invasive treatment for the bacteremia.

ABSTRACT NO. 20

IDENTIFYING LIGANDS FOR ODORANT RECEPTORS

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The ability of animals to sense distinctive scents is attributed to the activity of odorant receptors (ORs) that interact with volatile molecules in the environment. Humans possess approximately 400 ORs, whereas mice have over 1,000 ORs. However, the mechanisms through which ORs of diverse species perceive odors remains unclear. In this study, we focused on Class I mouse ORs, specifically MOR 31-7 (also known as Olfr 649, Or52h2), MOR 7-1 (Olfr 578, Or51g1) and OR-S6 (MOR42-3, Olfr5444, Or55b4) in addition to the engineered human consensus ORs consOR51 and consOR52. Previous research has shown that Class I ORs respond to carboxylic acids; hence, the focus of this study was to identify the agonists for these particular ORs via cell-based screenings against a panel of 53 carboxylic acids. Our findings revealed that medium chain carboxylic acids function as the agonists for MOR31-7. For MOR7-1, consOR51 and consOR52, the agonists were identified as medium to long chain carboxylic acids, while the agonists for OR-S6 were determined to be long chain dicarboxylic acids. This research provides further insight into the molecular underpinnings of odor perception.

ABSTRACT NO. 21

DISCHARGE, READMISSIONS, ANALYSIS, AND MANAGEMENT IN SEPSIS (DReAMS)

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Sepsis is the body's extreme reaction to infection that could trigger life-threatening organ dysfunction. This can lead to many complications beyond higher mortality and morbidity such as more readmissions and a greater cost to the healthcare system. Sepsis is the single most expensive cause of hospitalization in the United States; however, little is known about risk factors that lead to readmissions in these patients. Historically, readmissions are higher in underserved populations. This prospective cohort study named Discharge, Readmissions, Analysis, Management in Sepsis (DReAMS) was designed to investigate the social determinants of health's (SDOH) association with readmission in septic patients. The factors of SDOH included were social identity factors (race, ethnicity, gender), health behaviors (smoking, substance use, physical activity), health insurance, financial strain (insecurity related to housing, food, and transportation), neighborhood characteristics, employment status, education level, social connections, and stress levels.
This study was performed among 182 patients. We screened patients then approached eligible ones with a valid questionnaire to gather data on SDOH. Then, we followed patients for 30 days after discharge to determine any readmission. Of

the 182 patients, 44 of them were readmitted. The mean age of the patients was 62.8 years (SD,15.8 years), 44% were female, 41.3% were a race other than White, and 92.3% reported non-Hispanic ethnicity. Pneumonia was the most common cause of sepsis (29.7%) followed by intra-abdominal causes (22%). The majority of patients were admitted to non-surgery wards (94.5%) and approximately half of them (56%) had an infectious disease consult.
Our hypothesis is that there will be higher readmission rates among individuals from underserved social backgrounds. Through this work, we hope to address factors associated with readmission in septic patients to reduce this health problem by sensitizing decision-makers on this issue.

ABSTRACT NO. 22

BIDIRECTIONAL REGULATION OF ARC USING EPIGENOME EDITING TOOLS

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The ability to learn and form memories is a crucial part of survival. At a cellular level, these processes occur through the adaptation of neuron synapses as a response to stimulation. Upon external sensory stimulus, there is a rapid and transient induction of transcription of specific genes, called Immediate Early Genes (IEGs) that coordinate downstream processes essential for behavior. One specific IEG, Activity Regulated Cytoskeleton associated protein (Arc), is specifically important for synaptic plasticity and memory consolidation because it acts directly at synapses. Arc functions to modulate the strength of synapses through the endocytosis of AMPA receptors, a type of glutamate receptor that mediates the excitatory signal of neurons. To better understand the role of Arc in synaptic plasticity, we will study the regulatory mechanism mediating its expression. Like all other genes, IEGs are regulated by activity-regulated transcription factors that bind to DNA elements such as promoters and enhancers. Promoters are required for all transcription whereas the enhancer region works with the promoter to maximize transcription. However, for Arc the activity-regulated transcription factors bind predominantly at the enhancer, suggesting that activity-dependent induction of Arc required its enhancer. To better understand the role of Arc in synaptic plasticity, we will manipulate the expression of Arc by targeting repressors and activators at both the enhancer and promoter to dissect the contribution of both regulatory elements. In this study, we are developing these viral tools to bidirectionally regulate Arc at its promoter and enhancer. Future experiments will use these tools to modulate expression in culture and in vivo.

SURPH

ABSTRACT NO. 23

TARGETING OF PROTEIN TYROSINE PHOSPHATE RECEPTOR TYPE D FOR ANTI-ADDICTION THERAPEUTICS

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The illicit use of opioids and stimulants pose a significant and urgent public health concern, as addiction to these drugs disrupts a great number of lives and overdose deaths have surged in recent years. Methadone and Buprenorphine are current therapeutics for individuals who suffer from opioid use disorder (OUD) as they alleviate withdrawal symptoms. However, these drugs pose a significant risk of dependence and unfavorable side effects, while also neglecting the issue of relapse behaviors. Treatment for stimulant abuse remains problematic. Recent research has identified receptor protein tyrosine kinases (RPTKs) as potential targets for anti-addiction therapeutics due to their regulation of synaptic transmission and role in synaptic plasticity. Protein tyrosine phosphate receptor type D (PTPRD) is a

transmembrane RPTK found in high concentrations within dopamine neurons. Due to dopamine's key position in reward and reinforcement brain circuits and the role of RPTKs, PTPRD inhibition should reduce rewarding drug-related neural changes in synaptic formation and signaling, reducing drug self-administration. In this study, we assessed the effectiveness of Pentilludin, a PTPRD inhibitor, in reducing the self-administration of the opioid drug remifentanil and the stimulant drug amphetamine. We assessed the effectiveness of intermittent Pentilludin injections on the self-administration rates of these drugs in Sprague-Dawley rats. Intermittent dosing was used to help reduce the development of tolerance to the drug. We have documented Pentilludin's effectiveness in decreasing self-administration of remifentanil and preliminary results indicate decreases in amphetamine self-administration. In the future Pentilludin could be tested with alcohol and nicotine due to their shared actions on dopamine systems. In adjunct to current OUD therapeutics, we believe Pentilludin can serve as a powerful tool in helping individuals with substance use disorder overcome the challenges of relapse.

ABSTRACT NO. 24

INVESTIGATING EPH/EPHRIN SIGNALING IN NEURONAL PRIMARY CILIA

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The primary cilium is an antennae-like organelle present on most vertebrate cells and serves as an environment for many cell signaling pathways important in neuronal development. Furthermore, dysfunctional cilia have been implicated in several neurodevelopmental disorders as a result of improper Hedgehog signaling. To identify additional pathways associated with primary cilia in neuronal migration and maintenance we previously employed a biotin-based proximity labeling strategy. From this screen we identified components of the Eph/ephrin pathway, which mediates axon guidance, as enriched in the cilium. However, the details surrounding the neuronal cilium's participation in the Eph/ephrin pathway are not well known. Here we investigate this relationship by examining ciliary Eph/ephrin trafficking in mammalian cell lines. By overexpressing these pathway components in IMCD3 cells, we observed ciliary localization. By generating stable cell lines through retroviral infection, we will investigate trafficking of this pathway in response to different stimuli, such as serum withdrawal or addition of ligand. Accomplishing this will allow for the elucidation of the role of the primary cilium in neuronal axon guidance, and thus provide molecular context to human neurological conditions caused by the malformation of primary cilia.

ABSTRACT NO. 25

INCREASING THE RADIOSENSITIVITY OF CANCER CELLS TO IMPROVE RADIATION TREATMENT EFFICACY

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Radiation therapy is one of the most common treatment measures for a wide range of cancers. Its effectiveness heavily relies on its ability to trigger the accumulation of lethal DNA damage. Ionizing radiation induces various forms of DNA lesions, with DNA double-strand breaks being the most detrimental to the cell. Such lesions activate the DNA damage response pathway, which involves DNA damage sensing, cell cycle arrest, and DNA repair. However, cancer cells with highly efficient DNA repair capacities are radioresistant. This radioresistance continues to be a major limitation for therapeutic applications. Here we show that targeting genes or proteins involved in the DNA damage response pathway may be a promising therapeutic strategy for overcoming radioresistance and increasing cancer cells' sensitivity to radiation treatment. After identifying multiple candidate hits through a genome-wide CRISPR screen, we administered small molecule

inhibitors to investigate the effects of inhibiting Rac1 and Wdr5 function in the SMA-560 mouse glioma cell line. A synergistic reduction in cell viability was observed for two of the five inhibitors administered in combination with radiation treatment. Furthermore, we have generated SMA-560 gene knockouts of hits from the CRISPR screen that are implicated in cancer progression but have not been shown to be involved in radiosensitization. Our in vitro assays have served as a starting point for more sophisticated experiments in vivo. Moving forward, we hope to measure the phenotypic effects of the gene knockouts using both brain slice and mouse models. Such findings could bring new therapeutic combinations into the clinic for future cancer patients needing radiation treatment.

ABSTRACT NO. 26

QUANTITATIVE ANALYSIS OF N-CADHERIN EXPRESSION THROUGH PROSTATE CANCER PROGRESSION

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In prostate cancer, the progression from the androgen-dependent to castration-resistant type marks a lethal change through different mechanisms. One of the mechanisms currently being investigated is the increase in N-cadherin levels which confers many advantages for prostate cancer growth and metastasis. To better characterize this mechanism, quantitative changes in N-cadherin expression were monitored weekly. This process involved an assay of transferring androgen-dependent prostate cancer cells into an ADT (androgen-deprivation therapy) medium, which simulates the standard treatment for prostate cancer clinically. Quantitative analysis of the RNA transcript and protein expression levels was collected from the weekly samples and compared to the control samples. A general increase in the expression of the N-cadherin at the mRNA level was observed. Also, there was an increase in the level of the N-cadherin protein expression. Overall, these results support the hypothesis that increases in N-cadherin expression are correlated with the progression of early-stage prostate cancer to the more lethal late-stage type. In the future, knowing the degree of the N-cadherin expression changes can provide vital information for developing new therapeutic strategies for prostate cancer that becomes resistant to androgen deprivation therapy.

ABSTRACT NO. 27

MEASUREMENT OF OROFACIAL PAIN IN A MOUSE MODEL OF CHRONIC PRIMARY PAIN

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Chronic primary pain conditions (CPPCs), including pelvic pain, lower back pain, and temporomandibular disorder, affect one in three Americans. Previous work in our lab demonstrated that low activity of the catechol-o-methyltransferase (COMT) enzyme and corresponding increases in catecholamine levels cause widespread pain affecting abdominal, back, and plantar sites through activation of adrenergic receptor β3 (Adbr3). Yet, pain at orofacial sites characteristic of temporomandibular disorder has not been evaluated in our mouse model of CPPCs. Thus, here three groups of female wild-type or COMT+/- mice were exposed to three days of swim stress or sham stress, followed by a molar extraction or sham surgery. Using this model, we conducted three behavioral tests on the orofacial region of the mouse. We measured grimace (spontaneous pain), feeding behavior (non-evoked pain), and orofacial Von Frey (evoked pain) over 14 days, with the operator blinded to

the conditions of the mice. While data collection and analysis are ongoing, we predict that compared to wildtype mice COMT+/- mice undergoing the stress and molar surgery intervention will exhibit greater grimace scores, reduced attempts to drink condensed milk, and increased hyperalgesic responses to punctate von Frey stimuli. Future studies may be required to refine assessments and test mechanisms of orofacial pain.

AMGEN SCHOLARS PROGRAM

ABSTRACT NO. 28

A REG4+ NICHE CELL POPULATION IN COLON CANCER

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Colorectal cancer (CRC) is a leading cause of cancer-related mortality in the United States. Unraveling the underlying mechanisms that fuel CRC aggressiveness is paramount to developing effective therapeutic strategies. The cancer stem cell hypothesis posits that a minority subpopulation of tumorigenic cells (i.e., cancer stem cells) gives rise to non-stem cancer cells and drives tumor expansion. Herein, we investigate the intricate involvement of a distinct subpopulation of Reg4+ colon cancer epithelial cells in tumor progression. Employing single-cell RNA sequencing, we delineate and characterize these Reg4+ cells to elucidate their impact on tumor growth and development. We generated a novel genetically engineered mouse model of colon cancer in which Reg4+ cells are labeled with DsRed and inducible diphtheria toxin receptors for targeted elimination of Reg4+ cells. Precise colonoscopy-guided injection techniques are employed to initiate tumors in the distal colon, with subsequent selective elimination of Reg4+ cells through targeted DT (diphtheria toxin) treatment. Our findings demonstrate a significant reduction in tumor size following the selective elimination of Reg4+ cells. These results unveil fundamental insights into the intricate mechanisms and the pivotal role of Reg4+ cells in facilitating the growth of cancerous cells. By shedding light on the distinctive function of Reg4+ cells in promoting CRC progression, our study paves the way for promising targeted interventions in the treatment of colon cancer.

ABSTRACT NO. 29

AN INJECTABLE THERMALLY RESPONSIVE POLYPEPTIDE SCAFFOLD FOR PERIPHERAL NERVE REPAIR

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Despite affecting over 20 million people in the US, only 50% of patients with peripheral nerve injuries achieve meaningful sensorimotor recovery and the majority of patients continue to experience chronic pain. Thus, there is a pressing need for the development of therapeutics to enhance peripheral nerve repair.
Partially ordered polypeptides (POPs) are an artificial recombinant protein designed to mimic native elastin, one of the most abundant proteins in the human body. POPs transition from an injectable liquid at room temperature to a porous network in vivo that rapidly integrates into surrounding tissue with minimal inflammation. Furthermore, the molecular tunability of POPs allows for precise control over matrix properties based on concentration and composition, providing a structure facilitating axonal migration, neovascularization, and providing the needed mechanical support for successful neuroaxonal regeneration.
With a sequence precisely modifiable at the genetic level, POPs can be fused with bioactive sequences to encourage nerve repair. Nerve Growth Factor (NGF) has previously been shown to improve neurite sprouting and neuroaxonal regeneration.

Therefore, we hypothesize that an NGF-POPs fusion scaffold would improve peripheral nerve repair by promoting neovascularization and forming a local microenvironment supportive of neuro-regeneration by giving needed mechanical support for the nascent axon, and providing localized delivery of necessary growth factors.
Here we demonstrate proof of concept that a POPs-NGF fusion protein can be produced and purified based on a modified iterative thermal cycling (ITC) purification protocol, despite overall low yield and high impurity. The scaffold also maintains the lower critical solution temperature (LCST) phase behavior of unmodified POPs, allowing it to be injected as a liquid while forming a stable solid scaffold in vivo. Future work is required to further characterize the protein, optimize the purification protocol to improve yield and purity, and to test biological activity of the NGF-POPs fusion protein scaffold.

ABSTRACT NO. 30

UNDERSTANDING AND MANIPULATING THE METAL HOMEOSTASIS OF *Candida albicans*

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The lack of current treatment methods for fungi pathogens remains an important problem in basic science research. Pathogenic fungi are eukaryotic organisms that present a complex problem to conventional treatments because of limited options for selectively targeting the pathogen while sparing human cells, given their shared features. Fluconazole, one of the current antifungal drugs, works by inhibiting Erg11, a Fe-enzyme required for ergosterol synthesis which leads to alterations in the metal homeostasis of *Candida albicans*. To determine how fluconazole impacts the metal homeostasis of *C. albicans* and to take advantage of this change in metal status, we have employed a two-pronged approach. First, we investigated how fluconazole impacts Cu-associated proteins critical for respiration and control of radical oxygen species (ROS) by monitoring Cytochrome c oxidase (COX) and bulk Superoxide Dismutase (Sod) activity. Second, our lab has discovered metal chelators that can enhance fluconazole activity against *C. albicans*. To determine if these chelators work by a metal-dependent mechanism, we made Synthetic Defined (SD) growth media in-house that allows for the removal of specific transition metals (Cu, Fe, Mn, Zn). *C. albicans* was grown in an SD-metal medium, treated simultaneously with fluconazole and a metal chelator, and a specific metal was titrated to determine changes in overall activity. Preliminary results for the first portion of my project suggest that fluconazole does not significantly change COX activity as compared to Cu-extracellular chelator BCS. Similarly, fluconazole does impact overall Sod activity. In addition, I have found that in the presence of fluconazole, chelator activity is impacted by Cu and Mn. Overall these findings suggest changes in metal homeostasis could be a potential avenue for anti-fungal drug discovery. Future work would focus on determining how pro-chelators, which are masked-chelators activated under specific conditions, impact fluconazole activity and if they also have a metal-dependent mechanism.

ABSTRACT NO. 31

THE MTRR TRANSCRIPTIONAL REGULATORS ROLE IN THE OXIDATIVE STRESS RESPONSE IN *Neisseria gonorrhoeae*

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Multidrug resistance (MDR) is a rising global health problem. In *Neisseria gonorrhoeae*, the causative agent of gonorrhea, the multidrug efflux pump, MtrCDE, contributes to MDR by exporting cytotoxic molecules from the cell. The genes encoding MtrCDE are repressed directly by MtrR (Multiple transferable resistance Repressor). In addition to MtrR involvement in MDR, this protein has an unknown role in the oxidative stress response. MtrR binds and represses the rpoH operator, which encodes the oxidative stress sigma factor RpoH (σ 32). Due to

the presence of four cysteines (C66, C72, C116, C206) and that MtrR regulates rpoH, we hypothesized that MtrR may sense reactive oxidative species (ROS) by one or more cysteines thus derepressing the rpoH regulon. In order to determine the reactivity of each cysteine, we need to create via site-directed mutagenesis MtrR proteins which in which each cysteine is changed to the isosteric amino acid, serine, thereby allowing us to study the biochemical properties of individual cysteines. Furthermore, we need to ensure that the mutation does not affect the DNA-binding function of each protein. Using a fluorescence polarization-based DNA binding assay we determined the binding affinity of MtrR mutants for cognate DNA sites and compared them to previously determined MtrR WT binding constant. I found that MtrR C66S had a lower binding affinity (higher Kd) than MtrR WT. I have also been able to crystalize C116S and expect its structure to inform future studies. Additional mutations of residue C66 and the remaining cysteines must be tested. In the future we shall utilize these mutations to determine the reactivity of each individual cysteine and define its physiological relevance.

ABSTRACT NO. 32

THE REGULATION OF GENETICALLY-ENCODED M6A SENSOR BY RNA DEMETHYLASES

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Motor learning in the cerebellum is thought to rely on motor error messages that drive changes in learned behavior. Recent discoveries have shown that circuits in the cerebellum also respond to and predict reward after learning, positioning the cerebellum as a potential novel site of reward-based learning. The current hypothesis concerning cerebellar learning is that Purkinje Cells (PCs), the sole output cells of the cerebellar cortex, decrease or pause their firing to disinhibit premotor neurons in the deep cerebellar nuclei and execute learned behaviors. Molecular Layer Interneurons (MLIs) in the cerebellar cortex are spontaneously active interneurons that receive contextual input and inhibit PCs. As such, their position in the circuit potentially implicates them in learned changes in PC firing. We record neural activity during a classical conditioning task using multi-site silicon electrode during awake behavior. PCs and MLIs are identified in vivo by searching for characteristic complex spikes and analyzing inhibitory cross-correlograms with PCs, respectively. We discover an increase in MLI response to the conditioned stimulus after learning and investigate the extent to which MLIs are encoding learned rewards as opposed to solely participating in pre-motor activities related to licking or running. We also discover various distinct MLI learned responses and contribute to the characterization of MLI electrophysiological profile, including average waveform, interspike interval, and firing rate. By establishing a complete electrophysiological profile and improving our understanding of the role MLIs play in behavior, we hope to accelerate research efforts and the generation of therapies for psychopathology with cerebellar involvement such as Autism Spectrum Disorder and Alzheimer's Disease.

