
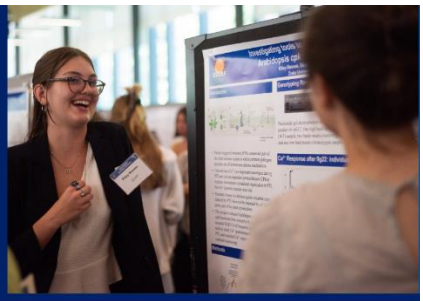

DUKE SUMMER RESEARCH SHOWCASE

Friday, July 26
10:00 am - 12:00 pm
Trent Semans Great Hall

Presented by Duke | UNDERGRADUATE RESEARCH SUPPORT OFFICE
Duke | OFFICE of UNDERGRADUATE EDUCATION

Participating Programs

Duke MARGOLIS INSTITUTE for Health Policy

SUMMER SCHOLARS Genome Sciences & Medicine For Underrepresented in STEM

PRIME CANCER

Duke PRATT SCHOOL of ENGINEERING

DUKE THE GRADUATE SCHOOL SUMMER RESEARCH OPPORTUNITY PROGRAM

Duke EXPERIENTIAL EDUCATION OFFICE of UNDERGRADUATE EDUCATION

Duke University · NC Central · D-CARE Medical Research & Education

Summer Undergraduate Research Fellowship SURF

SURPH@Duke
Summer Undergraduate Research in Pharmacology & Cancer Biology

AMGEN Scholars Program

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ABOUT THE ORGANIZATIONS

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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.

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Duke Undergraduate and Research Support Office

The Undergraduate Research Support (URS) Office facilitates undergraduate research by providing scaffolded training, programming, and funding resources to students. Our focus is on the entry points to research and the transition to the ensuing stages of future research opportunities. More about our resources and opportunities can be found on our website.

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.

Summer Undergraduate Research Fellowship (SURF)

SURF is an eight-week summer program offering rising Duke sophomores the opportunities for mentored research in a broad range of disciplines. There are two arms of the program: 1. Biological and Brain Sciences and 2. Social Sciences and Humanities. In these programs, students engage with faculty mentors and program directors to conduct disciplinary-specific research and learn effective research communication skills with both professional and lay audiences. Through a series of cohort discussions and faculty talks, students have explored various aspects of inquiry-based learning, such as: mentoring, designing a research question, public communication, ethical practices and social responsibility, and more.

Duke PRIME-Cancer Research Program

The Duke PRIME-Cancer undergraduate research program is an 8-week summer program in which rising juniors and seniors from US institutions participate in a mentored research experience in a Duke cancer research laboratory. The program also includes complementary activities to support career readiness, including building research skills, additional cancer biology content, and professional development. Scholars continue to engage virtually in structured professional development opportunities with their cohort throughout the following academic year and can return for a second year to continue their research and serve as a near-peer mentor.

Duke-Margolis Institute for Health Policy

Summer Experience Internship Program

The mission of the Robert J. Margolis, MD, Institute 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 Internship Experience Program is a collaborative and mentored 10-week program where undergraduate and graduate students contribute towards a variety of health policy research projects.

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.

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 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. Learn more about the Duke SROP.

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.

LIST OF STUDENT PRESENTERS

Name	Poster #
Akewusola, Fareeda	20 A
Amare, Ruth	56 B
Amodeo, Olivia	49 A
Andonov, Ella	17 A
Armijo, Brian	44 A
Bash, Reima	31 B
Belton, Colin	57 A
Bersche, Carissa	5 B
Bethke, Anna	20 B
Brown, Ursula	57 B
Bush, Ashley	17 B
Caldera, Alica	49 B
Carl, Kahlia	37 A
Cherkas, Shelby	21 A
Chetkof, Lindsay	19 A
Coley, Aaron	58 A
Colon, Aracelys	16 A
Colón, Alexander	50 A
Coonai, Cael	21 B
Cordova, Emily	37 B
Dahlgren, Sofia	22 A
de Leon, Courtney	50B
De Silva, Dinuk	22B
Debayo-Doherty, Ireoluwatomi	7A
DeBerry, Simone	58 B
Ding, Cynthia	59 A
Dono, Grace	6A
Du, Kunyu (Kimi)	23A
Eppers, Daelyn	23 B
Fan, Jasmine	59 B
Fargo, Isabel	60 A
Ferguson, Caly	38 A
Fraser, Justin	7 B
Gaines, Andrew	16 B
Gazi, Sameeha	44 B
Gillespie, Bennett	60 B