ABSTRACT NO. 33

INHIBITION OF TREHALOSE-6-PHOSPHATE SYNTHASE, TPS1, IN *Candida albicans*

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Candida albicans is a common fungal pathogen that disproportionately affects the immunocompromised population. This pathogen causes both superficial and invasive infections as a result of disruption of the growth of healthy bacteria and an overgrowth in yeast in the body. Due to the increase in its toxic effects and resistance to current antifungal drugs, new antifungal drugs are needed. The trehalose biosynthesis pathway is being studied as a

potential antifungal drug target as it is essential to the survival of many pathogenic fungi. This pathway is not found in humans, which will likely limit possible off-target effects. The pathway is composed of two steps. In the first step, trehalose-6-phosphate synthase (Tps1) converts UDP-glucose and glucose-6-phosphate to trehalose-6-phosphate (T6P). In the second step, trehalose-6-phosphate phosphatase (Tps2) converts T6P to trehalose. Here we have studied the inhibition of the *C. albicans* Tps1 (CaTps1) protein in order to further investigate this enzyme as a drug target. Another fungal pathogen, *C. neoformans*, which is responsible for cryptococcal meningitis, especially in the immunocompromised population and is similar to *C. albicans*, also contains the trehalose biosynthesis pathway. In previous studies, a small compound derivative was found to inhibit the activity of CnTps1. In an effort to learn if this compound affects CaTps1, we have first expressed and purified the CaTps1 protein. To determine the effect of this small molecule compound on CaTps1 catalytic activity, two approaches were taken: 1) enzyme activity assays were done to learn if this compound inhibits CaTps1, and 2) thermal shift assays were carried out to test for its binding to CaTps1. The results of this work will contribute to our further understanding of the trehalose biosynthesis pathway in *C. albicans* and the potential development of new antifungal therapeutics.

ABSTRACT NO. 34

ELUCIDATING AMILORIDE-BASED SMALL MOLECULE RECOGNITION OF SARS-COV-2 REGULATORY STRUCTURES

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The COVID-19 pandemic demonstrated the imperative need for novel antivirals to prevent any future coronavirus outbreaks. SARS-CoV-2, a positive-sense single-stranded RNA virus, is the causative agent of COVID-19. The 5' untranslated region (UTR) of this RNA is evolutionarily conserved and previously determined to be implicated in viral replication. Recently, small molecules featuring an amiloride-based scaffold have been found to inhibit SARS-CoV-2 viral replication by targeting this region. However, the mechanism of action of these small molecules with SARS-CoV-2 5' UTR secondary structures still requires further investigation. In this study, we evaluated the binding activity of novel amiloride small molecules with stem loop (SL) 1 and 5A of the 5' UTR. SL1 and SL5A were both previously determined to have bulges and apical loops, structural characteristics amilorides have preferential affinity for. As a result, SL1 and SL5A are attractive targets for small-molecule targeting of SARS-CoV-2 RNA. Through fluorescent indicator displacement assays (IDA), our findings demonstrated preliminary structure-activity relationship trends specifically at the C6, C5, and newly accessible C3 positions on the pyrazine core. In particular, dimethylamine at C5 and bulky aromatic groups at C6 improved affinity to SL1 and SL5A. At the C3 position, mono-substituted amines demonstrated stronger binding affinity compared to di-substituted amines. Our findings will advance the expansion and tuning of our current amiloride library. We anticipate these amilorides to be chemical probes to further understand SARS-CoV-2 RNA biology and small-molecule targeting of viral RNA motifs.

ABSTRACT NO. 35

NONLINEAR PUMP PROBE MICROSCOPY AND MACHINE LEARNING FOR EARLY DETECTION OF METASTATIC MELANOMA.

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In the realm of cancer detection, advanced imaging techniques play a crucial role in early diagnosis and facilitating effective treatment. However, the absence of reliable biomarkers for diagnosing metastatic melanoma poses a significant challenge in early detection, leading to a higher mortality rate for patients

diagnosed with stage I (local) melanoma compared to any other stage. Although effective, the aggressive nature of the treatment creates a dilemma in determining which patients should receive it. To address this issue, we utilize non-linear, pump-probe microscopy of melanin, a prevalent pigment in most melanoma, as a means of early detection of metastatic melanoma and to facilitate treatment. Unlike traditional approaches such as visual inspection, pump-probe microscopy offers the capability to probe transient, non-linear interactions in the excitation dynamics of melanin that provide predictive insights into the metastatic status of melanoma. But, the complex combinations of multiple nonlinear processes in melanin signals presents an interpretational challenge. To address this limitation, we employ binary classification techniques, such as Support Vector Machines (SVM), to classify transient absorption curves with respect to their metastatic status. Additionally, due to the black box nature of machine learning, we apply dimension reduction techniques to probe deeper into the latent mechanisms of the classifiers. First, we utilize a biexponential fit with three amplitudes and two lifetime parameters that model the transient absorption, decay dynamics of melanin. This maintains the expected relationship in the classifier with minimal loss of accuracy. Additionally, we leverage algorithmic techniques including Recursive Feature Elimination and normalization to further reduce dimensionality and systematically investigate the impact of each parameter on the classification of metastatic melanoma. Overall, these proposed methodologies have the potential in advancing diagnostic methods, opening doors for broader impact in the personalized treatment strategies of melanoma.

ABSTRACT NO. 36

ALLOSTERIC ACTIVATION OF THE ERK MAPK BY β-ARRESTIN

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ABSTRACT NOT PROVIDED: CONFIDENTIAL

ABSTRACT NO. 37

ENGINEERING HUMAN INDUCED IPS CELL DERIVED PODOCYTES TO UNCOVER THE ROLE OF TRPC6 RISK VARIANTS IN PODOCYTOPATHIES

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Chronic Kidney Disease (CKD) is a global health crisis for which successful targeted therapies remain elusive. In the United States, about 15% of the adult population suffers from CKD, which costs ~$48 billion annually to treat less than 1% of the affected population. Because CKD patients are often asymptomatic, around 90% of the affected patients are unaware of their disease status. Kidney disease can arise from a multitude of genes; however, one such genetic mutation affects the “transient receptor potential cation channel, subfamily C, number 6” gene (TRPC6), which encodes calcium channels found in the slit diaphragm of the glomerular podocytes. Kidney damage often originates in the glomerulus, the major site of blood filtration in the kidney. The podocytes are terminally differentiated cells that work with the glomerulus to create the ultrafiltration barrier. Once damaged, these podocytes have minimal capacity for regeneration. The TRPC6 gene is crucial in controlling calcium channels in the podocytes that maintain the ultrafiltration barrier. We hypothesize that the pathogenicity of the TRPC6 risk variants might primarily occur in kidney podocytes – the specialized epithelium that encases kidney glomerular capillaries. Here, we extended our podocyte differentiation strategy to help understand how TRPC6 variants affect the development and function of human kidney

podocytes and how these processes influence disease progression. Our preliminary results show that mutations in TRPC6 lead to protein trafficking defects where Nephrin and Podocin are stuck in the endoplasmic reticulum of the podocytes. Here, we developed a drug screening pipeline to repurpose FDA-approved drugs to ameliorate protein trafficking defect-mediated cellular pathophysiology. After treatment of the podocytes with the drugs, data will be obtained through the staining of cells associated with the trafficking of podocyte lineage-specific markers and compared with that of the wild-type podocytes. This study will provide a viable platform for future therapeutic discovery.

ABSTRACT NO. 38

OXIDATIVE AMINATION USING O-BENZOYLHYDROXYLAMINES FOR SYNTHESIS OF ALLYLIC AMINE-CONTAINING HETEROCYCLES

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Tertiary allylic amines are prevalent structures found in small molecule therapeutics, natural products and intermediates in complex molecule synthesis. As such, expedient methodologies for their synthesis are desirable. Modern methods deploy oxidative coupling of amines and alkenes with recent works extending the scope of compatible amines from electronically deactivated nitrogens (e.g. sulfonamides and carbamates) to include electron rich alkyl-substituted amino groups. Here, we report a copper-catalyzed allylic amination of alkenes using O-benzoylhydroxylamines as an electrophilic amination reagent for the coupling of alkylamino groups. This simple method affords tertiary allylic amines from a wide scope of alkene and amine reaction partners. Notably, the allylic amination of endocyclic alkenes is achieved. Such allylic amines are known to possess potent bioactivity. We demonstrate further diversification of these endocyclic allylic amines, leveraging the alkene towards a variety of useful transformations. Thus, the potential of our method to efficiently access structurally complex, amino-substituted heterocycles is demonstrated.

ABSTRACT NO. 39

STUDYING THE EFFECTS OF NF1 BONE MARROW TRANSPLANTS ON FRACTURE HEALING IN NEUROFIBROMATOSIS TYPE 1

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The NF1 gene, also known as Neurofibromin 1, is a crucial gene responsible for the development and regulation of various cellular processes and is often associated with the genetic disorder Neurofibromatosis type 1. Patients who present with tibial pseudoarthrosis are often co-indicated with Neurofibromatosis type 1. Often, in cases of tibial arthrosis, patients possessing a Neurofibromatosis type 1 genotype display delayed fracture healing and an upregulation of fibrous tissue production at the fracture site. These phenotypes are similarly reflected in murine models. In severe instances, patients may experience non-unionization and chronic impairment of the tibia leading to higher mortality and poor quality of life. To better elucidate the role of the NF1 gene in fracture repair, we used a surgically induced tibial fracture model in conditional knockout (KO) NF1flox/flox mice while manipulating the presence of NF1 through two conditions of bone marrow transplants. Fracture healing was subsequently analyzed through micro-CT and bone histology.

ABSTRACT NO. 40

DECIPHERING HUMAN GENETIC SUSCEPTIBILITY TO ZIKA VIRUS

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Zika Virus (ZIKV) is a mosquito-borne RNA flavivirus that causes mild symptoms including fever, headache, and general malaise in most infected hosts. However, complications occur in a small subset of people which may be fatal and in pregnant women, ZIKV has been linked to congenital Zika syndrome and neonatal microcephaly. There are currently no approved ZIKV vaccines or anti-viral therapeutics, underscoring the need to resolve the underlying basis for infection and understand the genetic basis responsible for the clinical spectrum of the disease. The goal of this study was thus to decipher the link between human genetic variation and differences in susceptibility to ZIKV using cellular GWAS. A pilot panel of four lymphoblastoid cell lines (LCLs) from genetically diverse individuals was used to assess infection levels with three ZIKV strains. We found that there is a dynamic range of infection levels among different LCLs. The relative levels of infection were consistent among all the ZIKV strains tested, but they varied in the absolute percentage of cells infected. Our results suggest that there is a genetic component that impacts an individual's susceptibility to ZIKV. To validate this and identify potential genetic differences that confer susceptibility and resistance to ZIKV, we will use single-cell high-throughput in vitro susceptibility testing (scHi-HOST), a cellular GWAS platform that uses single-cell RNA sequencing to identify genetic differences associated with host variance in viral burden. A scHi-HOST experiment of 96 LCLs has been submitted for sequencing. We predict that this method will elucidate gene variants that are related to the differential ZIKV susceptibility seen in human populations.

ABSTRACT NO. 41

NANOBODIES AS ALLOSTERIC MODULATORS OF G-PROTEIN COUPLED RECEPTORS: INSIGHTS FROM THE BETA 2 ADRENERGIC RECEPTOR

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G-protein coupled receptors (GPCRs) play a crucial role in cellular signaling and are targeted by about 30 percent of FDA-approved therapeutics. The β-2 adrenergic receptor (β2AR) is a key regulator of several cardiovascular and pulmonary functions. Binding of an agonist such as the endogenous ligand—epinephrine, to the β2AR results in conformational changes within the receptor leading to the activation of the G-protein Gs-mediated cAMP signaling in cells. GPCRs are highly dynamic in nature and exist as an ensemble of inactive and active conformational states. In recent years, remarkable progress has been made toward developing antibodies to stabilize conformations of GPCRs. Specifically, a class of camelid-derived heavy chain-only antibodies, referred to as nanobodies (Nbs), have been used successfully to visualize high-resolution structures of several GPCRs. The first collection of β2AR conformation stabilizing Nbs studied in the Lefkowitz laboratory were developed in llamas by the research groups of Brian Kobilka and Jan Steyaert. Amongst these Nbs, Nb60 and Nb80 were used to respectively determine crystal structures of an inactive and the first active conformation of the β2AR. Here, we expand upon the application of Nb60 and Nb80 as allosteric modulators of the β2AR. Using a combination of biochemical, pharmacological, and biophysical assays we demonstrate the distinct cooperative effects of these Nbs on the β2AR. While Nb80 selectively couples to agonist-bound β2AR and is positively cooperative for agonist binding, Nb60 prefers the antagonist-bound inactive state of the receptor and is negatively cooperative for agonist binding. As a proof-of-concept application, we

propose the utility of allosteric Nbs as potential tools for affinity isolation of functional GPCRs.

ABSTRACT NO. 42

INVESTIGATION OF THE C-TERMINAL DOMAIN OF *Plasmodium* HEAT SHOCK PROTEIN 90 AS A TARGET FOR NOVEL ANTIMALARIALS

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The parasitic disease malaria continues to be a world health concern, with over 240 million cases and 600,000 deaths in 2022. Despite current small molecule drugs for treatment, there is increasing drug resistance among the *Plasmodium* parasites that cause malaria, including the most lethal species *P. falciparum*. The *P. falciparum* protein Heat Shock Protein 90 (PfHsp90) has been identified as a conserved and essential protein for parasite survival, making it a promising target for novel antimalarials. PfHsp90 functions as a homodimer chaperone protein responsible for the proper folding and heat stabilization of protein substrates, termed clients. The N-terminal domain of PfHsp90 has been previously explored for drug targeting at its ATP active site, but ATP-competitive inhibitors often lead to a compensatory heat shock response (HSR). Moreover, the ATP-binding site is highly conserved between PfHsp90 and its human host's Hsp90 homolog, limiting the potential of species-selective inhibitors required to reduce host toxicity and off-target effects. However, the less conserved C-terminal domain responsible for the dimerization of PfHsp90 is a possible allosteric site for PfHsp90 targeting drugs uninvestigated in *Plasmodium*. To explore potential inhibitors, we used thermal shift assays using truncated PfHsp90 protein containing the C-terminal and Middle domains. We found that the antibiotics novobiocin and coumermycin A1 have a destabilizing effect on the C-terminal truncation of PfHsp90. This destabilization of PfHsp90 by novobiocin may be promoted by the formation of oligomers as shown by Native PAGE. These inhibitors have been previously shown to bind to the human Hsp90 C-terminal domain, but their effects in *Plasmodium* and mechanism of inhibition was unknown. Our finding demonstrates that these antibiotics destabilize the C-terminal domain of PfHsp90 by disrupting the quaternary structure and promoting oligomerization. These small molecules can be used to inhibit PfHsp90 and inform future studies on the proteome of *Plasmodium* following inhibition.

ABSTRACT NO. 43

INVESTIGATING THE ROLE OF RUNX1 IN DRIVING TUMOR PLASTICITY IN OLFACTORY NEUROBLASTOMA

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ABSTRACT NOT PROVIDED: CONFIDENTIAL

ABSTRACT NO. 44

PKN2 IS A DEPENDENCY IN CELL LINES FOLLOWING EPITHELIAL MESENCHYMAL TRANSITION

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For epithelial cancers, the process of epithelial-mesenchymal transition (EMT) is critical for metastasis and advancement of disease. Through this process, cancer cells can lose their adhesive properties and acquire the migratory and invasive properties of mesenchymal stem cells. This can lead to the spread of disease and development of drug resistance. However, little research has explored differential dependencies of the post-transition state, leaving few known targets following metastasis or failure of primary therapy. Our project seeks to uncover novel targets for cancers following EMT in order to address growing therapy resistance. Using publicly available

cancer dependency data, we identified PKN2, a little studied kinase, as a target in cell lines following EMT. We have shown mesenchymal-like cancer cell lines are uniquely sensitive to PKN2 genetic knockout. Additionally, SKMEL-28 melanoma cells develop dependence on PKN2 following induction of EMT through derived resistance to a BRAF inhibitor. Quantitative RT-PCR data suggests that PKN2 is capable of modulating YAP/TAZ signaling, a pathway involved in cell proliferation and growth, potentially suggesting why this kinase becomes a genetic dependency. We will further validate PKN2 as an activator of this pathway by expressing constitutively active YAP/TAZ mutants to see if viability is recovered following PKN2 knockout. We are seeking to elucidate the mechanism through which PKN2 modulates this pathway through manipulation of the kinase domain to create a constitutively active kinase domain to measure effects on signaling and co-immunoprecipitation with regulators of YAP/TAZ signaling. We have nominated PKN2 as a potential target for cells primed to undergo metastasis and resistant to targeted therapy, and future work will help to elucidate the mechanism through which this kinase acts.

HUANG FELLOWS

ABSTRACT NO. 45

TAKE FIVE: BINDING ENERGETICS AND KINETICS OF THE FIVE DOMAINS OF *Staphylococcus aureus* PROTEIN A

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Staphylococcus aureus is a bacterium found on the skin and in the human respiratory tract.

S. aureus is a dangerous bacterium because it evolves quickly and causes life-threatening sepsis and pneumonia, especially in hospital settings. These symptoms can be exacerbated by the presence of staphylococcal protein A (SpA), found abundantly on the surface of *S. aureus*. SpA has five nearly identical domains that bind to various ligands with the similar binding affinity. Research suggests that SpA assists the formation of biofilms, structures made of slimy bacteria matrices. We hypothesize that SpA stabilizes these biofilms by binding to extracellular polysaccharides. Using biolayer interferometry, we investigated the energetics of binding and unbinding of the extracellular polysaccharide and the domains of protein A to test this hypothesis. We determined the optimal experimental conditions using computer simulations designed with Mathematica™ software. These simulations predict the association and dissociation curves of the binding and unbinding of the extracellular polysaccharides to each of the five SpA domains. The simulations assume that SpA domains more accessible to bulk solution bind to extracellular polysaccharides faster. We analyzed the binding energetics and kinetics of polysaccharides and protein A domains by comparing the association and dissociation curves from both simulated and biolayer interferometry data. Each polysaccharide has many subunits that can bind to SpA domains. This characteristic of polysaccharide potentially increases both the affinity and the complexity of the binding reaction. Our results inform the design of new experiments to further explore this complexity in the future.

ABSTRACT NO. 46

THE ROLE OF S1-S2 INTERSUBUNIT MUTATIONS IN ALTERTING THE THERMOSTABILITY OF THE SARS-COV-2 SPIKE PROTEIN

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SARS-CoV-2 virus is the causative agent of COVID-19. The SARS-CoV-2 spike, a glycoprotein responsible for host cell entry, contains two subunits, S1 and S2, which are responsible for host cell attachment and fusion, respectively. Following host cell receptor

engagement, S1 must detach to allow necessary structural rearrangements from pre- to post-fusion conformation to occur. Four mutations found in the SARS-CoV-2 Omicron variant, N764K, N856K, N969K, and L981F, are located in the interface of S1/S2 subunits' ectodomain. Due to their location on the spike, these mutations may influence key S1-S2 intersubunit interactions and either stabilize or destabilize the spike pre-fusion form. To elucidate how these mutations influence the stability of the spike, we measured the thermostability of the SARS-CoV-2 spike and its mutants. We hypothesize that each residue substitution will prompt a change in the thermal sensitivity profile of the spike relative to the SARS-CoV-2 wild type. The mutated spike proteins were expressed in human embryonic kidney (HEK) cells and purified through affinity and size exclusion chromatography. By conducting differential scanning fluorimetry (DSF) and differential scanning calorimetry (DSC) assays on the purified spikes of each desired substitution, comparisons of the unfolding profiles of these constructs can be drawn. Preliminary data suggests substitution L981F to be the most divergent from SARS-CoV-2 wild type profile. Understanding how naturally occurring mutations of the spike affect its thermostability provides information about how these mutations are affecting viral fitness as the virus evolves.

ABSTRACT NO. 47

INVESTIGATING THE ROLE OF INTESTINAL MUCIN ON CHEMICAL TOXICITY IN *C. elegans*

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Intestinal mucin plays a vital role in protecting many organs in humans, acting as the first line of defense against pathogens and environmental pollutants (Gillois et. al 2018). Our research aims to assess whether and how intestinal mucin modulates chemical uptake and susceptibility in *C. elegans*, a nematode and model organism for toxicological research. We focused on the mul-1 gene in C. elegans, which encodes a secreted surface protein for intestinal mucin homologous to the MUC2 mucin gene in humans (Kimura et al., 2012). Studies suggest that the mul-1 gene is involved in the innate immune response in *C. elegans* (Cui et al., 2007). Studies have also shown that mucin degrading bacteria has been linked to the progression of early Parkinson's Disease, a neurological disorder (Nishiwaki et al., 2022). Our research aims to assess how environmental pollutants, specifically cadmium and lead, alter the expression of the mul-1 gene, and whether the mul-1 gene impacts neurodegeneration after exposure. We hypothesized that *C. elegans* utilizes an innate defense pathway that involves increasing the protein secretion of mucin via upregulating mul-1 to decrease gut permeability, thus reducing chemical uptake. We also hypothesized that *C. elegans* without the mul-1 gene would be more susceptible to neurodegeneration from environmental pollutants due to increased gut permeability and chemical uptake. For our experiment, worm strains with a Green Fluorescent Protein (GFP) tagged to the mul-1 gene were analyzed for GFP expression after exposure to various concentrations of cadmium and lead. A cross strain between mul-1 knockout worms (mul-1 KO) with GFP tagged neurons (BY200) was also created in order to assess for neurodegeneration after exposure to cadmium and lead. Elucidating how intestinal mucin mediates toxicity allows us to further understand how different pollutants impact and alter human health outcomes.

ABSTRACT NO. 48

EFFECT OF NEURONAL SUBTYPE AND ACTIVITY ON IL34 EXPRESSION

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Synaptic pruning is a critical process in neurodevelopment. This occurs when microglia (immune cells in the brain) engulf neuronal

synapses and projections, helping refine and strengthen communication between neurons. The mechanisms involved in microglial pruning during development are not comprehensively understood. Previous work in the Bilbo lab has demonstrated that Interleuken-34 (IL34), which is expressed by neurons, is developmentally regulated. We believe this early production of IL34 is a vital part of microglial-neuronal interplay, however, the factors dictating its expression by neurons are unknown. This project aimed to test whether the expression of IL34 by neurons is dependent on neuronal subtype (excitatory or inhibitory) and/or neuronal activity. To do this, we used a Designer Receptors Exclusively Activated by Designer Drugs (DREADDS) approach. We administered either an excitatory receptor virus, an inhibitory receptor virus, or a control virus to wild type mice at postnatal day 1 (P1). At P8, P9, and P10, the mice received an injection of the designer drug that interacts with the designer receptor. Brains were collected at P10 and sectioned. Using RNA-Fluorescence in Situ Hybridization (FISH), we then stained for Gad2 (inhibitory neurons), Fos (active neurons), IL34, and DAPI (cell nuclei). Slides were then imaged at 30x using a confocal and analyzed with Imaris software. We quantified IL34 in excitatory and inhibitory neurons that were either active or inactive. This will allow us to determine how IL34 expression is regulated by neuronal firing and subtype, informing its potential role in microglial-neuronal interactions in neurodevelopment.

ABSTRACT NO. 49

ADVANCING THE QUEST FOR PARTICULATE DARK MATTER (DM): A NOVEL APPROACH FOR DETECTING METASTABLE CHARGED PARTICLES AT THE LARGE HADRON COLLIDER

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Although the discovery of Higgs Boson at the Large Hadron Collider (LHC) answered many important questions in relativistic quantum field theory of fundamental particles and their interactions– the standard model (SM) of particle physics, it has not been able to explain the gravitational interaction of dark matter (DM) on the cosmological scales. Many theories suggest that LHC might already be sufficiently producing metastable charged partners of the DM particles. In this case, if we describe a triggering scheme for “disappearing tracks” of massive particles that do not reach the outermost muon detectors, we can progress towards understanding new-physics scenarios related to particulate DM or other new neutral particles. We propose a novel algorithm for detecting charged particles which decay invisibly after traveling a short distance of 25 cm in the collider. Our method uses probabilistic calculations and detector geometry to cluster spacepoints registered by two-dimensional silicon pixel detectors into mathematically-defined patterns. Then it uses graph computing to look for helical trajectories of appropriate geometric characteristics– formed due to the magnetic field effect on produced charged particles. The algorithm is deployable on a highly-parallelized graph computing architecture and achieves extremely rapid particle trajectory reconstruction in the high energy collisions at LHC. Hence, our method may be embedded on silicon-based integrated circuits using commercial FPGAs to augment or replace traditional computing apparatus.

ABSTRACT NO. 50

IDENTIFYING SELECTIVE ANTAGONISTS TO RABBIT OLFACTORY RECEPTOR RESPONDING TO MOTHER’S PHEROMONE

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Critical to mammalian development is the newborn’s ability to locate the mother’s milk and begin suckling. Rabbit pups rely on specialized olfactory pathways, detecting pheromones in the

mother's milk. Exposure to 2-methylbut-2-enal, 2MB2, which is present in the mother's milk, leads to newborn rabbit behaviors such as oral grasping mouth movements and head searching patterns. Our lab previously established olfactory receptor OR2D2-LIKE as the receptor activated by 2MB2. However, whether 2D2-LIKE mediates newborn suckling remains unclear. We aimed to identify an antagonist for 2D2-LIKE, which serves as a useful tool to investigate whether receptor inhibition also inhibits newborn suckling. We used a human cell culture based system of HEK293T cells, which were transfected to express the olfactory receptor and stimulated with each chemical. Olfactory receptor activities were measured with Glosensor cAMP assays. Through screening 376 odorants, we identified beta-damascenone and other similarly structured ketones as a potent and effective antagonist to 2D2-LIKE. Beta-damascenone did not inhibit other olfactory receptors tested, which suggests selectivity to 2D2-LIKE. This work provides an avenue to test the hypothesis that 2D2-LIKE responds to 2MB2 to cause newborn behaviors. We will share this data with our collaborators in France for in vivo analysis. If successful, we can suggest a causal relationship and molecular pathway for 2MB2 binding to 2D2-LIKE, leading to the innate newborn behavior of responding to this pheromone in the mother's milk.

ABSTRACT NO. 51

EVALUATING ARTIFICIAL INTELLIGENCE BIAS IN LARGE LANGUAGE MODELS

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Computational linguistics and machine learning encourage the current development of chatbots and virtual assistants. Chatbots, specifically, function through a series of prediction modeling to generate subsequent words and phrases while encouraging speech variety. Sequence-to-sequence modeling, among other input-output techniques, facilitates more accurate language generation by training chatbots through heavy data sets, following organized rules and patterns. Chatbots, however, rely on extensive collections of texts or corpora, decreasing response accuracy and increasing bias for low-resource languages. Chatbot technology could, therefore, positively impact marginalized speech communities through archival recovery. Additionally, professionals will soon face ethical impediments in occupations requiring creative thought. Consultations with field professionals reveal chatbots' current and future developments and limitations, specifically through both corpus and prediction restrictions and ethical concerns regarding creative ownership. Further, these corpus restrictions hinder access to reliable information for marginalized communities, particularly for low-resource languages. Findings indicate a diverse review of chatbots and their applications across disciplines. While professionals and academics appreciate chatbots for their utility in creative generation beyond austere text, conflicts arise regarding the extent to which chatbots and virtual assistants can be utilized for guidance. Additionally, speakers of low-resource languages undergo technological burdens where less-commonly spoken languages face systems undermining their pertinence. These accounts thereby construct a hesitant acceptance of chatbots and their utility in creative and academic fields, particularly regarding professionalism and creative ownership. Additionally, these marginalized groups whose limited corpora hinder their access to text-generation tools could benefit by expanding data collection retrieval.

ABSTRACT NO. 52

A NEW SYSTEM TO TEST AND CALIBRATE A DEVICE THAT AUTOMATICALLY TRACKS URINE AND STOOL IN HOSPITAL SETTINGS

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We have created a smart toilet medical device that automates the process of monitoring stool and urine output of hospitalized patients, which is often a messy, yet clinically significant task for nurses. Fluid balance and stool consistency are important measures of a patient's response to therapy, organ transplant, or surgery. The current standard of testing the smart toilet medical device involves recruiting human subjects to urinate into the device or repeatedly pouring water into the device to simulate urination. These testing processes are time-consuming, making data collection a lengthy and difficult task. To address the need for efficient testing of the medical device, we have developed a testing appliance that automatically dispenses liquid into the toilet to simulate urination. The testing appliance consists of an embedded system featuring a peristaltic pump that is controlled by an Arduino microcontroller and a Raspberry Pi computer. It is Wi-Fi connected, so that tests can be configured and run remotely. Currently, the dispensing mechanism is accurate within two percent of a given volume. In the upcoming weeks, the testing appliance we have developed will be used to test five different smart toilet medical devices to assess their readiness for a clinical trial in the Duke University Hospital.

ABSTRACT NO. 53

DO PFOS AND PFOA CAUSE NEUROTOXICITY?

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Per- and polyfluoroalkyl substances (PFAS) are synthetic chemicals found in many consumer products including cookware, food packaging, cosmetics, adhesives, and electrical insulation. Exposure to PFAS is linked to adverse health outcomes such as cancer and damage to the liver and immune system. Previous studies have shown that the PFAS compound, perfluorooctane sulfonate (PFOS), causes dopaminergic neurodegeneration in *Caenorhabditis elegans*. It is unknown whether PFOS and other PFAS chemicals, such as perfluorooctanoic acid (PFOA), cause neurodegeneration in mammalian systems. We hypothesize that PFOS and PFOA cause DNA damage and cell death in mammalian cells. Poly(ADP-ribose) polymerase-1 (PARP-1) is a protein that signals DNA damage and initiates DNA repair. Poly(ADP-ribose) (PAR) is a product of PARP-1 activity and signals cell death. We are currently testing whether there is an increase in PAR activation in PFOS and PFOA-treated cells via immunoblotting. This study will provide insight into the impact of PFAS on cells and their mechanism of action. This knowledge will help us better understand potential underlying mechanisms of neurodegenerative diseases, such as Parkinson's disease.

ABSTRACT NO. 54

EVALUATING A FUNCTIONAL VERTICAL RANGE FOR PRECISE INTERCRANIAL TUMOR BOUNDARY IDENTIFICATION

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Approximately 270,000 individuals worldwide receive a primary brain tumor diagnosis annually. Neurosurgeons face unique challenges preserving non-trivial surrounding tissue while fully removing tumors, and addressing these complications could greatly improve patient prognoses. Fluorescent markers such as 5-ALA enable surgeons to detect and excise residual malignant tissue at the edges of intracranial cavities. An alternative method, laser-

induced fluorescence (LIF) spectroscopy, offers improved precision without the need for injected dyes.

LIF-based approaches for identifying tumor boundaries have primarily been studied in controlled environments concerning their positioning relative to tissue samples. This study aims to investigate the impact of the distance between the objective lens of the LIF system (Tumor ID) and the tissue on the tissue's spectral signature.

The working distance of objective lenses dictates a distance for accurate optical readings. This study will evaluate a vertical range of distances from as close as possible to the objective lens to twice its working distance. Five points on the phantom tissue sample will be identified, and scans will be conducted at each point at 1 mm intervals within the vertical range and at every 0.5 mm within +/- 5 mm of the working distance. The use of multiple xy positions controls for any variations in the phantom tissue.

Spectral intensity within the 450-700 nm wavelength range will be assessed as a function of the z-distance from the objective lens. If the spectra exhibit scaling outside the working distance, scaling factors as well as any potential shape errors will be evaluated as a function of z-distance.

This study aims to establish a functional range for the Tumor ID, ensuring precise identification of intracranial tumor boundaries. Findings may contribute to advancements in automated tumor resection systems, including the potential correction or adjustment of classification errors caused by positioning discrepancies.

ABSTRACT NO. 55

FACTORS INFLUENCING CHOICE OF DEMOGRAPHIC FORMS AMONGST LATINX COLLEGE STUDENTS

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Filling out demographic forms can be difficult for Latinx individuals because there is no consensus about whether Latinx is a race or an ethnicity. The current research uses qualitative, focus group methodology to explore how U.S.-born, Latin American-born, and multiracial Latinx college students prefer to see their Latinx identity displayed on demographic forms. In groups of 3-6 students, Latinx-identifying college students self-reported skin-tone and country of origin and asked their opinions on three different demographic forms. One listed Latinx as an ethnicity, another listed Latinx as a race, and a third listed Latinx as both a race and an ethnicity. Results indicated that Latinx college students overwhelmingly prefer to fill out the demographic form that listed Latinx as a race option. Skin-tone, country of origin, and multiracial identity seem to be the most influential factors students consider when filling out demographic forms. Specifically, U.S.-born Latinx participants who self-report medium-to-brown skin tones are less likely to identify as White or Black, and thus prefer Hispanic Latino as a race option. Latin American-born students report more confusion when filling out demographic forms because international students say race did not become a salient identity until they came to the US. Finally, multiracial students report they feel most included when they are able to select more than one race option on demographic forms. This research is among the first to examine factors influencing demographic form preferences, and explore how demographic forms can act as proxies for displaying racial/ethnic identity.

ABSTRACT NO. 56

UNDERSTANDING THE COMMENT LANDSCAPE FOR FEDERAL HEALTH REGULATIONS IN THE DIGITAL ERA

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In the realm of administrative law, the notice-and-comment rulemaking process plays a

crucial role in shaping regulations, empowering members of the general public and interested stakeholders to leave comments on proposed rules before their final revision. This scholarship examines the notice-and-comment rulemaking process, focusing on the commenting landscape of federal health regulations since the process was moved online to regulations.gov in 2003. While past literature has analyzed the impact of comments on rulemaking and the degree of interest group involvement in a subset of rules prior to the implementation of online commenting, there is a significant gap in understanding the commenting landscape since the digitization of the notice-and-comment process. Our study aims to address this gap by providing a comprehensive view of comments on Physician Fee Schedule regulations since 2005. We utilize bulk downloading methods to retrieve hundreds of thousands of comments on rules spanning the past two decades. Through this analysis, we will shed light on how the quantity, quality, and makeup of comments have changed since 2005. By exploring the 21st century commenting landscape, this research fills an important void in the literature and contributes to a deeper understanding of the digital notice-and-comment rulemaking process. The findings of this study have the potential to inform policymakers, regulatory agencies, and interested stakeholders about the evolving dynamics of public participation in health regulations and its implications for health policy decision-making.

ABSTRACT NO. 57

INHIBITION OF CD47-SIRP-ALPHA SIGNALING IN TRIPLE NEGATIVE BREAST CANCER TREATMENT

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Previous treatments for Triple Negative Breast Cancer (TNBC) have relied on chemotherapy such as Doxorubicin, and additional treatment options include immune checkpoint blockade of PD-1/PD-L1. Although PD-1/PD-L1 blockade showed great efficacy in melanoma, it only slightly increases survival of metastatic TNBC patients. Therefore, additional research is needed to improve treatment efficacy of immune checkpoint inhibition in TNBC. Previously, our lab explored inhibition of the CD47-SIRP-alpha checkpoint in HER2-positive breast cancer. This checkpoint inhibits phagocytosis and activation of innate immune cells (macrophages and dendritic cells). We discovered that addition of CD47 blockade to Trastuzumab synergistically improved treatment efficacy for HER2-positive breast cancer. Similarly, we hypothesize that disruption of the CD47-SIRP-alpha innate immune checkpoint combined with existing treatment for TNBC can further suppress tumors. The treatment we propose is Doxorubicin combined with SIRP-alpha disruption. To test our proposed treatment, we used syngeneic mouse TNBC tumor cell lines for in vitro studies and implanted tumors in mice for in vivo studies. In vitro, we found that doxorubicin treatment increases CRT expression on the tumor cell surface. This result lays the foundation for combining Doxorubicin with SIRP-alpha inhibition, because surface CRT is one of the pro-phagocytic signals inhibited by CD47-SIRP-alpha signaling. In vivo, we implanted E0771 tumor cells into wildtype and SIRP-alpha knockout mice and treated these mice with either control treatment or Doxorubicin. The anti-tumor effect of doxorubicin combined with SIRP-alpha disruption is inconclusive. However, this experiment reveals that SIRP-alpha inhibition combined with Doxorubicin worsens anemia than either treatment alone. In conclusion, the efficacy of the proposed treatment requires additional experiments to assess. We plan to repeat the in vivo study testing the combination of doxorubicin and SIRP-alpha inhibition. We also plan to perform in vitro assays to measure the effect of the proposed treatment on macrophage phagocytosis and activation.

ABSTRACT NO. 58

ESTABLISH HIGH-TITER LENTIVIRUS PRODUCTION PROCEDURE IN THE VELMESHEV LAB

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Developing methods to understand cell lineage in in vitro models is of critical interest when advancing research. The STICR (scRNA-seq-compatible tracer for identifying clonal relationships) tool allows for the massive parallel tagging of single cells with a high-diversity lentiviral library of unique oligonucleotide sequences, or lineage “barcodes”. My goal is to establish a high-titer lentivirus production procedure in the Velmeshev lab, which will be used to employ a STICR lentiviral library. We hypothesize that generating high-titer lentivirus will enable the effective infection of a cell population by our STICR lentiviral library, and aid in determining barcode inheritance and thus cell lineage in that model. Testing protocols with two different transfection reagents, PEI and LIPO, revealed that the LIPO transfection reagent created an infectious lentivirus, while PEI did not. We expect to produce up to 1x10^9TU/ml functional viral particles for the effective infection of different types of cells, including iPSCs. Establishing a high-titer lentivirus procedure will aid the usage of the STICR tool in in vitro models, and hopefully supplement understanding of how cells relate to each other in different projects in the Velmeshev lab.

ABSTRACT NO. 59

THE GROUND REACTION FORCES OF COMPLIANT AND STIFF GAITS IN HUMANS

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The relatively smaller joints of human ancestors suggest that they may have experienced lower forces on their limbs. These lower forces may be explained by a compliant walking gait, in which knees and hips are bent, in comparison to the stiffer behavior of modern human walking. In a compliant gait, the limbs yield such that the leg imitates a spring, which may lead to lower ground reaction forces (GRF; the force that the ground exerts on the body during movement). We hypothesize that compliant gaits produce lower peak forces than stiff gaits. To test this, humans walked on a force plate to record vertical forces applied during a step. Additionally, OpenCap, a new cost-effective but untested software, was used to calculate forces and angles with the goal of testing this new method. To validate the software, forces were compared between the force plate and OpenCap. Knee and hip angles were calculated with video software using digital markers from the time of heel strike to toe off during a step and compared to angles calculated by OpenCap. Using Statistical Parametric Mapping, OpenCap GRF values were significantly different from standard methods in midstance but were consistent during heel strike and toe off. Additionally, the stiff walking forces and angles were compared to compliant values. It is expected that the complaint gait will produce lower peaks values, signifying lower GRF. Studying human ancestors from millions of years ago can suggest practices that could be important in clinical settings today.
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ABSTRACT NO. 60

ANTIANGIOGENIC THERAPY MAINTAINS THE SURVIVAL BENEFITS OF IMMUNOTOXIN-αCD40 THERAPY IN GLIOBLASTOMA MODELS

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D2C7-immunotoxin is a novel cytotoxic therapy against glioblastoma that effectively

induces tumor cell killing by targeting glioblastoma-specific oncogenes, EGFRwt and EGFRvIII. We previously showed that combining D2C7-immunotoxin with αCD40 costimulation of antigen-presenting cells successfully generated cures in preclinical models. However, in clinical settings, the proinflammatory environment induced by immunotoxin-αCD40 immunotherapy exacerbates cerebral edema (brain swelling) in patients with glioblastoma. Traditional edema treatment with corticosteroids cause numerous side effects and hinder the survival benefits of immunotherapies. Recently, antiangiogenic agents that block vascular endothelial growth factor (VEGF) emerged as a promising treatment for edema, but it is unclear whether anti-VEGF therapy improves or hinders the effectiveness of immunotoxin-αCD40 immunotherapy by altering the antitumorigenic immune cell infiltration into the brain. Here, we show that anti-VEGF does not reduce the survival benefits of the immunotoxin-αCD40 therapy in murine glioblastoma models. Compared to the group receiving immunotoxin-αCD40 alone, where 4 out of 8 mice survived, co-administration of low-dose anti-VEGF increased the survival rate to 6 out of 8 mice while maintaining the same median survival time (> 58 days). These findings support the continued use of anti-VEGF to control edema in glioblastoma patients undergoing immunotoxin-αCD40 therapy. For future research, we will rechallenge the surviving mice with glioblastoma to evaluate the long-term immunologic memory response after anti-VEGF co-administration. We will then analyze tumor micro-environment and T cell infiltration to elucidate the role of anti-VEGF in immunotoxin-αCD40 induced antitumor response.

Biological Sciences Undergraduate Research Fellows (BSURF)

ABSTRACT NO. 61

RESCUE OF GLYCOGEN STORAGE DISEASE IA IN MICE BY LIVER-DIRECTED THERAPIES

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Glycogen Storage Disease Ia (GSD Ia) is a rare inherited metabolic disease caused by a mutation in the G6PC1 gene, which codes for an important protein called glucose-6-phosphatase-alpha (G6Pase-alpha), primarily active in the liver. Without G6Pase-alpha, a key enzyme in gluconeogenesis, the patient is unable to break down glycogen into glucose. Consequently, GSD Ia patients experience low glucose levels, glycogen accumulation in the liver, and toxic metabolite build-up in other organs of the body including the kidney, intestines and in some cases the brain. Long-term implications may include liver cancer and end-stage kidney disease. The primary treatment option for GSD Ia involves a dietary approach; however, patients' quality of life remains considerably compromised. Additionally, the dietary regimen does not provide a preventive measure against long-term complications. A viable gene therapy would significantly increase the quality of life of these patients, but it has yet to be found. One key obstacle in delivering gene therapy lies in hindrance caused by glycogen accumulation in the liver. To address this issue, we are focused on developing a solution comprised of a drug and gene-editing therapy using liver-specific G6pc-knockout mice. Through this approach, we hope to enhance gene editing efficiency for GSD Ia and come closer to a promising therapeutic solution for the victims of this debilitating disease.