Name	Poster #
Grimminger, Ethan	15 A
Grossman, Kira	45 A
Gupta, Deven	32 A
Haggler, Jayden	38 B
Hammond, Francisca	32 B
Haque, Huda	33 A
Harris, Assata	24 A
Hatchett, Seth	24 B
Hawk, Jacob	51 A
Heeb, Riley	8A
Heverly, Lauren	45 B
Ho, Lauren	13 B
Hoffmann, Ryan	39 A
Holman, Olivia	39 B
Hool, Alexander	19 B
Jackson, Kate	46 A
Jagadeesh, Aashika	1 B
Jantz, Elise	25 A
Jastrzembski, Mia	46 B
Jeffries, Kaleb	61 A
Jiang, Chi	30 B
Jimenez, Camila	61 B
Johnson, Faith	8 B
Joshi, Shreya	62 A
Kaniyur, Mira	43 B
Khayamian, Ariana	33 B
Kikerkov, Emma	31 A
Kmitch, Laura	34 A
Knapp, Cristen	40 A
Kotelanski, Maia	11A
Kubovsky, Monique	6 B
Kuess, Morgan	51 B
Kumar, Anika	62 B
Lapidot, Lia	63 A
Larbie-Mensah, Glen	40B
Lazo, Sophia	52 A

Name	Poster #
Li, Renee	63 B
Lloyd, Kameryn	41 A
Lynfatt, Elizabeth	64 A
Macabangon Jr, Abol	52B
Marin, Daniel	64 B
Marshall-Kirk, Veronica	34B
Mathis, Chase	2A
Mechelke, Annika	13 A
Meesala, Srijan	47 A
Mesarick, Giuliana	18 B
Mirembe, Tracey	9 B
Mishra, Alek	53 A
Mitchell, Olivia	35 A
Mojekwu, Debbie	10A
Montes, Carlos	2 B
Myers, Tyler	47 B
Nakimuli, Bellise	25 B
Ojuba, Mezisashe	30 A
Okotcha, Danielle	12 B
Osman, Salma	53 B
Patel, Nikhil	35 B
Patel, Nirali	14 A
Pequeno, Alexandria	26 A
Pickett, Grace	36 A
Pirtle, Makyla	65 A
Post, Emily	5A
Powe, Kendall	26 B
Rajeev, Sanjay	55 A
Rawlings, Maxwell	27 A
Reeve, Ella	36 B
Regassa, Hanna	41 B
Rispoli, Erika	3A
Rodriguez, Patrick	31 A
Ruley, Joshua	48 A
Santos, Marino	27 B
Schonhorst, Nolan	28 A
Sharpe, Julianne	48 B
Shen, Sophia	65 B
Shiell, Lauren	3 B
Shivaramakrishnan, Akhilesh	42 A
Silverstein, Matthew	1A
Song, Emily	28 B
Soto Torres, Yadielis	15B
Spruill, Jaleah'	12A
St.Brice, Shanell	10B

Name	Poster #
Stahl, Sara	42 B
Stockwell, Alexander	14 B
Talaski, Grayson	29 A
Tang, Rachel	66 A
Thrasybule, Brielle	9A
Torres, Sara	66 B
Wang, Stephen	19 A
Wang, Grace	67 A
Watts, Andrew	54 A
Weaver, Cole	55 B
Wilson, Gabrielle	11 B
Xavier, Jackson	29 B
Yang, Chaoran	30 B
Zalloumm, Reem	56 A
Zhang, Yunjia	18 A
Zhang, Yuhuan	67 B
Zimbwa, Murisi	43 A

ABSTRACT INDEX

SCHEDULE

Group A | 10 – 10:30 a.m.

Group B | 10:30 – 11 a.m.

Group A | 11 – 11:30 a.m.

Group B: | 11:30 a.m. – 12 p.m.