ABSTRACT NO. 62

PSEUDOURIDINE AS A KEY PLAYER IN PLANT IMMUNE RESPONSE

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Pseudouridine, an isomer of the uracil nucleotide, is a common RNA modification. However, its function is not fully understood, especially during plant immunity. In collaboration with Dr. Chuan He's laboratory in University of Chicago, we applied a new technique, BID-Seq,

to quantitatively measure pseudouridine modification in plant RNAs at base resolution. This revealed that this modification is widely present in plant mRNAs. After being used in COVID vaccines in previous studies, it was found that pseudouridine helped in suppressing immune responses in humans from the vaccines. Due to this, we hypothesize that mRNA pseudouridylation plays a role in regulating plant immune response as well. In order to understand the impact of pseudouridine on plant immunity, we have taken seedlings of *Arabidopsis* and subjected them to various pathogen treatments. By measuring the pseudouridine levels in mRNAs, we are looking to see dynamic changes of pseudouridine levels which could be an important trigger for the plant's immune response. Furthermore, we seek to identify what proteins are involved in the pseudouridine synthetic pathway during immunity by using a tagger on known proteins involved in the pathway. If we can understand the importance and mechanisms of pseudouridine in plant immunity, we believe it would be a significant step towards strengthening agriculture as understanding plant immune response mechanisms to pathogens will help us benefit our crops which ultimately will benefit our communities.

ABSTRACT NO. 63

TESTING DIFFERENT GUIDE RNA SEQUENCES TO ACTIVATE GENES IN HUMAN CELLS

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The CRISPR/Cas-9 system is an RNA-based DNA targeting system that is used to localize effector proteins to manipulate specific regions of DNA. For instance, null-nuclease Cas9 (dCas9) proteins can be fused to epigenome modifiers to activate or repress target genes.Cas9 proteins can locate specific target genes with the help of guide RNAs(gRNAs). Cas9 proteins are derived from different bacterial species. The most commonly used Cas9 proteins are *S. pyogenes* and *S. aureus* Cas9. However, existing Cas9 proteins have limitations such as the potential for pre-existing immunity in the human population. The lab has identified 4 novel Cas9 proteins from different bacterial species. This study aims to determine if these novel Cas9 proteins can activate the HBG1 gene within human embryonic kidney (HEK) cells given a specific gRNA. We hypothesize that in conjunction with the appropriate gRNA that targets the promoter of HBG1, these dCas9-p300 fusions can activate HGB1 expression. We first deactivated the catalytic sites in each Cas9 protein to ablate its nuclease activity and we fused it with p300, a protein that acts as an activator. Then, we transfected HEK with these dCas9-p300 plasmids and the corresponding gRNA plasmids. By running quantitative PCR tests at the end of the process, we can see which samples had higher HGB1 RNA expression.This would mean that that specific dCas9-p300 worked together with a specific gRNA sequence to activate the HBG1 gene. Overall, the discovery of new, working Cas9 proteins could help problems of immunogenicity in gene therapy patients.

ABSTRACT NO. 64

RNAI PATHWAY COMPONENTS MAY CONTRIBUTE TO STARVATION-INDUCED GONAD ABNORMALITIES IN *Caenorhabditis elegans*

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Caenorhabditis elegans that hatch into an environment without any nutrients are arrested in the first larval stage of development, L1. Larvae can remain in L1 arrest for weeks and resume normal development once they receive food. However, many *C. elegans* that experience extended L1 arrest develop abnormal gonads in

adulthood, including germ-cell tumors and uterine masses. These growths suggest a misregulation of cell growth. Previous results indicate that genes involved in processing somatic RNA interference (RNAi) could be causing abnormality formation. RNAi refers to a cell's response to exogenous or endogenous double-stranded RNA. It functions as an internal regulatory mechanism as well as an immune response, allowing sequence-specific suppression of corresponding genes. We hypothesize that endogenous RNAi pathways are involved in the occurrence of starvation-induced gonad abnormalities. It is possible that aberrant small RNAs produced by somatic RNAi machinery are transported to the germline, causing abnormalities to form. We examined rrf-1, ppw-1, rde-1, dcr-1, rde-4, sid-1, alg-1, and rrf-3, which correspond to components of various RNAi pathway branches. Knockout strains and RNAi were used to evaluate the impact of these genes on gonad abnormality frequency in adults following 8 days of L1 arrest. So far, results align with previous findings about somatic RNAi and our transportation hypothesis. We expect future results to further corroborate these findings and clarify the role of different RNAi pathway branches in gonad abnormality formation. Overall, these experiments provide greater insight into the little-known mechanisms regulating pathologies that result from early-life starvation.

ABSTRACT NO. 65

DETERMINING THE ROLE OF K63 UBIQUITINATION IN ER TRANSLATION DURING OXIDATIVE STRESS

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Oxidative stress is a pervasive environmental challenge linked to the development and progression of several diseases, including cardiovascular disease, cancer, and immunodeficiency. Understanding various cellular responses to oxidative stress is essential in developing therapeutic interventions. The Ubiquitin Proteasome System (UPS) regulates several cellular processes, including protein degradation, synthesis, and gene expression. The Silva lab investigates protein translation by K63 ubiquitination during oxidative stress. Recent literature indicates significant translational regulation occurs in the endoplasmic reticulum (ER), and our lab highlighted preferential K63 ubiquitination of ER-bound ribosomes under oxidative stress in mammalian cells. Despite this, numerous functions of ER-localized translation remain unsolved. This study will determine how stress-induced K63 ubiquitination plays a role in ER-localized translation regulation using *Saccharomyces cerevisiae* (yeast) as a model. To investigate this process, we will utilize several techniques, including cellular fractionation using differential centrifugation. We will further validate differences in accumulation between cellular compartments by performing western blot analysis targeting ubiquitin conjugates. These studies will allow us to better understand whether ER-localized K63 ubiquitination is conserved across species and provide avenues for understanding its essentiality for cellular responses to oxidative stress. Eventually, this will enable us to develop targeted therapies that leverage the power of this cellular modification to better control and alleviate the detrimental effects of oxidative stress and pave the way for future treatments and interventions.

ABSTRACT NO. 66

FABRICATING MICROFLUIDIC DEVICES FOR MODELING MICROVASCULATURE

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Microfluidic devices are tools used to study cell behaviors and interactions with their microenvironments. Typical in vitro models, like 2D-culture dishes, insufficiently capture the complex structure of the extracellular matrix, whereas in vivo models like animal testing make it difficult to control experimental conditions. A

microfluidic device is a small chip that permits 3D cell cultures while still allowing control over desired variables, such as flow rate and growth factor concentrations in the cell media. Although there are commercially available devices, these options normally lack design variability and are costly. Therefore, there is a need in the lab for a method to design and fabricate personalized chips for our specific applications. My project is to investigate existing protocols and formulate a procedure for producing microfluidic devices in our lab. The main fabrication method is lithography, which involves printing a design onto a silicon wafer and using it to mold several chips. Most current protocols leave the photoresist, or the “ink,” on the wafers when molding ; instead, we physically etched our designs into the wafer to more economically achieve the feature depths needed for our lab’s application. By testing different elements, such as etching and sterilization, we hope to find the most effective method for promoting blood vessel formation in these chips. If perfected, our lab can readily fabricate its own chips for experimental use to advance our current in vitro models and improve the quality of our experiments.

ABSTRACT NO. 67

OPTIMIZING CYANOBACTERIA DETECTION FOR COMPARING LICHENIZED AND ENVIRONMENTAL CYANOBACTERIAL COMMUNITIES

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Cyanolichens are symbiotic associations between fungi and cyanobacteria. When lichenized fungi reproduce sexually, the fungal spores are dispersed without the cyanobacteria, and they must find a new partner to form a cyanolichen thallus. However, how common these potential cyanobacterial partners are in the substrates where the cyanolichens grow is unknown. A robust sequencing procedure is necessary to compare the communities of lichenized and environmental cyanobacteria. This study aims to optimize the procedure for sequencing 1800 environmental samples from Alberta, Canada. We tested the sensitivity of the 16S rRNA and rbcLX genetic markers for cyanobacteria detection and the role of substrate depth on cyanobacterial community composition. The rbcLX genetic marker is more variable but is single-copy, while the 16S rRNA gene is less variable but exists in multiple copies. Sequencing the 16S rRNA gene may be better for detecting trace amounts of cyanobacteria in environmental samples. Additionally, cyanobacteria are expected to be more diverse in top substrate layers because they need light for photosynthesis, so sampling from deeper depths may not be necessary. We sequenced the two markers from 112 environmental samples, including 12 with known taxonomic compositions. The remaining 100 samples have unknown compositions and include both top and bottom substrate layers. We will use the sequence data to compare the detection sensitivity of the two genetic markers. Preliminary results favor the 16S rRNA gene. The results will inform the procedure for large-scale characterization of environmental cyanobacteria to understand the formation of the cyanolichen symbiosis.

ABSTRACT NO. 68

WHAT IS THE GENETIC CARGO NECESSARY FOR FERROPTOSIS SENSITIZATION OF MCF7 CELLS?

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Ferroptosis is a form of programmed cell death characterized by the accumulation of reactive oxygen species, which lead to lipid peroxidation and membrane rupture. To search for novel ferroptosis inducers and inhibitors, we combined two ferroptosis inducers: erastin and RSL3 with different drug-like compounds from Pandemic Response Box, a compound library for possible Malaria treatment. We identified tipifarnib as a candidate, which was shown to be

particularly effective in sensitizing MCF7 cells to ferroptosis. Aside from the known target of farnesyltransferase we believe that tipifarnib has other targets that lead to the observed phenotype. We performed a one-pot assay and identified exportin/importins as the potential targets of tipifarnib to trigger ferroptosis. We hypothesize that tipifarnib disrupts certain import/exportation of "cargos" resulting in the sensitization to ferroptosis. We treated MCF7 cells with compound inhibitors of exportin, importin, and tipifarnib. Also we shRNA to knockdown exportin, importin, to look for potential pathways that results in the phenotypic change. Through the usage of RT-PCR assays we have data that suggests possible targets and non-targets that make MCF7 cells sensitive to ferroptosis treatment. With further investigation, this provides an avenue for an alternative strategy to treating tumors.

ABSTRACT NO. 69

ASSESSING *C. elegans* INNEXIN LOCATION PHENOTYPES IN TOUCH-SENSITIVE NEURONS

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Gap junctions are intercellular channels made up of hexameric units, connexins in vertebrates or innexins in invertebrates, that allow ions and small molecules to pass between adjacent cells. Although gap junctions are essential to the survival and function of organisms, relatively little is understood about them. To understand more about gap junctions, we used TurboID, a proximity biotinylation enzyme fused to a neuronal innexin, UNC-7, followed by HPLC Mass Spectrometry to identify proteins of interest. We generated single gene deletion strains, guided by the TurboID data to gauge its effect, if any, on innexin localization. The effect the proteins of interest have on innexin regulation was assessed by introducing deletion alleles into a strain that labels an innexin closely associated with UNC-7, UNC-9, with GFP and expressed in a single pair of touch-sensitive neurons in the animal's tail, the PLM neurons. PLM neurons form gap junctions with several other important neurons in C. elegans, including the PVC, PVR, and LUA neurons. These neurons should appear as bright GFP puncta on the PLM axon. Using this system, we found that the deletion of syg-1, unc-116, vab-1, and src-1 lead to phenotypes in the localization of the GFP labeled UNC-9 innexin. When looking at these genes, we sought to find out whether the deletions affected function – forming nonfunctional gap junctions, interrupting cell-cell communication, or not forming gap junctions – trafficking, or positioning at the correct synaptic face.

ABSTRACT NO. 70

THE CONTRIBUTION OF NRG1/ERBB4 SIGNALING TO THE HOMEOSTATIC EFFECTS OF SEIZURES IN EPILEPSY MODELS

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Temporal lobe epilepsy (TLE) is known to be induced by seizures themselves, although there is much to learn about the mechanisms by which TLE develops and progresses ("epileptogenesis"). Briefly inhibiting BDNF/TrkB signaling induces regression of epileptogenesis, yet only if introduced after a seizure. Thus, we propose that seizures also activate signaling pathways that inhibit epileptogenesis. The receptor tyrosine kinase ErbB4 is expressed exclusively in the interneurons of the hippocampus, where the activation and inhibition of ErbB4 signaling exerts anti- and pro-convulsant effects respectively in diverse seizure models. We hypothesize Nrg1 activated ErbB4 to be involved in this seizure-activated, anti-epileptogenic signaling pathway. Kainic-acid status epilepticus mice cohorts and PBS control mice cohorts were studied using in situ

hybridization techniques such as RNAscope to label targeted mRNA sequences with fluorescent tags. Charting the spatial profile of KA-SE induced Nrg1/ErbB4 signaling was achieved using ImageJ software that produced image based, semi-quantitative analyses of the RNAscope data. We expect to be able to quantify and localize the increases in Nrg1 mRNA expression seen in our preliminary data. ErbB4 receptors are expressed in hippocampal interneurons, and parvalbumin (PV) interneurons are required for the anticonvulsant effects of Nrg1, suggesting that seizures may enhance PV neuron-mediated synaptic inhibition. Understanding the circuits and cells in which KA-SE activates Nrg1/ErbB4 signaling would facilitate elucidating its functional consequences.

ABSTRACT NO. 71

ALPHA-ACTININ IN ZASP52 MUTANTS DURING DORSAL CLOSURE

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Dorsal closure is a stage of *Drosophila* embryogenesis in which lateral epidermal cell sheets bordering an eye-shaped dorsal opening ”zip” together to form a seamed and then seamless epithelium. Understanding this process is important because it models cell sheet movements such as neural tube closure and palate formation as well as wound healing in vertebrates. The dorsal opening itself is filled by a layer of thin, flat amnioserosal cells. The amnioserosa is bordered by actomyosin-rich purse strings that provide tension and maintain the shape of the opening as it closes. The expression of Echinoid in the lateral epidermis and the lack of expression in the amnioserosa is known to be essential for actomyosin cable formation, but what proteins govern the formation and stability of the purse string are not fully understood. I used a GFP-tagged alpha-Actinin fusion protein to visualize alpha-Actinin localization in Zasp52 and Echinoid double mutants as well as in Echinoid mutants only. Fluorescent imaging revealed that in Zasp52 and Echinoid double mutants, alpha-Actinin does not appear to localize to the purse string, while in Echinoid mutants it does. This provides evidence that it is Zasp52 that recruits alpha-Actinin to the purse string.

ABSTRACT NO. 72

INVESTIGATING TOOLS TO STUDY CALCIUM DYNAMICS IN *Arabidopsis* CPK MUTANT RESPONSE

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Pattern-triggered immunity (PTI) is an ancient, conserved branch of the plant immune system activated by pathogen-associated molecular patterns. Calcium signaling is an important part of the immune pathway and plant responses to stress, yet the spatiotemporal dynamics of calcium during PTI are not well understood. Previous research has demonstrated the role of calcium-dependent protein kinases (CPKs) in downstream cytoskeletal regulation and actin reorganization, but the role of calcium in these pathways is unknown. Here, we validate tools to study calcium dynamics using the model plant system *Arabidopsis thaliana*, and mutations in CPK3-2 and CPK6, which have previously shown cytoskeletal phenotypes during PTI. T-DNA insertional knockout lines cpk3-2 and cpk6 were used to explore the connection between CPK pathways, calcium signaling, and the cytoskeletal PTI response induced by the bacterial flagellum-derived protein flg22. The knockouts were crossed with the genetically encoded calcium biosensor RGECO1/mTurquoise. Seed lines were bulked and genotyped to select homozygote lines for the T-DNA insertional mutant, as well as screened via confocal microscopy to check the fluorescence and functionality of the RGECO1/mTurquoise cassette. Time-lapse images were taken of selected plants with the confocal microscope after inoculation with flg22, and their initial calcium responses were compared with the wildtype RGECO1 cross. The

preliminary results presented here give further insight into the roles CPK and calcium play in the PTI response, and how best to continue studying calcium and cytoskeletal dynamics in plant cells.

ABSTRACT NO. 73

PRENATAL ENVIRONMENTAL TOXIN EXPOSURE AS A RISK FACTOR FOR NEURODEVELOPMENTAL DISORDER PATHOLOGY IN ADOLESCENCE

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The prevalence of neurodevelopmental disorders (NDDs) has increased rapidly in recent decades. Genetic mechanisms of these disorders have been studied extensively; however, environmental factors contributing to NDD development remain less understood. Current evidence suggests that alterations in synaptogenesis and pruning underlie NDD pathology. Sleep is essential to this synaptic remodeling process. Disturbed sleep is a highly conserved trait affecting nearly 86% of NDD patients. Additionally, sleep appears to be particularly sensitive to environmental perturbations, as negative sleep outcomes have been strongly linked to exposure to air pollutants. The Diesel Exhaust Particle and Maternal Stress (DEP/MS) paradigm was used to co-expose pregnant mice to DEP and a maternal stressor, modeling epidemiological data suggesting that combined prenatal exposure to DEP is strongly linked to socioeconomic stressors. Previous studies have revealed that DEP/MS offspring show male-specific social and behavioral traits consistent with NDD pathology. Based on preliminary data demonstrating sleep deficits in DEP/MS adult offspring, this study aims to characterize NDD phenotype of DEP/MS offspring during adolescence, focusing on possible female-specific sleep and behavioral alterations. To analyze sleep patterns in DEP/MS and control offspring, we performed electroencephalography and electromyography recordings from P37 to P40. Additionally, we isolated astrocyte and microglia populations from parietal and frontal cortex tissue. Lastly, we conducted the forced-swim test to analyze depressive-like behavior, a common comorbidity in female NDD patients. We hypothesize that DEP/MS offspring will exhibit sex-specific depressive-like behavior and sleep deficits driven by changes in astrocyte gene expression.

ABSTRACT NO. 74

ELASTIN-LIKE POLYPEPTIDES WITH MODIFIED CDC-19 AMYLOID INSERTS

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Elastin-like polypeptides (ELPs) have the ability to phase separate in liquid which provides many applications (like protein purification), and with modifications they can have pH dependent properties to form functional materials. ELPs reversibly change solubility based on temperature, becoming insoluble after reaching a critical solution temperature. CDC-19 amyloids are found in yeast and sequester proteins during stress. When added to ELPs, the ELPs become irreversible below a certain pH threshold. However, this threshold is below physiological conditions and pH changes alter ELP transition temperatures, limiting use and predictability. It was hypothesized that 1) substituting the aromatic amino acids will increase the threshold pH and 2) adding positively charged amino acids to neutralize the amyloid's negative charge will stabilize the phase transition temperature across pHs. Polypeptides were placed into a UV-Vis spectrophotometer at various pHs, then heated and cooled to record transition behavior and measure phase reversibility. Polypeptides were also imaged under a microscope to show phase behavior assemblies (such as droplets and solids) at different pHs. It was found that the substitution of aromatic amino acids increases the pH threshold of polypeptides. In contrast, the addition of positively charged amino acids, arginine and lysine, abolished pH sensitivity. A material that is pH sensitive potentially has many

applications, such as researching cancer as cancerous cells have distinct pHs. Future research should seek to increase the pH at which the ELPs change to a physiological one and stabilize the temperature-dependent behavior at various pHs.

ABSTRACT NO. 75

LOCALIZATION AND FUNCTION OF ARC6 IN CELL DIVISION

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Chloroplast division of photosynthetic eukaryotes is a highly regulated process with divisionary machinery involving a division ring and other essential components. To gain insights into this process, our lab uses the green alga *Chlamydomonas reinhardtii*, which possesses a single chloroplast that coordinates with the rest of the cell during division. We investigate the role of the ARC6 protein, a potential linker between the inner chloroplast membrane and the FtsZ division ring. We aim to investigate the dynamics of ARC6 localization and its potential role in the context of various division components and the FtsZ ring. While previous studies have indicated that ARC6 localizes at the division site, the underlying mechanisms and its relationship with FtsZ and other divisionary machinery are not fully understood. In our study, by employing fluorescent microscopy, we characterized the localization patterns of ARC6 during cell division. Our findings reveal a dynamic assembly and disassembly behavior of ARC6 at the division site, enabling movement along the chloroplast membrane to subsequent division sites. Previous research has suggested that cytoskeletal actin may be important for the formation of the inner division ring. Surprisingly, we found an apparent loss of ARC6 at the division site in the absence of actin in our experiments. This result suggests that the cell uses the cytoplasmic F-actin to regulate the localization of ARC6 in the chloroplast inner envelope. Possible mechanisms for this regulation and the consequences of loss of ARC6 from the division site are being examined.

ABSTRACT NO. 76

DIFFERENCES IN GROUND REACTION FORCES BETWEEN A STIFF AND COMPLIANT GAIT

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Orthopedic injuries often occur while the knee is extended, in a relatively stiff (limited change in angle) position that generates relatively high ground reaction forces (GRF, forces applied to the body from the ground). Modern humans walk with their knees in this relatively stiff position while apes, our closest relatives, utilize a compliant gait that features greater knee joint yield (decrease in knee angle). Compliant walking has been predicted to lead to lower GRFs, but there is limited data to test that presumption in walking. The Animal Locomotion Lab sought to compare the differences in GRFs, using 28 participants walking with a stiff and compliant gait. If participants walking compliantly are shown to have lower GRFs compared to when they walked stiffly, implications span from orthopedics to evolutionary anthropology. The data was collected using two methods to determine the validity of an open-source and marker-less gait analysis technique (OpenCap). Traditional gait analysis requires force plates and markers to gather force and joint angle data. This method, though accurate, is resource intensive and hard to utilize in nontraditional settings. OpenCap performs the same data analysis with fewer resources and is applicable in various settings. Even though we found significant differences in the numeric values of minimums of the force traces, Open Cap still calculated accurate data for peak forces that was not statistically different, which can still provide insight into how athletes, non-athletes, healthy, and injured people move.

ABSTRACT NO. 77

EVALUATING THE PHENOTYPIC CHARACTERIZATION OF *Cryptococcus neoformans* CLINICAL ISOLATES

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Cryptococcus neoformans is a human fungal pathogen that can infect the lungs and later spread to the central nervous system. This disease is most associated with immunosuppressed individuals. *C. neoformans* is distinctive compared to other fungi because of its ability to produce a thick capsule comprised of polysaccharides, proteins, and other molecules, which shield this yeast from environmental stresses. The capsule can also interfere with the hosts' immune response by dampening the response and preventing phagocytic cells from engulfing the yeast due to its increased size. We hypothesize that variation in capsule size among clinical isolates could result in different patient outcomes, as it could aid the cells in establishing disease and avoiding immune detection. For instance, smaller capsules may enable this yeast to survive better within macrophages through adaptation. These infected macrophages can then travel to other parts of the body and spread the infection, while yeast with large capsules pose a challenge for immune cells to engulf. To test this hypothesis, we carried out in vitro analyses to examine which conditions caused optimal capsule production in *C. neoformans* isolates from temperature, growth duration, media volume, and other growth conditions. In addition, 162 clinical isolates were evaluated for sensitivity to cell stressors, SDS detergent, and caffeine, that affect cell membrane and cell wall integrity. By identifying the conditions that promote optimal capsule growth–a major virulence factor– for this yeast cell, and those that hinder it, more comprehensive research can be conducted on *C. neoformans* and other fungi.

ABSTRACT NO. 78

OPTIMIZING ASSEMBLY OF ASYMMETRIC PEPTIDE NANOFIBER VACCINES FOR DELIVERY THROUGH MUCOSAL MEMBRANES

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Mucosal vaccines are gaining increased attention due to their potential to tackle distinct bodily mucosae and induce immune responses to prevent and treat infectious diseases and autoimmune conditions such as inflammatory bowel disease (IBD). Some benefits over traditional vaccination methods include needle-free delivery and localized action through the production of IgA and tissue resident T cells. Firstly, materials need to cross a dense layer of mucus before reaching the epithelium and achieving the desired therapeutic goal. Moreover, each mucosal membrane is distinct and presents its own properties, for instance, pH, immune cell type, turnover rate, etc, that call for specific biomaterial properties for successful delivery. Inspired by infectious organisms that naturally cross human mucus to impair cellular function (e.g., Influenza A virus), this project aims to develop a safe and effective carrier platform that can both attach to and cross mucosae in time before being carried away by natural mucus turnover in the host organism. The asymmetry of the fibers is essential so that they can perform a Brownian ratchet-like motion, where one subunit of the fiber is constantly cleaving mucus whereas the other provides support by attaching to mucus. After conjugating each subunit with a fluorophore, we observed through confocal microscopy that they combine most effectively at 95°C for 10 minutes. We also tested the binding activity of two mucin-binding peptides identified from the literature as well as epitopes of interest through a mucoadhesion assay. C3a1 showed the highest binding activity. Knowing this, we aim to conjugate this binding subunit with a mucus cleaving enzyme and assess their overall dynamics in mucus.

SUMMER RESEARCH OPPORTUNITY PROGRAM (SROP)

ABSTRACT NO. 79

THE ROLE OF UBE2A MUTATIONS IN THE DEVELOPMENT OF THE NASCIMENTO DISEASE

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Nascimento syndrome is a X-linked intellectual disability discovered in 2006 characterized by developmental delay, moderate to severe Intellectual development, seizures, dimorphisms, skin anomalies. The hypothesis of this project is that the presence of disease-related mutation in the UBE2A sequence compromises the UBE2A gene leading to the development of the Nascimento disease. The goal of this project is to confirm if Rad6 affects cellular growth in yeast cells. It shows the Western blot experiment and sizes. The PCR and Western blot were important for the identification and comparison of the proteins on the growth curve, UBE2A, UBE2A Mutations, Rad6, RAD6. From our experiments, it was concluded that UBE2A mutations affect cellular health and growth. The absence of rad6 in our proposed model made our cells sicker. The other mutation as described by researchers showed little decline in growth and confirmed that the effects from the mutation were mild and severe respectively. The big question following the confirmation concerning the cellular health hypothesis is to find out if it is connected to the Nascimento disease – the functions altered remain unknown – and if the UBE2A mutation is even actually the cause of the disease.

ABSTRACT NO. 80

TARGETING PREDETERMINED AFRICAN AMERICAN GENES ASSOCIATED WITH INCREASED RISK OF METASTATIC PROSTATE CANCER USING DOCUMENTED SMALL MOLECULE INHIBITORS

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Prostate cancer (PC) health disparity is the largest cancer disparity. PC incidence rates are 73% higher for African American men (AA) versus Caucasian American men (CA). Even in equal-access settings, AA are 84% more likely to have high-grade PC compared to CA. Although socioeconomic determinants heavily influence disparity across all health sectors, the statistics suggest an inherent genetic difference between AA and CA at play. Consequently, there is a need for translational research using genomic data and precision medicine approaches to combat the increased risks of fatal PC in AA. Our hypothesis is that there is a subset of actionable genes essential for enhanced PC progression in AA. To identify genes associated with PC lethality in AA, we utilized a Durham VA gene expression data set from 300 AA and 300 CA with PC. We conducted a CRISPR knockout screen to find druggable genes associated with metastasis in AA with PC. 11 AA hits were found, of which the following were prioritized given that they have documented small molecule inhibitors: Tyrosine threonine kinase (TTK), Ribonucleotide reductase catalytic subunit M1 (RRM1), and Mediator complex subunit 25 (MED25). The IC50s of the corresponding inhibitors were tested in 22RV1 cells. Complementary studies using gene knockdown are being conducted to validate our targets and their corresponding small molecule inhibitors. Furthermore, the downstream genetic effects of inhibiting our hits in vitro are to be analyzed via western blotting. Findings from the exploratory in vitro studies highlight the role of our hits in reducing PC cell proliferation and metastasis rates. As such, this research lays the groundwork to justify further studies, such as ex vivo assays in which PC patient-derived explants from AA and CA are treated with the relevant inhibitors. Such studies can more accurately reveal the therapeutic potential of targeting our race specific hits.

ABSTRACT NO. 81

INVESTIGATING THE ROLE OF THE RIOK2-NFKB INTERACTION IN PROSTATE CANCER

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Right Open Reading Frame Kinase (RIOK2) is critical in the assembly and maturation of ribosomes, which are necessary for the high proliferation of cancer cells. Targeting RIOK2 genetically and pharmacologically is shown to decrease tumor growth and metastatic potential, likely due to impairment of ribosome biogenesis. Our group discovered that RIOK2 has novel DNA binding activity. There remain unknowns regarding RIOK2-DNA binding including which cofactors it binds. Mass spectroscopy studies indicate that RIOK2 interacts with RELA, a subunit of Nuclear Factor Kappa-light-chain-enhancer (NF-kB). NF-kB is a proinflammatory cytokine, influencing cell proliferation and processes essential for cancer cells. The RELA subunit in canonical NF-kB signaling is a nuclear localization sequence whose exposure results in NF-kB nuclear translocation. This study hypothesizes the RIOK2-NF-kB, specifically the RELA subunit, interaction supports tumor cell proliferation and progression. A nuclear fractionation experiment exhibited that RIOK2 is present in both the nucleus and the cytoplasm. Following that, an immunoprecipitation assay of 22RV1 and PC3 cells indicated that RIOK2 and NF-kB were bound when RIOK2 was not part of a ribosome complex. A combination proliferation experiment indicated an additive effect on tumor cell proliferation when targeting NF-kB and RIOK2 simultaneously. The results of these assays validated the presence of an NF-kB-RIOK2 interaction. Next, we will conduct a nuclear fractionation assay with genetic and pharmacological targeting of RIOK2 or NF-kB to understand where the interaction occurs and how it is disrupted. Conversely, we will use NF-kB activating ligands to determine how activation of NF-kB affects RIOK2-NFkB binding. An understanding of this interaction is important to understand cancer cell biology and for translational interventions. Currently, there are no drugs in clinical trials targeting NF-kB, whereas RIOK2 is highly actionable. If there is a significance to this interaction it may be possible to target NF-kB by focusing on the RIOK2 interaction.

ABSTRACT NO. 82

LEVERAGING OPTOGENETIC STIMULATION DATA TO VALIDATE LOCAL FIELD POTENTIALS AND THEIR FEATURES

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Optogenetic stimulation is a popular method to alter the neural activity of various organisms in a localized manner. To better understand the effect of optogenetic stimulation across different regions of the brain, we analyzed the results of an experiment involving mice with 6 different opto ports located in different regions as well as 32 electrophysiology channels that collect local field potential (LFP) and single neuron spike data. We used a feature representation of LFP data called directed spectrum and were able to lend evidence to its legitimacy using the data. These features illustrate the effects of optogenetic stimulation through interactions between areas of the brain showing regions that have more widespread impacts and regions that stay more contained. Through the opto experiment we were also able to better understand how LFPs and spike data are linked, investigating firing rate and phase relationships. Applying these insights to a practical example, directed spectrum features were able to add novel information to machine learning models using a more common LFP representation.

ABSTRACT NO. 83

THE EFFECTS OF ANXIOLYYTIC CHANGES ON MITOPHAGY IN AN ALS MODEL

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Mitochondria are dynamic organelles that are vital for neuronal health. Mitophagy is a mitochondrial quality control pathway where damaged or aged mitochondria are removed from the cell. Specifically, PINK1 and Parkin phospho-ubiquitinate outer mitochondrial membrane proteins that target damaged organelles for engulfment by LC3-anchored phagophores and degradation via lysosome fusion. Genetic and pathology studies have implicated deficits in the PINK1/Parkin mitophagy pathway to the onset of Amyotrophic Lateral Sclerosis (ALS), a neurodegenerative disease involving the loss of motor neurons followed by muscular atrophy. Research suggests that there are similar changes in mitophagy in anxiety induced by chronic psychogenic stress. Mitophagy is enhanced due to the increased stress, which causes mitochondrial loss and downstream synaptic weakening in the anxiolytic pathways, as also seen in ALS. Here, we explored the relationship between chronic social defeat (CSD) and mitophagy using immunohistochemistry in mouse brains. To see whether there were changes in mitophagy following CSD, we visualized TOMM20 (a subunit of the Translocase of the Outer Mitochondrial Membrane) to label the mitochondrion in the brain tissues and confocal imaging to quantify the number of mitochondria throughout the brain in wild type and defeated mice. Investigating these changes in various brain regions: prefrontal cortex, amygdala, dorsal hippocampus, and primary motor cortex, we can pinpoint the area that is most affected. This highlights the importance of targeting the mitophagy pathway to ameliorate the detrimental effects of chronic social defeat that models the mitochondrial changes in many neurodegenerative diseases. These mechanisms are critical for neuronal health, as neurons are vulnerable to impairment in mitochondrial quality, we hope to target the PINK1/Parkin pathway in regions that are most affected by CSD to further investigate its significance in ALS.

ABSTRACT NO. 84

INVESTIGATING THE ROLE OF THE MD-TO-PRL PATHWAY IN GOAL-SEEKING BEHAVIOR

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In the natural world, organisms have evolved to actively seek out rewards, a fundamental behavior that is reinforced as they approach the anticipated goal. In the context of the brain and reward anticipation, goal progress can be understood as the behavioral measures reflecting an individual's advancement toward an expected reward. Previous research has utilized machine learning and multi-site electrophysiology to define a specific pattern of synchronized neural activity called an electome network that signals for goal progress. This electome network is dominated by a connection leading from the mediodorsal thalamus (MD) converging onto the prelimbic cortex (PrL). To further investigate this specific pathways relevance to goal oriented behavior, we utilized a DREADD-based (Designer Receptors Exclusively Activated by Designer Drugs) inhibition of the MD-to-PrL circuitry in a mouse model. We then examined their behavior in a social seeking paradigm using the standard social preference assay. We hypothesize that inhibiting the Md-to-PrL pathway will result in behavioral deficiencies in goal progress, operationalized as the number of visits to the social chamber in the social preference assay. Understanding how this specific pathway contributes to the regulation of goal-oriented behaviors has the potential to shed light on the underlying mechanisms of neuropsychiatric disorders characterized by dysregulated reward processing and impaired goal-directed behaviors.

D-CARE

ABSTRACT NO. 85

NEUROBEHAVIORAL TOXICITY WITH COMBINED LEAD AND ETHANOL EXPOSURE DURING DEVELOPMENT IN ZEBRAFISH

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Both lead and ethanol exposure during early development have long been known to cause long-term neurobehavioral impairment. Exposure to lead during pregnancy and childhood has been linked to long-lasting cognitive and emotional impairments. However, people are not only exposed to single toxicants. In addition to daily lead exposure, most people have interactions with many other toxicants. Prenatal exposure to ethanol can cause cognitive impairment typically diagnosed as Fetal Alcohol Spectrum Disorder. Little research has been done to show the effects between lead and ethanol despite the fact that many people have this dual exposure. This study sought to examine the effects of the two toxicants and determine whether or not lead and ethanol have additive or synergistic effects. In this study, zebrafish were on a five-day schedule where they were individually exposed to water, ethanol, lead, or a lead and ethanol mixture. Following this, they were examined for deformities and tested for locomotion under light and dark conditions using Daniovision at six days post fertilization. The data collected is hypothesized to show that the zebrafish exposed to both toxicants will have the lowest levels of locomotion and the highest deviation in behavior when compared to the control. Furthermore, it is hypothesized that ethanol and lead will potentiate each others' long-lasting effects into adolescence and adulthood. This zebrafish study will help us better understand the neurobehavioral effects that these toxicants have on brain development and the mechanisms for these impairments.

ABSTRACT NO. 86

NO INFLUENCE OF SEX ON CYP2E1 LEVELS IN A DEPENDENT OR NON-DEPENDENT ALCOHOL USE DISORDER MODEL

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Compared to women, men are more likely to consume larger amounts of alcohol. In fact, men consume nearly 3 times more alcohol per year as women. However, women tend to have more severe pathological effects due to excessive ethanol levels. For example, binge-drinking overwhelms Alcohol Dehydrogenase (ADH) leading to the oxidation of ethanol by Cyp2e1. Cyp2e1 is associated with reactive oxygen species production which can increase liver damage. Few studies have been published on the effects of gender on ethanol-induced Cyp2e1 in the liver. This study tested the hypothesis that Cyp2e1 will be more elevated after ethanol in females compared with their male counterparts. Liver samples were taken from 2 cohorts of animals. The first underwent the Drinking in the Dark model, a non-dependent model of a binge; whereas, the second group were gavaged for 10 days with 5g/kg of ethanol in a model of alcohol-induced cell death. Samples were then homogenized, followed by undergoing Bicinchoninic Acid Assays (BCA) and Cyp2e1 ELISAs. The BCA was used to determine total protein concentrations, but the ELISA was utilized specifically to measure Cyp2e1. The CYP2E1 levels were comparable between ethanol and sucrose and across both sexes after the DID. However, in our "dependence" model with higher blood ethanol concentrations, ethanol led to an increase in CYP2E1 compared to water across both sexes. This suggests that while gender does play a role in the intensity and damage associated with ethanol, it does not affect the levels of Cyp2e1 in the liver, but there were distinct differences in ethanol's effects across the

two models. Heavier consumption could lead to more ROS production and damage due to changes in CYP2E1 compared with non-dependent binge drinking.

ABSTRACT NO. 87

CRISPR-CAS9 PROBES THE IMPACT OF PRDM1 GENE ON ALCOHOL-ASSOCIATED LIMB MALFORMATION USING A ZEBRAFISH MODEL

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Alcohol exposure during embryonic development is known to cause a broad range of defects in an organism, including physical malformation and cognitive deficits. However, the genetic mechanism by which alcohol can cause such a consistent pattern of defects is largely unknown. In the present study, the gene PRDM1, a transcription vector crucial to limb development, is evaluated for its role in alcohol-induced limb deformities, using CRISPR-Cas9 gene-editing techniques and a zebrafish model. The CRISPR-Cas9 system for genome editing uses a short guide RNA (sgRNA) matching a target sequence within the gene of interest to create a double stranded break in a cell's genome and introduce a mutation, turning off or "knocking out" the translation of that gene. When injected into the yolk during the zygote stage, this technique produces a biallelic null mutation of the gene of interest. Additionally, using a set of four different target sequences attached to the Cas9 endonuclease has been found to increase the efficiency of gene mutation, ensuring a complete knockout in the majority of cells in the developing organism. After synthesizing four sgRNAs matching four sequences within the PRDM1 gene of zebrafish, zygotes were injected with the Cas9-sgRNA complex. Their phenotypes will be compared with an uninjected control group and an alcohol-exposed group to determine the potential role of PRDM1 in mediating alcohol's effect on limb development. The ability to create homologous mutants in the manipulated generation differentiates the CRISPR-Cas9 approach from previous recombinant DNA technologies and opens the door for a more efficient analysis of the role of specific genes in a wide range of pathologies.

ABSTRACT NO. 88

LONG-TERM EFFECTS OF ADOLESCENT ALCOHOL EXPOSURE, AND PREVENTATIVE CHOLINE SUPPLEMENTATION ON CHOLINERGIC MARKERS IN THE MEDIAL PREFRONTAL CORTEX.

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Adolescent binge-drinking causes adverse effects on brain development that persist into adulthood. Adolescent intermittent ethanol (AIE) exposure, a rat model that mimics adolescent binge-drinking patterns, causes deficits in cholinergic tone in adulthood within the medial prefrontal cortex (mPFC) – a region important for memory, decision-making, and self-regulation. Notably, previous studies have shown that choline supplementation can reverse cholinergic deficits and persistent neurodegeneration induced by fetal alcohol exposure. As such, this study aims to investigate the long-term effects of AIE on cholinergic tone within the mPFC, and the potential preventive effects of choline supplementation administered during AIE. We hypothesized that rats exposed to concurrent AIE exposure and choline supplementation will not manifest the cholinergic deficits induced by AIE alone, resulting in levels of mPFC cholinergic markers that are similar to those observed in control animals that were not exposed to AIE. Male and female adolescent Sprague-Dawley rats received 14 doses of ethanol (DOSE, intragastric) or isovolumetric water over 23 days. The daily choline supplements (DOSE) were given in condensed milk or the rats were given regular condensed milk at PND 24 continuing until PND 56. In

adulthood (PND 70) rats were sacrificed, and their brains were harvested for immunohistochemical analysis of vesicular acetylcholine transporter (VAChT). The investigation of the mPFC is currently ongoing. After images of the infralimbic and prelimbic regions of the mPFC are obtained, VAChT immunoreactivity (IR) will be measured using densitometry. We predict that AIE will reduce VAChT in the mPFC as in previous studies and that preventative dietary choline supplementation will ameliorate the AIE-induced deficit, resulting in VAChT+IR comparable to those observed in non-AIE-exposed controls. This would suggest that preventive dietary choline supplementation, combined with binge drinking, may protect against the neurological deficits associated with adolescent binge drinking.

ABSTRACT NO. 89

CHOLINE SUPPLEMENTATION AS A POTENTIAL PROTECTIVE MEASURE AGAINST ADOLESCENT INTERMITTENT ETHANOL-INDUCED CHOLINERGIC DEFICITS WITHIN THE MSDB

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Binge-drinking, a prevalent adolescent ethanol consumption pattern, yields acute cognitive deficits, particularly in learning and memory mediated by specific brain pathways. Adolescent intermittent ethanol (AIE) exposure, a rodent model for adolescent binge-drinking, causes memory impairments and reductions of cholinergic neurons in the Medial Septum Diagonal Band of Broca (MSDB). The MSDB is a hub of memory-related cholinergic innervation that is divided into subregions Ch1, 2 (medial septal nucleus and diagonal band's vertical limb nucleus) and Ch 3 (lateral portion of the diagonal band's horizontal limb nucleus). Choline supplementation during adolescence may mitigate AIE effects in the MSDB, as choline supplementation has neuroprotective effects against neurodegeneration. Therefore, we hypothesized that dietary choline supplementation during adolescence would ameliorate AIE-induced cholinergic deficits within the MSDB. Adolescent Sprague-Dawley rats received daily choline (100 mg/kg in 6% sweetened condensed milk) or vehicle (6% sweetened condensed milk) (PND 24-56) while concurrently being exposed to 14 ethanol (5 g/kg; intragastric gavage; AIE) or isovolumetric water doses (PND 29-52). Brains were harvested in adulthood (PND 70) for Choline Acetyltransferase (ChAT) expression, a marker for cholinergic neurons in the MSDB. Densitometry and cell count methods were used to measure ChAT immunoreactivity (IR). We expect to replicate previously reported AIE deficits in ChAT-IR and we predict dietary choline will prevent these deficits.

ABSTRACT NO. 90

PATERNAL CANNABIS EXPOSURE EFFECTS ON OFFSPRING GLUTAMATERGIC AND CHOLINERGIC FUNCTION

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Cannabis use is increasing, particularly in the US; however, little is known of the trans-generational effects of cannabis. Previous research shows that paternal cannabis use alters DNA methylation in sperm, and increases drug-seeking behavior in offspring, indicating an altered response in brain regions involved in reward processing such as the nucleus accumbens (NAc). Excitatory transmission, both glutamatergic and cholinergic, is important for reward processing in the NAc, and disruptions in these systems can lead to dysregulated reward response. Adolescent offspring of male rats exposed to cannabis extract (CE, containing 4 mg/kg Δ9-THC) were expected to have increased glutamatergic function in the NAc. Male rats were

subcutaneously exposed to CE either daily (7xWeek) or using a “weekend” model (2xWeek, 5xWeek vehicle), or control (vehicle) for 28 days. 24 hours after the last exposure, males were mated with drug-naïve females. Offspring aged into adolescence and brains were harvested for analysis of vesicular glutamate transporter (VGluT) and vesicular acetylcholine transporter (VAChT) expression in NAc subregions. “Weekend” paternal cannabis exposure increased VAChT expression in the NAc core of female offspring compared to control female offspring, but had no effect in male offspring. There was no effect of daily paternal CE exposure on VGluT expression, and no effect of either CE exposure on VAChT expression. These data indicate weekend paternal cannabis use may alter the glutamatergic system in reward regions in a sex-specific manner, highlighting the need for continued research on the effects of paternal cannabis exposure research.

ABSTRACT NO. 91

SEX-SPECIFIC, ENDURING EFFECTS OF ADOLESCENT INTERMITTENT ETHANOL EXPOSURE-INDUCED DYSREGULATION OF ASTROCYTES IN THE AMYGDALA

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Adolescent binge-drinking is widely prevalent in the United States and is the most commonly abused substance amongst youth. Adolescent binge drinking is known to have long-term effects on hippocampal astrocytes in both males and females leading to increased gliosis. However, less information is known about alcohol’s long-term influence on the amygdala and whether biological sex factors into its dysregulation. The amygdala, which continues to develop into early adulthood, is critical for regulating emotion and encoding memory. Further, the amygdala is traditionally larger in males, which makes it critical to assess its impacts on both sexes. In this study, immunohistochemistry for glial fibrillary acidic protein (GFAP), an astrocyte-specific cell marker, was applied to brains from rats exposed to the Adolescent Intermittent Ethanol (AIE) model. Cell counts and cell density in the basolateral amygdala (BLA), central nucleus of the amygdala (CeA), and medial amygdala (MeA) were analyzed separately. It was found that ethanol exposure significantly decreased the cell count of astrocytes in the BLA and MeA in both sexes. While no sex difference was observed in the MeA, females showed a greater BLA cell count than males even in the control. There were no notable differences in GFAP cell count or density for neither ethanol nor sex in the CeA. These results indicate that both sexes are susceptible to having decreased cell counts in the BLA and MeA due to ethanol exposure, but there are regional differences in the ethanol response considering our findings in the amygdala compared with the hippocampus. More studies must be done to further assess the impacts of cell death in the amygdala due to ethanol exposure and possible strategies to combat ethanol-induced astrocytic loss.

EVOLUTIONARY ANTHROPOLOGY

ABSTRACT NO. 92

AGE & SEX: FACTORS OF NEOPHOBIA IN EULEMUR FLAVIFRONS

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Neophobia, the fear of novelty, is a major contributor to how animals interact with their environment. It has been well documented that age can affect reaction to novelty, such that younger individuals are less neophobic than older individuals because they have not been exposed to as much risk. However, less is known about sex related neophobia, which may be more prominent in the dominant sex, such as lemurs, which exhibit strong female dominance.

Individuals of the less dominant sex could be less neophobic as they have less access to resources, thus needing to more flexibly exploit resources. Alternatively, individuals of the more dominant sex may be less neophobic if the boldness they show in social contexts, also translates to increased boldness in non-social contexts. We studied neophobia and its relationship to age and sex in captive Eulemur flavifrons (blue-eyed black lemurs, n = 10) at the Duke Lemur Center in Durham, N.C. To do so, we allowed lemurs to interact with a novel object and familiar food, and then measured latency to approach and order in which the lemurs explored both. We then compared averages in males vs females and in younger vs. older adults. Our preliminary data shows that both males, the less dominant sex, and older adults took longer to approach their first choice of either the food or the novel object (5.85 vs 33.54 sec and 1.75 vs 37.64 sec, respectively). We also found that females approached the novel object more times than males as did older adults when compared to younger adults. From these findings, it appears that both age and sex affect E. flavrifrons neophobia, however, more trials need to be done for confirmation.

ABSTRACT NO. 93

INFLUENCES OF LOCOMOTOR MODE ON HAND AND FOOT BONE SCALING IN PRIMATES

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In quadrupedal primates, the hands and feet are homologous structures and perform similar functions due to similar functional demands of locomotion (e.g., weight bearing, propulsion). In primates with functionally differentiated limbs (e.g., suspensory taxa) the limbs have likely undergone subsequent morphological diversification, causing homologous structures to diverge from one another. We test the hypothesis that different biomechanical pressures on the limbs impact scaling of homologous hand and foot bones. We predicted that, across primates, the talus (foot bone) will show less size variability than the scaphoid (hand bone), while scaphoid size will correlate to locomotor mode. Volume and surface areas of the sample were measured using GeoMagic Studio v.2014. All data analysis was conducted in R studio v.4.2.0. Preliminary results support our predictions. First, the scaphoid exhibits a higher range of size across locomotor modes than the talus. Second, scaphoid size variation tends to group according to locomotor mode, while groupings of the talus are less distinct. These results preliminarily support our hypothesis that locomotor mode impacts scaling of serially homologous bones, suggesting that the biomechanical demands of specific locomotor modes may influence reduced size covariation of serially homologous bones. Future research will incorporate additional pairs of serially homologous bones.

SUMMER NEUROSCIENCE PROGRAM (SNP)

ABSTRACT NO. 94

TRAUMA AND MEMORY: EXAMINING THE RELATIONSHIP BETWEEN GENERAL EPISODIC MEMORY PERFORMANCE AND CHILDHOOD ADVERSE EXPERIENCES IN ADULTS

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Episodic memory (EM), unique from other memory systems, entails the reimagination of past experiences, supported by neural structures and pathways in the medial temporal lobe. Exposure to maltreatment and abuse during childhood, a period crucial to neural development, has been shown to reduce adult EM task performance, along with structural and

functional changes to the hippocampus. However, these past studies were limited, only focusing on patients with diagnosed psychopathologies or tested EM related to the trauma. In the current study, we aim to measure if this relationship between childhood trauma (CT) exposure and adult EM performance holds true for nontraumatic-related tasks, along with analyzing potential mediating variables in this relationship, such as anatomical distinctions and demographic factors. The study is a collaborative secondary data analysis using a cohort-designed longitudinal study on elderly participants from the Rush Alzheimer's Disease Center. Countering the initial hypothesis, CT exposure correlates to an elevated general EM; however, it was affirmed that hippocampal and amygdala volumes were associated with higher performance on these tests. These findings could emphasize the time-dependent effects of trauma on memory. The cohort studies followed elderly participants, who may have limited recollection of any trauma they experienced and therefore, their EM performance is not impaired as expected. It was also discovered that CT was only significantly positively associated with amygdala volumes, diverging from current understandings of the hippocampus's role in mediating this relationship between CT and EM. These positive correlations between CT, neural volumes, and EM could underline a "resilience" response to trauma, unlike what previous studies have shown. The results of this study underline the importance of studying CT neurological effects on memory and related neural systems beyond memory related to the trauma, improving our understanding of CT's impacts holistically on neural structure and function.

ABSTRACT NO. 95

PROTEINS IN ALZHEIMER'S DISEASE

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It is estimated over 5.5 million people in the US are diagnosed with Alzheimer's Disease (AD), with over half being women. Since 1991, the Amyloid Hypothesis has been the focus of much research into AD pathology and interventions. However, different genes have recently been associated with mouse models of AD, like TOMM40 and APOE. The roles of these genes and their products in the onset, development, and symptoms of AD is largely unknown. In this investigation, it is important to be able to quantify the amount of the gene and associated proteins present in the mouse models to confirm the synthesis (or lack of) in the knockout, heterozygote, and wild type mice. In the current study, this is accomplished with the use of three major techniques: 1) cell fractionization and homogenization of the brain from the different mice to prepare the sample, 2) the enzyme linked immunosorbent assay (ELISA) to measure protein concentration within the fractions, and 3) Western blots of fractions and antibody staining to detect the desired proteins. The goals of this project are to examine at which fraction of the cell the genes and proteins of interest are found and to identify any sex differences, as well as develop a streamlined and standardized protocol to increase efficiency, efficacy, and ease. After the completion of the protocol for mice of the differing genotypes is completed, the data can be analyzed and used to further improve the procedures. Further directions include behavior assays with the mouse models to confirm the genes' potential impact in AD and its symptoms, and possibly identify interventions.

ABSTRACT NO. 96

INVESTIGATING Col4a1 mRNA LOCALIZATION TO RADIAL GLIAL BASAL ENDFEET ACROSS MOUSE EMBRYONIC DEVELOPMENT

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Radial glial cells (RGCs) are neural stem cells that play a critical role in embryonic brain development. RGCs produce both neurons and

glia, and their basal processes constitute a physical structure that guides migrating neurons to facilitate cortical organization. RGCs have a unique bipolar morphology featuring a long basal process that spans across the developing cortex, ending in subcellular compartments called endfeet organized just beneath the basement membrane (BM) at the pia. Current research aims to characterize molecular mechanisms underlying RGC function, especially concerning their endfeet. One hypothesized role of RGC endfeet is the secretion of extracellular matrix (ECM) components, which organize into a scaffolding necessary for adequate survival and organization of brain cells. ECM may also impact RGCs by influencing basal process and endfoot organization or neurogenesis. There is evidence that local production of ECM may be conserved across elongated cell types, and the recent discovery of the RGC endfoot proteome identified ECM components as the largest category of proteins specifically enriched in RGC endfeet as compared to the cell body. Among these enriched proteins is COL4A1, part of a collagen essential to the formation of BMs. Both the COL4A1 protein and its associated mRNA are significantly and specifically enriched in RGC endfeet, suggesting local translation and function. Using a mouse model, Col4a1 mRNA localization to RGC endfeet was assessed at different developmental time points. This is significant for understanding the developmental dynamics of ECM RNA localization as well as temporal regulation of Col4a1 expression in RGC endfeet. This informs future work with Col4a1 by providing evidence of the time period during which this gene is the most developmentally significant.

ABSTRACT NO. 97

SOCIAL ISOLATION DURING ADOLESCENCE INFLUENCES DOPAMINE SYSTEM DEVELOPMENT

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Adolescence is a period of increased reward seeking, risk taking and social behaviors. The dopamine (DA) system is an important mediator of these behaviors and undergoes maturation during adolescence. Microglia, the resident immune cells of the brain, are involved in DA system maturation through engulfment of the dopamine D1 receptor (D1r) in the nucleus accumbens (NAc) of male rats. This engulfment facilitates the termination of adolescent social play behavior. Social isolation (SI) has been linked to many neuropsychiatric disorders, and adolescent SI has been shown to impact DA system development. The mechanisms underlying the impacts of adolescent SI on DA system development, and how it may alter microglia-dopamine system interactions, remain unclear. To investigate this, rats were isolated upon weaning at P21 and until P38. We examined social behavior along with D1r and Iba1 (microglia) levels in the NAc at several developmental timepoints. D1r and Iba1 were measured through immunohistochemical staining and subsequent fluorescent imaging and analysis. Behavior tests included social preference and social novelty tests. Due to the widespread isolation experienced in recent years as a result of the Covid-19 pandemic, understanding the mechanisms and effects of SI, particularly during critical periods such as adolescence, has become increasingly important.

ABSTRACT NO. 98

DISSECTING THE RELATIONSHIP BETWEEN THE SIZE OF THE OLFACTORY BULB AND THE DEVELOPMENT OF DEMENTIA IN THE DUNEDIN STUDY CONTRIBUTION OF TRPV4 AND SEX HORMONES IN MAST CELLS TO MIGRAINE PAIN

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Dementia and Alzheimer's disease are neurodegenerative disorders marked by cognitive decline and early olfactory dysfunction.

The olfactory bulb's involvement in these conditions is under investigation due to its critical role in our sense of smell. Understanding the olfactory bulb's role and its association with brain pathology holds promise for enhancing diagnostic techniques and developing targeted treatments. This study presents preliminary results from an analysis of olfactory bulb sizes in healthy individuals categorized into low and high-risk groups for dementia and Alzheimer's. Our hypothesis posited that subjects at higher risk for Alzheimer's will exhibit a smaller olfactory bulb.The olfactory bulb volumes were measured semi automatically on T2 MRI brain scans. Statistical analysis revealed that high-risk subjects displayed smaller olfactory bulbs than low-risk individuals. These findings highlight the olfactory bulb's potential as a promising indicator for early detection of dementia and Alzheimer's.

ABSTRACT NO. 99

CONTRIBUTION OF TRPV4 AND SEX HORMONES IN MAST CELLS TO MIGRAINE PAIN

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Migraine is estimated to affect over 10 percent of people worldwide. Women are disproportionately affected, being three times as likely to experience migraines and with greater comorbidities. One particularly salient finding is the involvement of transient receptor potential (TRP) channels, specifically TRPV4, in the manifestation of migraine-like symptoms. Moreover, mast cells, an integral component of the immune system, have emerged as potential contributors to migraine-associated pain. Studies have shown that the sex hormone progesterone can bind to TRPV4 and inhibit its activity and expression. Our aim was to explore the potential relationship between the TRPV4 channel in mast cells, their susceptibility to hormonal regulation, and plausible involvement in the observed sexual dimorphism. We examined mast cells from the meninges of wild-type mice and bone marrow of Trpv4 gene-targeted mice to test our hypothesis that progesterone can inhibit TRPV4 to reduce mast cell degranulation as observed in migraine models. To investigate this, we conducted β-hexosaminidase release assays and fluorescent microscopy of meningeal tissues. We observed that meningeal and cultured mast cells stimulated with compound 48/80 showed increased degranulation over baseline; additionally, mast cells pretreated with progesterone before stimulation with 48/80 showed decreased degranulation compared to 48/80 alone. We show that activation of TRPV4 via agonist GSK101 can induce degranulation in meningeal mast cells compared to baseline. Conversely, mast cells pretreated with progesterone and stimulated with GSK101 showed similar degranulation to GSK101 alone. Furthermore, male TRPV4 knockout BMMCs exhibited lower degranulation rates across all treatment groups compared to wild-type male cells. Female TRPV4 knockout cells also showed reduced degranulation compared to wild-type female cells at baseline and mixed results upon degranulation stimulation. These results suggest that while mast cell degranulation is regulated by both TRPV4 and progesterone, TRPV4 regulation is independent of progesterone in both male and female mice.

ABSTRACT NO. 100

DEVELOPMENT OF QUANTITATIVE TOOLS FOR CERVICAL DYSTONIA

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Dystonia is an involuntary movement disorder characterized by sustained or intermittent muscle contractions causing abnormal postures. The conventional rating scales of dystonia are subjective and highly dependent on the inter-rater and their experience. Therefore, this study aims to develop an objective, novel measure that could capture the key aspects of cervical dystonia. To achieve this overall purpose, the study applied a commercially

available quantitative 3D neck sensor device to measure the abnormality in neck movements in patients with cervical dystonia. Subjects completed two research visits, before and after their clinical treatment of either botulinum toxin injection or deep brain stimulation (DBS). At each visit, participants performed trials of neck movements in three axes (x,y,z) while wearing 3D neck sensors on their head and neck. The mean change in neck movements with 3D sensors concluded correlation within the sensor data before and after the patient's treatment by showing a statistically meaningful difference between the two visits. Furthermore, the study was able to calculate the minimal detectable change of 3D neck sensor that corresponds to the change in patient reported outcomes after clinical treatment. This demonstrates the efficacy of the sensor system in measuring and rating cervical dystonia.

ABSTRACT NO. 101

LEARNING BEHAVIORAL ACTION SEQUENCES IN CORTICO-STRIATAL NETWORK VIA ELIGIBILITY TRACES

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Sparse, sequential neural activity has been observed in the striatum for skilled, sequential behaviors. Though the cortico-striatal loop appears to coordinate the sequence, the circuit mechanism is not well understood. We model the cortico-striatal loop, characterized by temporally symmetric and asymmetric Hebbian rules in sparsely connected recurrent networks. We demonstrate that after learning, during which random patterns are used to update the synaptic weights of the networks, transient correlation with each pattern is observed in the correct sequence. The speed of the sequence can be rescaled to be consistent with experimental observations. Furthermore, we model a biologically plausible learning mechanism of the sequence via synaptic eligibility traces applied to reward-based learning. We add random noise to the striatal network such that the model explores different patterns, during which an eligibility trace is imprinted if there is co-activation of the pre and postsynaptic neurons. The synaptic weights are updated upon receiving a reward. We trained mice to perform a stereotyped reaching behavior and recorded extracellular spiking activity in the dorsal and ventral striatum to constrain the model.

ABSTRACT NO. 102

OBSERVING THE STRUCTURAL LANDSCAPE AND PATHOLOGY OF NOVEL ALPHA-SYNUCLEIN FIBRIL ASSEMBLIES IN TRANSGENIC MICE

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Alpha-synuclein structure adopts either a conformation of α-helical loops with the ability to bind to the membrane or exists in a disordered unfolded form exposed in the cytoplasm of the cells. In Lewy body diseases, such as Parkinson's disease (PD), α-synuclein undergoes conformational changes and assembles into β-sheet enriched amyloid fibrils. Recent studies have shown that regardless of having identical amino acid sequences, fibril structures can vary in conformation and function. In this study, we observe the structural landscape and pathology of novel alpha-synuclein fibril assemblies. We implemented a novel mouse model using Human-a-syn-PAC-FVB strain expressing human alpha-synuclein without endogenous presence of mouse synuclein variant. Transgenic mice (N-7-10) underwent intracranial injections of alpha-synuclein strains A(13) and B(17) along with the control recombinant fibril preparations. Three months post-injection mice were collected for immunohistochemistry and biochemistry in order to investigate the pattern and severity of alpha-synuclein fibril-induced pathology regardless of the strain injected. Herein, we observed that pS129-a-synuclein inclusions varied

considerably between the different fibril assemblies, suggesting a diverse and complex structural pathology associated with PD. Further studies are aimed to explore specific pathophysiological properties of α-synuclein fibril conformers associated with PD.

ABSTRACT NO. 103

A FEM COMPUTATIONAL MODEL OF DEEP BRAIN STIMULATION IN THE BASAL GANGLIA

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The application of electric current in the basal ganglia circuit has been established as a potent therapy for severe Parkinson's disease. Computational modeling is an essential tool to elucidate the mechanism behind deep brain stimulation's therapeutic efficacy and target electrode implantation in the clinic. We constructed a flexible segmented electrode FEM model in COMSOL Multiphysics and extracted electric potential distributions from the surrounding neural tissue medium. Using NEURON software to model key neural circuits in the basal ganglia involved in Parkinson's disease, we applied the electric potentials from the FEM model and recorded activity evoked in the subthalamic nucleus, a common target for deep brain stimulation. We found higher evoked potential activity in the FEM model compared to the previous static equation model due to its more complex voltage gradient. The FEM model can also create geometrically complex electric potential distributions that can be used to target specific brain structures, such as the dorsal subthalamic nucleus or globus pallidus internus. The precision upgrade from an equation-based model to an FEM model gives clinicians and researchers greater insight into the mechanisms of deep brain stimulation, and the FEM model's flexible design allows it to keep pace with evolving electrode designs.

ABSTRACT NO. 104

FORGIVING AND FORGETTING: EXPLORING CONNECTIONS BETWEEN MEMORY AND FORGIVENESS IN DURHAM

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Despite clinical and social psychology research into forgiveness, (Worthington, 2006; Fehr, Gelfand and Nag, 2010; Worthington and Wade, 2020) little is known about the exact cognitive mechanisms that underlie the process of forgiving. Our current hypothesis is that forgiveness involves the reactivation of an autobiographical memory and that forgiveness is the result of reappraisal and reconsolidation that can become modified with affective content. Thus, we aimed to explore whether the modification of this content is related to or independent of the cognitive content. This was done through a series of experiments in which participants were asked to recall autobiographical memories with various degrees of questionnaires and tools to measure the physiological attributes of each participant. For this particular portion of the overall project, 60 participants were asked to recall two memories: a neutral condition and one in which they experienced harm by another person. A neutral memory consisted of baseline autobiographical events that had no extreme emotion attached to them, while the negative memories were used to show the potential changes found in participants. BIOPAC was used to measure skin conductance, heart rate, respiration as well as muscle activity in the corrugator and zygomaticus muscles. This was done while the participant thought of these autobiographical memories to determine if there were any potential indicators attached to these memories. As stated, not much research has been done into the various factors which may indicate the process of forgiveness and if there

are any cognitive or psychological changes brought on by forgiveness, or if the act of forgiveness is completely independent. Thus, this research can have broad implications on the role of emotion, memory, and physiology into forgiveness. Additionally, forgiveness may be affected by using well-established cognitive and emotional reappraisal techniques to facilitate forgiveness.

ABSTRACT NO. 105

INVESTIGATING THE INFLUENCE OF ANXIETY AND THREAT ON COGNITIVE MAP LEARNING

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Anxiety is one of the most common mental illnesses worldwide and has been studied extensively, but one area in which the literature is lacking is investigations into anxiety's impact on the learning of cognitive maps. Cognitive maps are the internal representations we create about associations in the external world that are critical for understanding relationships and accomplishing goals in our everyday lives. Our aim is to answer whether learning of cognitive maps is enhanced or impaired when the maps contain threatening stimuli, and whether this interacts with people's levels of trait anxiety. To this end, we had human participants (N=105) learn a map of network locations associated with images of either negative (threat) or neutral valence. Participants' success at learning the structure of the cognitive map was tested through a series of gamified tasks. We conducted statistical analyses to draw comparisons between participants with different trait anxiety levels and their learning performance across the tasks and among threat versus neutral images in the network structure. Analysis is still ongoing, but initial results suggest that people were better at learning the location of threatening images than neutral images regardless of trait anxiety level. In addition, individuals with high trait anxiety were better at learning the cognitive map structure overall, regardless of image valence. The results of this study help advance our understanding of the contribution of threat to cognitive map learning, and the effect of anxiety on higher-level cognition.

ABSTRACT NO. 106

OPENING THE GAP: CURIOSITY AND PREDICTION ERROR PERPETUATE INFORMATION SEEKING AND INFLUENCE MEMORY

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The world is filled with massive amounts of information, forcing us to choose what we learn and remember. Curiosity exerts a key influence on these decisions by directing information-seeking and enhancing memory. Curiosity is thought to arise due to an "information gap" - a discrepancy between what one knows versus wants to know. Gaining information is typically thought to "close" this gap, therefore reducing curiosity. However, it is also possible that additional information reveals a lack of knowledge, broadening the information gap and increasing curiosity. The idea that additional information can open information gaps implies that curiosity has self-perpetuating properties, yet these properties remain untested, and their impact on memory remains unclear. The current study aims to test how acquisition of knowledge furthers information-seeking and how this self-perpetuating information-seeking may influence the relationship between curiosity and memory. Participants complete an online trivia task during which they predict the answers to trivia questions, view the answers, and have multiple opportunities to receive follow-up information about each trivia fact. They rate their curiosity both before the answer is revealed and after receiving additional information about the trivia fact and later undergo memory tests for the information encountered during the task. Preliminary results show that even after the answer is revealed, high initial curiosity about the trivia statement, as well as experiencing a strong

negative prediction error (high confidence incorrect response), predict a higher likelihood of seeking additional information, providing evidence that new information can perpetuate curiosity-driven information-seeking. We are currently exploring how curiosity after receiving additional information might contribute to information-seeking and how this relates to memory. The results should provide further insight into the mechanisms through which curiosity improves memory, enhancing our ability to harness curiosity as a tool for improving memory in contexts ranging from education to public policy.

ABSTRACT NO. 107

UTILIZING DRUG ACUTELY RESTRICTED BY TETHERING (DART) TECHNOLOGY TO ACHIEVE SOMATODENDRITIC-SPECIFIC PHARMACOLOGY

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While the basic structure of neurons is well established, it remains unclear how the same receptors in different compartments of the neuron (the axon, soma, dendrites) serve different functions. To address this fundamental question, we build on the Drug Acutely Restricted by Tethering (DART) technology to manipulate receptors in different subcellular compartments of the neuron. DART works by genetically encoding a HaloTag protein (HTP) in the cell type of interest. This protein covalently captures any drug conjugated to its cognate HaloTag ligand (HTL), concentrating the drug only on cells expressing HTP. To enable subcellular targeting, we engineer variants of the HaloTag protein that are targeted to distinct subcellular compartments. Here, we focus on developing a somatodendritic-targeted HTP by fusing it to somatodendritic trafficking motifs. To construct this fusion protein, we utilized molecular cloning to insert the DNA sequence encoding the trafficking motifs into the DNA sequence of HTP. We will validate the subcellular location of these HTP variants by transfecting them into cultured neurons and labeling them with a fluorescent dye conjugated to HTL. By restricting drug capture to the somatodendritic region, we will be able to distinguish the roles of somatodendritic and axonal receptors, which have conceptually been associated with presynaptic and postsynaptic neuronal functions but have been technically challenging to test causally. This tool is compatible with use in free-behaving mice, enabling neuroscientists to study both circuit-wide and behavioral effects of subcellular manipulations.

ABSTRACT NO. 108

EXPLORING INTERNEURON TRANSPLANTATION IN THE HUMAN BRAIN

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Loss of inhibitory GABAergic interneuron populations in the brain leads to abnormalities in cell circuits that can result in numerous neurological diseases including epilepsy – characterized by recurrent disabling seizures affecting 1% of the population. Unfortunately, 30-40% of patients suffer from drug-resistant epilepsy and are left with surgical resection to improve their quality of life. These operations have strict selection criteria and may have limited seizure reduction in some populations; therefore, therapeutic alternatives are needed to improve treatments options. Given seizure pathophysiology involves interneuron hypofunction, there is growing evidence in the literature and in ongoing clinical trials that using interneuron transplantation, a novel cell-based therapy, increases inhibitory signaling and reduces seizures. In rodent models of epilepsy, transplantation of interneuron precursors derived from a brain region known as the medial ganglionic eminence (MGE) have been shown to survive, migrate, differentiate into mature interneurons which modify diseases phenotypes in vivo. However, the mechanism of how transplants improve seizure phenotypes is

unknown; specifically, how transplants attract afferent inputs in mature cell circuits lacking stage appropriate developmental extracellular cues. The purpose of this study was to develop a viral transsynaptic tracing method to determine the identity of presynaptic inputs onto transplants. Here we used human temporal cortex resected from epilepsy patients and wild type mouse organotypic hippocampal slice cultures (OHSCs), a model of epileptogenesis that generate spontaneous seizure-like activity, to develop viral transsynaptic tracing and explore interneuron transplantation. Transplants were exposed to a TVA expressing helper virus followed by a G deleted rabies tracing virus to ensure monosynaptic infection and identify afferent inputs. Our findings suggest that the combination of transgenic transplants that express TVA coupled with direct application of a 1:10 TVA virus followed by a 1:10 rabies virus yields the greatest levels of transsynaptic efficiency and presynaptic labeling.

ABSTRACT NO. 109

NOVEL SMALL-MOLECULE DRUG CANDIDATE IMPROVES FUNCTIONAL OUTCOMES AFTER SUBARACHNOID HEMORRHAGE

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Subarachnoid hemorrhage (SAH) is a form of stroke that is physically, emotionally, and financially devastating for individuals and their families. Despite decades of research, there are currently no approved pharmacological treatments for SAH that can reduce neural damage and improve functional recovery. The inflammatory response to CNS injury has emerged as a promising therapeutic target, due to the potential of its regulation for neuroprotection. However, many drugs that modulate neuroinflammation are too big to cross the blood-brain barrier (BBB). To address this problem, researchers have developed a small-molecule, MW189, that is able to cross the BBB and selectively modulate neuroinflammation. Following promising results with traumatic brain injury and intracerebral hemorrhage, our lab has tested the drug candidate MW189 in a mouse model of SAH. We found that compared to mice who received no treatment, MW189 significantly improved body weight recovery and motor performance assessed by Rotarod and CatWalk across 35 days. While endpoint Sensory and Motor Neuroseverity Scores (NSS) were similar for both groups, the recovery curve showed a much earlier improvement and overall smaller drop in motor function following MW189. These results have positive implications for MW189's viability as a therapeutic for SAH, and future work will assess MW189's capacity to decrease neural damage by analyzing fluoro-jade staining on brain tissue of mice with and without treatment.

ABSTRACT NO. 110

MECHANISMS OF PAIN INHIBITION IN MICE PRIMARY SENSORY NEURON MODELS

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Chronic pain affects millions of patients around the world as both a medical condition and a complication of medical treatment. Ineffective methods of pain alleviation lead to the abuse of drugs and medication, with one namely case being the current opioid epidemic; thus, understanding the mechanisms of pain and how to effectively manage it is imperative to modern society. The transmission of pain is initiated in nociceptors, free nerve endings in the skin that fire in response to painful stimuli such as heat or tissue damage. These nociceptor cell bodies are localized in the dorsal root ganglia (DRG). Their axons converge on the spinal cord, where the pain signal is then propagated to upstream targets in the central nervous system. This investigation seeks to explore the effects of SBI-810, a novel agonist of neurotensin (a

neuropeptide with known analgesic effects), in blocking signal transduction in nociceptors. First, DRG will be surgically isolated from GCaMP6 reporter mice expressing calcium indicator, and primary DRG cultures will be prepared. The cultured neurons will then be treated with allyl isothiocyanate (AITC) and capsaicin, two compounds that trigger nociceptor firing and burning pain but act on different receptors. Next, calcium imaging will be conducted in cultured DRG neurons to detect whether SBI-810 successfully blocks nociception; behavioral analysis of experimental mice groups injected with AITC and capsaicin will confirm findings from calcium imaging. Final results will be summarized in an academic poster. The findings of this investigation will uncover pathways of pain inhibition and help identify alternate, more sustainable methods of pain alleviation – which in the long term may decrease the abuse of painkiller drugs.

ABSTRACT NO. 111

DEVELOPMENT OF LIPID-HYDROGELS TO DELIVER OMEGA-3 FATTY ACID DOCOSAHEXAENOIC ACID (DHA) FOR THE TREATMENT OF ISCHEMIC STROKE

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Traditional stroke therapies, such as mechanical thrombectomy and tissue plasminogen activators, are time limited in effectiveness (several hours post onset). To increase the rehabilitation period following stroke, hydrogel tissue scaffolds have emerged as effective therapeutics to deliver and release reparative cues to the brain by rehabilitating surviving cells in the tissue surrounding the stroke infarct to assist in driving neurocircuit regeneration. One such reparative cue is the polyunsaturated omega-3 fatty acid docosahexaenoic acid (DHA), a lipid constituent of the cellular membrane that plays a role in the brain's anti-inflammatory and neuroregenerative pathways. In this project, we aim to conjugate short lipids to the surface of hydrogel microparticles to increase local hydrophobicity and enable delivery of DHA via physical mixing of lipid-microgels and DHA. Before DHA can be added to the hydrogel scaffold, we must understand how lipid conjugation impacts the physical and chemical properties of microgels. We hypothesize that increasing lipid content on the surface of microgels will increase scaffold stiffness due to the interactions between the hydrophobic tails of neighboring beads. We additionally hypothesize that chemical annelation performed by tetrazine modified hyaluronic acid (HA) will be effective in crosslinking lipid-microgels due to excess surface norbornenes. The hydrophobicity of lipid-microgels will encourage cell migration and grow towards naked-microgels. To test these hypotheses, we generated microgels using oil in water emulsion on microfluidic devices. Physical interactions and degree of chemical annelation in scaffolds were measured via rheology. Preliminary results indicate that lipid-microgels have increased physical interactions between microgel particles, while not preventing tetrazine chemical annelation. These findings enable a variety of scaffold formation strategies, allowing customization in how microgel scaffold stiffness is modulated. In the future, we aim to quantify cell survival and migration in lipid-microgel scaffolds to determine whether local hydrophobicity impacts cell adhesion.

Pratt School of Engineering

ABSTRACT NO. 112

PRECISION AND CLARITY: INTEGRATING MACHINE LEARNING AND OPTICAL SENSOR PRECISION IN MICROWAVE IMAGING

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This comprehensive, interdisciplinary study explores the advancement of microwave

imaging quality, achieved by implementing machine learning (ML) algorithms and a precision-controlled sensor system. The research aims to significantly augment obscured object detection capabilities in microwave imaging. The findings are presented in two interconnected areas of exploration.

Firstly, the research dealt with image corruption due to noise from a metasurface antenna. We designed an advanced ML model and trained it on a dataset encompassing noise-free and noise-impacted images. The wide-ranging dataset, with a vast assortment of shapes, allowed the model to learn the intricate noise patterns extensively. The ML model significantly reduced noise and bridging corruption-induced gaps; evaluation metrics revealed an exceptional enhancement of images from 55% to 94% structural similarity. The substantial improvement in image clarity and noise reduction represents a breakthrough in microwave imaging, minimizing potential misinterpretations.

Concurrently, the second focus was to refine the scanning process by employing an Arduino-based optical sensor control system. The precision in measuring distance changes was critical, targeting an error threshold of less than half the wavelength. The project commenced with integrating the optical sensor into the Arduino and creating a customized library to accommodate the Arduino. The sensor was encased in a meticulously 3D-printed housing. This custom library facilitated the distance recording and returned precise x and y coordinates between stops, thus simplifying its integration with existing code. A rigorous calibration process was implemented, with adjustments made to the sensor's code and physical properties, as required. We also documented and analyzed the error introduced by sensor drift or inherent limitations, working steadily towards reducing error to less than half the wavelength.

These advancements signify a considerable leap in scanning precision and image clarity within the microwave imaging domain. As demonstrated in this project, the integration of machine learning with precision-controlled sensor mechanisms promises transformative potential for the future of microwave imaging technologies.

ABSTRACT NO. 113

TRANSISTORS USING ITO (INDIUM TIN OXIDE) FOR BEOL (BACK-END-OF-LINE) COMPATIBLE CMOS (COMPLEMENTARY METAL OXIDE SEMICONDUCTORS) TECHNOLOGY

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Amorphous oxide semiconductors are currently being considered for BEOL processes since they are easy to implement on a large scale and can be deposited at low temperatures. This study encompasses the electrical characterization of Field Effect Transistors (FETs) that used ITO as the channel with varying deposition times and channel lengths with two structures: back gate and top gate. At least 10 devices of each type were characterized. The top gate dielectric, Al2O3, was deposited using atomic layer deposition (ALD) technique. It is known that when H2O is used as one of the precursors for the ALD of Al2O3, the FET does not exhibit gate control. Hence, a seed layer of 1.2 nm of Al, allowed to oxidize to AlOx, was used prior to the ALD process. Using the back gate, a maximum drain current is recorded at 9.4 uA/um for a channel length of 10 um at a drain voltage of 2 V. The device fabrication processes are being optimized for improving sub-threshold swing to 60 mV/dec and drive current to 1 mA/um for VD = 1 V.

ABSTRACT NO. 114

MEASURING HYDROPHOBICITY OF NANOPARTICLES

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Nanoparticles (NP) have extensive applications in nanomedicine and industrial applications. It is important to characterize NP properties due to potential environmental and manufacturing exposures. In a biological environment, such as the lungs, NPs are exposed to proteins which can adsorb onto the surface of NPs, forming a protein corona. Hydrophobicity is an important property in characterizing the agglomeration state under biological and environmental conditions. The surface hydrophobicity influences the composition of this protein corona, which impacts its affinity for surrounding environmental surfaces and overall biological response. Current methods for determining hydrophobicity are limited and cannot be applied to all NPs due to NP size, shape, surface roughness, or heterogeneity. In this study, we used hydrophobic Rose bengal dye and hydrophilic Nile blue A dye to measure the hydrophobicity of carboxylate modified polystyrene, amine modified polystyrene, amine modified magnetic, and carboxylate modified magnetic NPs. Hydrophobicity is quantified using the partitioning quotient by varying concentrations of NPs with fixed concentrations of Rose bengal and Nile Blue A. We determined that both carboxylate modified polystyrene and amine modified polystyrene are hydrophilic.

ABSTRACT NO. 115

CONTROL SYSTEM COMPONENTS FOR TRAPPED ION QUANTUM COMPUTING

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Given the profound benefits quantum computing offers in solving certain problems deemed otherwise intractable via classical approaches, there is significant momentum toward the development of large-scale quantum computers to carry out such operations. In the Noel Lab at the Duke Quantum Center, trapped ions are used to encode the fundamental unit of quantum information (qubits); given their relative accuracy and ability to emulate crucial aspects of quantum mechanics, ion traps offer promise as an effective quantum computing architecture model.

In ion traps, lasers can be used both to control and enact quantum logic through the excitation of the trapped ion into different states. However, the development of effective control systems for such lasers is essential to developing a reliable quantum computer that drives state transitions (qubit logic) precisely when it needs to and otherwise robustly maintains the internal state. Quantum control software (namely ARTIQ, DAX), as well as optical setups, are used in concert to implement such a control system for the lasers.

Here, we discuss the details behind both the hardware and software that need to work in concert for a functional ion trap quantum computer. First, we cover a high-level introduction to the control system hardware-software interface. We then elaborate on the specific experiments and setups that constitute this laser control system.

ABSTRACT NO. 116

PHONEME CLUSTER MASKING FOR REVERB REMOVAL IN COCHLEAR IMPLANTS

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Cochlear implants (CIs) have transformed hearing restoration for individuals with severe hearing loss. However, speech comprehension in challenging acoustic environments remains a significant obstacle. Reverberation occurs when speech is layered with attenuated echoes, which are reflected sound waves within an enclosed room that have been reduced in volume. Due to physiological

impairments and the limited acoustic information provided by CIs compared to the human cochlea, reverberation significantly diminishes speech intelligibility. This project builds upon a novel solution that uses real-time phoneme recognition and signal processing to address this issue. By preprocessing reverberant speech with machine learning-trained, phoneme-specific masks, extraneous echoes are minimized and speech clarity is improved. However, the storage and utilization of individual masks of a large number of phonemes within a language may potentially demand significant processing power and onboard memory of CI processors. This project leverages the similarities between phonemes in the time and frequency domains to create "phoneme cluster" masks, potentially leading to a reduction in model complexity, as well as improved efficiency of speech enhancement within a CI system.

ABSTRACT NO. 117

EVALUATING THE ADVANTAGES OF DIRECT-PRINTED ON-SKIN ELECTRODES FOR IONTOPHORETIC DRUG DELIVERY

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Iontophoresis is a non-invasive transdermal drug delivery (TDD) clinical method. Improvements in iontophoretic technology has led to the development of transdermal patches that offer slow and sustained drug release, improving patient prescription adherence. However, its prevalence is currently limited due to reports of patient discomfort, lack of dosage control, and an inability to deliver large biomolecules, such as insulin. In prior work, it was demonstrated that conductive circuits could be printed onto human skin with an aerosol jet printer (AJP) and a water-based ink containing metallic silver nanowires (AgNWs). It is proposed that drug throughput can be improved by decreasing the skin-electrode distance, which is achieved using this direct-printing approach. The overarching vision of this research is to improve therapy for patients by developing a Direct-printed On-Skin Electronic Drug-delivery (DOSED) technology.

In this work, AgNW inks were formulated, their printing process was optimized, and performance experiments were conducted to validate the advantage of using direct-printed electrodes versus transferred electrodes for iontophoresis. Printing AgNW electrodes at room temperature on glass yielded conductive traces at a 100% yield without any sintering process. Furthermore, by increasing the platen temperature to 80 ºC, sheet resistance was decreased to below 1 Ω/sq. AgNWs of various dimensions were printed onto porcine skin; however, multiple printing passes and therefore longer printing times were required to achieve sheet resistances below 100 Ω/sq. Electrical characterization of the electrodes in a Franz cell indicates that printed electrodes have lower voltage requirements than transferred electrodes of the same surface area. We also observed that printed electrodes could reproducibly operate at maximum safe current density (MSCD) at sub-2 V potential bias. Printed electrodes were exposed to 1x PBS for 24 hours with no loss is sheet resistance. Furthermore, a 2 V static bias was applied, resulting in currents well above MSCD, and still there was no loss in cathode sheet resistance over the same time period, suggesting that AgNW electrodes can be used as cathodes for iontophoresis.

ABSTRACT NO. 118

SYNERGY OF MACHINE LEARNING AND MIE-TRONICS: TAILORING RESONANT RESPONSE OF META-ATOMS ON DEMAND

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Metamaterials are engineered electromagnetic structures with unusual properties not readily found in nature. Their unit cells, meta-atoms, usually represent a set of

electric and magnetic multipoles. All-dielectric-based metamaterials have recently attracted significant attention owing to their virtually lossless transmission properties at optical frequencies. A majority of reported dielectric metamaterials are composed of regular and relatively simple meta-atoms such as spheres, cubes, and cylinders, whose electromagnetic response is dominated by the electric dipole. However, magnetic dipoles and higher-order multipoles may enable a number of functionalities including directional scattering, beam steering, and new frequency generation. Despite impressive progress in the field of optical metamaterials and nanofabrication technologies, engineering meta-atoms that support such higher-order resonances is still challenging. Here, we demonstrate that designed titanium dioxide meta-atoms can enable dominant magnetic dipole response. We apply a machine-learning model to predict a meta-atom shape with a strong magnetic dipole resonant mode at the operating wavelength of 750 nm. Using finite-element-based numerical simulations implemented in COMSOL Multiphysics, we find that the predicted meta-atom is robust against experimental variations such as an added substrate, significant incident angles of light, and a 2D array of meta-atoms. Subsequently, we developed an electron beam lithography recipe followed by reactive ion etching to fabricate the optimized meta-atoms. Next, the fabricated samples will be experimentally characterized using a white light spectroscopy setup to further validate our theoretical design and optimization. To the best of our knowledge, this is the first experimental realization of a machine-learning-based optimization of a magnetic dipole mode at optical frequencies.

ABSTRACT NO. 119

SCALING TRANSISTORS VIA END BONDED CONTACTS TO CARBON NANOTUBE CHANNELS

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Silicon field effect transistors (Si-FETs) are the elementary components of many electronic devices. The miniaturization of Si-FETs has reached physical limits that motivate research in
exploring materials that allow further scaling of the device. Carbon nanotubes (CNTs) are a semiconductor that has proven to be a good candidate for transistor channels due to their exceptional electrical conductivity and high on/off current ratio. Here, we fabricated CNT transistors with traditional top and bottom contact schemes and a novel end bonded contact scheme. When scaling CNT transistors to dimensions in the tens of nanometers, using traditional contact schemes is limiting due to increased contact resistance. It has been shown that improving electrical contact between electrodes and a CNT channel with end bonded contact resulting from the formation of covalent bonds alleviates the contact resistance obstacle. However, formation of covalent bonds via annealing requires high temperatures making fabrication cumbersome. We demonstrate CNT end bonded transistors via an oxygen plasma etching process to facilitate fabrication. To test the performance of the transistors we performed electrical measurements in a variety of environments including air, vacuum, mineral oil, and passivated with zirconium oxide.

ABSTRACT NO. 120

APOE GENOTYPE, DIET, SEX, AND AGE EFFECTS ON FUNCTIONAL CONNECTOMES OF MOUSE MODELS OF ALZHEIMER'S DISEASE

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Alzheimer's Disease (AD) is a progressive brain disorder characterized by memory loss, cognitive decline, brain atrophy, and potentially altered structural and functional connectivity. The Apolipoprotein E (APOE) gene, a well-known risk factor, transports cholesterol and fat in the bloodstream. The APOE2, APOE3,

and APOE4 genes exhibit protective, neutral, and promoting effects on AD, respectively. Rodent models can serve as a proxy for understanding APOE genotype effects on the functional connectome. Resting-state functional magnetic resonance imaging provides in vivo measurement of the BOLD (blood oxygen level dependent) signal to approximate blood flow and neural activity. We have developed methods for processing functional connectomes in mouse models with humanized APOE genotypes. Our aims were to examine the effects of APOE genotype, sex, diet, and age on mice resting state functional networks. Data preprocessing steps include skull stripping, slice time correction, volume registration, atlas alignment, despiking, blurring, scaling, cerebrospinal fluid and white matter denoising, and bandpassing. Independent component analysis (ICA) is used to decompose spatial and temporal data into distinct networks. Group-level analysis, voxel-wise analysis, and statistical tests are performed to compare the networks among subjects. Future work will examine seed-based connectivity for relevant brain regions including the hippocampus and amygdala. A limitation of the study was due to the presence of imaging artifacts such as ghosting, which will be addressed by changing the number of echoes, and phase encoding steps. This study aims to provide valuable insights into the impact of APOE genotype, sex, diet, and age on the functional connectome in mouse models, contributing to our understanding of AD.

ABSTRACT NO. 121

IMPLEMENTING A CENTER OF MASS MODEL FOR EDFA GAIN WITHIN MININET-OPTICAL

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Creating an accurate packet-optical network simulator is an important step in improving testing within the field of optical system research, allowing for cheaper, flexible, and scalable testing to be done. Mininet-optical is an emulation software built to emulate software-defined network (SDN) tools, and allows for the specification of important SDN network elements such as reconfigurable optical add-drop multiplexers (ROADM) and erbium-doped fiber amplifiers (EDFA). Mininet-optical has proven to be an improvement on previous testing methods in various aspects, but still has room for improvement in its accuracy. An important step in creating an accurate emulation of a network span is to model the wavelength-dependent gain (WDG) of the emulated EDFA, which varies based on a number of factors specific to each device. One way to model WDG is through a Center of Mass Model (CM), which can be used to predict the WDG of an EDFA at each channel in use. The CM model is excellent for fast testing at the cost of some accuracy, but has shown promise in use within SDN emulation. In order to test and train our CM model to be implemented in Mininet-optical, we will pull relevant data in an attempt to create a digital twin for the Cloud enhanced Open Software defined MObile wireless testbed for city-Scale deployment (COSMOS) which was chosen for its city-wide scalability and availability of test data. The COSMOS testbed provided data for 8 booster and 8 preamplifier gain data, with which we investigate the application of the CM model within Mininet-optical and its effects on the output gain of our EDFAs.

ABSTRACT NO. 122

INVESTIGATING THE IMPACT OF IMAGE PROPERTIES ON OBJECT DETECTION PERFORMANCE IN AUGMENTED REALITY SCENARIOS

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State-of-the-art machine learning models for image classification and object detection still underperform in augmented reality (AR) scenarios, due to the properties of real environments and user motion that introduce artifacts into the camera images used as input. In this work, I characterize the differences between

the images these models are trained on and images collected in real AR scenarios, how camera image properties relate to prediction performance, and explore techniques for better integration of these models with AR. I began by implementing a characterization pipeline in Python using OpenCV to quantify image properties such as brightness, contrast, entropy, edge strength, and the noise of a set of images. Using this pipeline, I characterized existing object detection datasets (e.g., Coco and RF100), as well as my own image datasets that I collected by capturing videos in conditions representative of realistic AR scenarios. I also measured image similarity in the consecutive frames of video datasets to inform how this relates to object detection results. I then measured image classification and object detection performance by implementing a state-of-the art solution, YOLOv8, along with metrics such as mAP (mean Average Precision) and IoU (intersection over union). Finally, I analyzed the relationships between image properties and object detection results to gain insights into how different conditions impact performance. My work is vital for understanding how to achieve high quality, robust AR experiences that incorporate image classification or object detection, and to improve their deployment for a diverse set of audiences in a wide range of environmental conditions.

ABSTRACT NO. 123

TWO EYES ARE BETTER THAN ONE - IMPROVED VISUAL INERTIAL SLAM USING DEEP LEARNING BASED OBJECT TRACKING

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Augmented Reality (AR) is the human endeavor to blend our digital and physical worlds, developing experiences at a level never seen before. It lets us immerse ourselves and interact with overlaid computer generated elements onto the real world. The limited hardware capabilities of handheld devices poses a hurdle in bringing this technology into the present. Accurate tracking and mapping of the environment is critical for a seamless AR experience, something that proves to be challenging. In the worlds of Augmented reality, Robotics and Drones the SLAM algorithm is one of the pillars of the system, its efficient and speedy computation goes a long way in developing the next generation of technology. In our summer long endeavor we work towards developing our visual and visual-inertial SLAM systems. [1] which we work towards improving with the supplementation of the concepts of EdgeSLAM and Object Tracking. 1. In line with the concepts of Edge assisted SLAM our mobile device will run a tracking thread using a local map, while the mapping and loop closure tasks will run on the edge server by virtue of maintaining the global map. 2. As the mobile device and the edge server perform their tasks we supplement it with the positional data retrieved through our StrongSORT based Object tracking system. 3. We shall then determine the accuracy of our system and ground truth using the Vicon motion tracking setup.

ABSTRACT NO. 124

ACUTE TO CHRONIC CHANGES IN BIOMARKERS GENERATED BY DEEP BRAIN STIMULATION

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Deep brain stimulation (DBS) is an implanted brain pacemaker that manages motor symptoms of Parkinson's Disease by delivery of electrical pulses to the subthalamic nucleus (STN). DBS can reduce these symptoms; however, DBS parameters are static while motor symptoms fluctuate throughout the day. To deliver optimal DBS, neural correlates indicating the effectiveness of DBS could be used to adjust stimulation parameters. However, it is unknown if these signals remain detectable over the lifetime of DBS leads. To address this issue, we examined local field potentials (LFPs) from the

STN as potential biomarkers during initial DBS electrode implantation surgeries (Stage 1, n = 38) and battery replacement surgeries (Stage 3, n = 13), which occur 3-17 years after implants. All study procedures were approved by Duke University Medical Center IRB and all participants provided informed consent. DBS local evoked potentials (DLEPs) are LFPs resulting from synchronous neural activation by DBS pulses and are thought to quantify DBS efficacy. We observed DLEP latencies during 130 and 185 Hz DBS and DLEP amplitudes during 130 Hz DBS. Analysis of STN recordings demonstrated a difference in DLEP latency across 130 Hz and 185 Hz DBS stimulation frequencies ($p < 0.001$, Wilcoxon ranked sum). Nevertheless, we did not detect a difference in DLEP latency between Stage 1 and Stage 3 for 130 Hz DBS ($p = 0.749$, Kruskal-Wallis) nor 185 Hz DBS ($p = 0.402$, Wilcoxon ranked sum). However, we observed a lower peak-to-peak DLEP amplitude during Stage 3 compared to Stage 1 during 130 Hz DBS ($p < 0.001$, Kruskal-Wallis). Our analysis indicates that DLEPs may provide a marker of DBS effectiveness. However, the difference in DLEP parameters between surgery stages (i.e., between acute and chronic contacts) suggests that a DLEP-based closed-loop system will need to account for changes in signal amplitude over time.

ABSTRACT NO. 125

MODELING AND TESTING 3D PRINTED AND GOLD PLATED ION REPELLER FOR MINIATURE MASS SPECTROMETER

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The miniature mass spectrometer plays a crucial role in rapidly identifying unknown compounds and determining their chemical structures and properties. This research focused on replacing the conventional machined ion repeller within the miniature mass spectrometer with a 3D printed alternative, reinforced with gold plating, while ensuring its functionality. The replacement of the machined ion repeller with a 3D printed version was an important task as it would speed up the process for creating these parts and allow for more parts to be produced at once.

To achieve this objective, the ion repeller's 3D CAD model underwent a comprehensive redesign, optimizing its printability by refining thread hole sizing and making other essential design modifications. Leveraging the expertise of Xometry, a reputable 3D printing company, the ion repeller was manufactured using titanium and subsequently gold plated with a Nickel-Phosphorous undercoat.

To evaluate the functionality of the new 3D printed ion repeller, a comprehensive understanding of the previous machined part's operation within the device was imperative. To this end, a series of tests were conducted on the miniature mass spectrometer using air as the test sample. The presence of oxygen and nitrogen in the air generated distinct peaks at m/q = 32 and m/q = 28, respectively. A MATLAB code was developed to analyze these peaks by comparing their height, width, and location over time. Additionally, a representative spectrum was plotted based on data accumulated from over 3000 trials.

The same test procedures will be executed on the 3D printed ion repeller, and the resultant graphs will be juxtaposed for comparative analysis. These experiments are scheduled for the upcoming week, and the outcomes will be presented on the accompanying poster.

ABSTRACT NO. 126

RETROSPECTIVE THREE-DIMENSIONAL ASSESSMENT OF SURGERY CHOICE WITH RESPECT TO JOINT SPACE WIDTH FOR END STAGE ANKLE ARTHROSIS: A PILOT STUDY 126

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INTRODUCTION: Degeneration of the ankle joint complex often causes severe pain and instability, necessitating surgical intervention. While total ankle replacement (TAR) is the standard procedure for most patients, extreme damage to the tibiotalar joint may require total ankle/total talus replacement (TATTR). However, proper patient selection is crucial to ensure post-operative ligamentous stability. This pilot study aimed to analyze preoperative imaging in TAR and TATTR cases using a three-dimensional distance mapping algorithm to understand the relationship between ankle joint health and surgery choice.

METHODS: Fourteen computed tomography (CT) scans were retrospectively collected and semi-automatically segmented. Subgroups were created based on surgery choice and imaging method: TAR with weightbearing CT (WBCT) (n=3), TATTR with WBCT (n=2), TAR with non-weightbearing CT (NWBCT) (n=5), and TATTR with NWBCT (n=4). A three-dimensional distance mapping algorithm was developed to measure joint space width (JSW) in the tibiotalar and subtalar joints. The tibiotalar joint analysis included the talar tome/distal tibia, while the subtalar joint analysis covered the sinus tarsi, posterior facet, middle facet, and anterior facet (divided into 1-3 sectors). Since this was a pilot study, results were described on an absolute scale.

RESULTS: The WBCT-TATTR cases showed narrower JSW in 12 out of 13 studied subtalar sectors compared to WBCT-TAR cases. Similarly, the NWBCT-TATTR cases had narrower JSW in 4 out of 13 studied subtalar sectors compared to NWBCT-TAR cases. Regardless of the imaging method, TATTR cases had narrower JSW within the tibiotalar joint.

CONCLUSION: In this pilot study, the decision of the surgeon was retrospectively compared to three-dimensional joint health measured by subtalar/tibiotalar JSW. For WBCT, total ankle replacement was performed in cases with greater JSW in almost every studied articulation, while NWBCT cases were more varied. Future plans for this study involve including more cases to conduct proper statistical analysis.

ABSTRACT NO. 127

QUANTUM STATE COMPRESSION VIA LIFTED POLAR CODES

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Our goal is the creation of an efficient quantum compression protocol that asymptotically achieves the source coding bound. In the lossless quantum compression scheme proposed by Schumacher – in which Alice and Bob compress and decompress a message, respectively – Alice first projects her message onto a typical subspace. Bob inverts this process using an isometry from the typical subspace to the higher-dimensional initial space. A similar procedure based on error-correcting codes involves treating the message to be compressed as an error pattern. If Alice's message is a correctable error (e.g., a coset leader) then Alice can use a syndrome table to convert an error to its syndrome. While theoretically significant, direct implementation of Schumacher compression is quite complex. Therefore, we propose the following modified protocol: Alice projects her message onto the subspace of correctable errors and performs a measurement to confirm its typicality, applies a lifted polar transform to her message, and stores the frozen qubits, which constitute a syndrome. To decompress Alice's state, Bob applies an isometry which maps syndromes to their higher-dimensional errors.

ABSTRACT NO. 128

LOCAL POLYMER INTERFACIAL MECHANICS: EFFECT OF CHEMICAL NANOPATTERNING

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The goal of this experiment is to determine a relationship between how different chemical treatments affect local interface mechanics like stiffness and friction. Example applications for the altered surface properties include various manufacturing advancements and composites for aerospace, biomedical, and dentistry industries. To make these measurements, atomic force microscopy (AFM) is conducted on nanoscale chemical patterns created via colloidal deposition using 5 micron nanoparticles. The nanoparticles create areas of different chemistry with altered friction coefficients, which will be measured with lateral force microscopy. Then, polystyrene is spin-coated on the chemical patterned surfaces. The surface chemistry should alter the stiffness of the nearby polystyrene which will be measured with fast-force mapping mode. Expected results include friction changes between different chemicals across the nanopatterned surface and stiffer surface moduli with thinner polystyrene coatings.

OTHER PROGRAMS

ABSTRACT NO. 129

BEHAVIORAL CHARACTERIZATION AND WHOLE-BRAIN ACTIVITY MAPPING OF PSYCHEDELICS IN ZEBRAFISH

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Psychedelics are emerging as promising therapeutics for multiple mental health disorders. However, most of the current research on the underlying neurobiological mechanisms of psychedelics have investigated only a few brain regions at a time, rather than studying the brain as a whole, so there lacks a holistic understanding of the effects of psychedelics. The larval zebrafish is an ideal model organism as it provides optical access to the entire brain at a single-cell resolution. Therefore, using larval zebrafish, we have generated a comprehensive behavioral characterization of the psychedelic 2,5-dimethoxy-4-iodoamphetamine (DOI), a serotonin 2A receptor agonist, and recorded immediate neural responses via volumetric two-photon microscopy. Specifically, we tested how zebrafish respond to a series of behavioral tests, including locomotor, photomotor, and optomotor behaviors, as well as responses to light, dark, and vibration startles before and after acute exposure to DOI. After the addition of DOI in their media, the zebrafish decreased their locomotor and photomotor activity in a dose-dependent manner. This decrease in activity was also observed for light and vibration startles, but not for dark startle. Interestingly, during the optomotor response experiments, the fish did not exhibit an overall decrease in motor activity. Instead, they performed stronger turns in response to left and right visual gratings. Finally, we performed two-photon imaging to record neural responses across the hindbrain region of zebrafish, where most motor behaviors are integrated and communicated to the spinal cord. Together, our findings demonstrate an inhibitory function for DOI during static visual input, whereas an enhancing one with dynamic gratings. Future work will include whole-brain imaging in the presence of visual stimuli to parse out the specific neural circuits, as well as determining changes in functional connectivity using recurrent neural network models.

ABSTRACT NO. 130

OPTOMOTOR RESPONSE IN LARVAL ZEBRAFISH VS. DANIONELLA CEREBRUM, A NEW COMPARATIVE FISH MODEL

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While many sensory cues appear continuously, animals often respond by moving discretely, with a defined start and end. Due to its experimental advantages, the larval zebrafish allows detailed analysis of these discrete motor

outputs. Specifically, during optomotor response (OMR), the larval zebrafish moves in short burst-and-glide swims (i.e., bouts) to stabilize its position in continuous optic flow. Yet, while the closely related fish species Danionella cerebrum inhabits similar aquatic environments, larval Danionella fail to burst and glide, instead preferring to move in continuous swims. To investigate these natural behavioral differences, direction and eye-specific motion patterns were presented to the larval fish (n = 9 Danionella, n = 9 zebrafish) in freely-swimming, closed loop tracking assays. 20 visual stimuli, each 35 seconds with 3 seconds of stationary, control gratings at the start, were presented for ≤ 7 non-consecutive trials. OMR kinematic metrics, such as cumulative distance, velocity, and locomotion duration, were compared between larval Danionella and zebrafish through posthoc analysis. To filter out “bad” OMR fish, those that did not follow direction of motion, the non-parametric Mann-Whitney U Test assessed distance traveled during stationary vs. moving gratings (p-value ≤ 0.05). Preliminary results show that “good” OMR Danionella follow direction of motion comparable to zebrafish but travel a smaller cumulative distance and swim at a faster speed on average. This study secondarily revealed that diligent Danionella husbandry and care are required to experimentally observe OMR. Future directions include correlating the visually evoked behaviors of Danionella and zebrafish with neural activity in the pre-tectum region using head-fixed volumetric two-photon calcium imaging and simultaneous high-speed tail tracking. Ultimately, the study aims to identify the mechanisms underlying discrete and continuous locomotion in vertebrate sensorimotor transformations.