ABSTRACT NO. 1A

COMPOSITION- AND TEMPERATURE-DEPENDENT ANHARMONIC PHONON DYNAMICS IN FORMAMIDINIUM LEAD HALIDE PEROVSKITES

M. Silverstein, P. Postec, O. Delaire
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Phonons, sound quanta in the form of collective vibrations in a periodic crystal lattice, significantly affect the thermal and electrical transport properties of materials. The halide perovskite (HP) family of materials with the formula ABX3, where A is a monovalent cation, B is a divalent metal, and X is a halogen anion, boast long charge carrier lifetimes and high photovoltaic efficiency. Previous studies have shown significant electron-phonon coupling, which suggests that investigating the phonon dynamics of these materials is key to understanding their optoelectronic properties. At high temperatures, HPs adopt a cubic structure, but diffuse scattering experiments have shown that there are localized regions of correlated tilts of the BX6 octahedra, corresponding to strongly anharmonic phonon modes. We hypothesized that changing the chemical environment of the octahedral lattice, via substitutional disorder on the halide site, should affect the phonon dynamics. We studied FAPbX3 (FA = formamidinium, X = Br mixed with Cl) with Raman spectroscopy to elucidate the compositional and temperature-dependence of phonon modes. Doping the halide sites causes increased energy and broadening of certain phonons, while leaving other modes relatively unchanged. We found two vibrational modes of interest, one of which varied with temperature, and the other which coupled strongly to composition, but neither coupled to both variables. We found these phonons to be strongly anharmonic as evidenced by peak broadening with increasing temperature. Based on literature findings, we determined that these are molecular modes, vibrations of covalent bonds in organic compounds. The changes in one mode's energy due to modification of the inorganic lattice suggests a coupling to formamidinium. These results can be used for rational design of photovoltaic materials, by helping us better understand the mechanism by which hybrid organic-inorganic materials derive their favorable optoelectronic properties.

ABSTRACT NO. 1B

DETERMINING THE EFFECTS OF RISK FACTORS FOR ALZHEIMER'S DISEASE ON FUNCTIONAL NETWORKS OF MOUSE MODELS

A. Jagadeesh, A. Mahzarnia, R.J. Anderson, J. Stout, Z. Han, A. Badea
Duke Pratt School of Engineering, Duke University; Durham, NC 27701

Alzheimer's disease (AD) is a major public health concern, affecting approximately 416 million people worldwide. Since AD is often diagnosed in the later stages of life, understanding the effect of risk factors on the brain is important for developing preventive approaches. To investigate how risk factors impact brain networks, we utilized mouse

models (n=346) carrying the three major human APOE alleles (E2, E3, E4). We studied the effects of APOE allelic variations, sex, diet, and age on functional brain networks using a high-field MRI. Resting-state functional and structural images (T1s) were preprocessed using a pipeline that includes FMRIB Software Library (FSL), Analysis of Functional Neuroimages (AFNI), and Advanced Normalization Tools (ANTs). We applied a group Independent Component Analysis (ICA) to sedentary mice (n=279) using FSL MELODIC, identifying 20 spatially and temporally distinct functional networks. From our ICA results, we performed dual regression while setting up contrasts (e.g., E4 vs. non-E4, High Fat Diet vs. Control Diet, Male vs. Female) and design matrices with covariate information. This resulted in a series of t-statistic maps ($p<0.05$) for each ICA component, showing that the high-fat diet group exhibited higher connectivity values than the control in the hypothalamus and olfactory regions. Using dual regression t-statistic maps, we developed gaussian mixture models to determine z-score thresholds for activation, deactivation, and non-signal regions in t-statistic maps. Our results indicate that risk factors for Alzheimer's disease impact the architecture of functional networks. We aim to use our findings from mouse models to identify early-warning signs of AD in functional networks, predict patient risk, and help identify targets for preventive therapies.

ABSTRACT NO. 2A

ONE PROXY PROXIMAL CAUSAL LEARNING WITH AN EPSILON-DELTA DIFFERENTIALLY PRIVATE ALGORITHM

C. Mathis, A. Volfovsky, R.J. Evans
Statistical Sience, Duke University; Durham, NC 27701

A fundamental problem in causal inference is the presence of confounders. A general solution is to control for confounders by conditioning on them. Ideally, the variable we measure is the true confounder, but oftentimes we only measure a proxy – a noisy measurement of the true confounder. Proximal causal learning demonstrates that two independent proxies of an unobserved confounder is sufficient in controlling for the unobserved confounder. We consider the possibility of having only one proxy for the unobserved confounder. We demonstrate that for multivariate normal data and an ordinal proxy, estimating the Average Treatment Effect (ATE) is possible with only one proxy. We use a Bayesian probit regression to simulate two conditionally independent proxies. Then, we use proximal two stage least squares to estimate the ATE. This method has lower mean squared error (MSE) than other naive methods commonly used such as conditioning on the noisy measurement. We also highlight the importance of cross-fitting in estimating to increase the stability of the estimate. Finally, we introduce an application of proximal causal learning in the field of differential privacy.

ABSTRACT NO. 2B

INVESTIGATING THE UNDERLYING MECHANISM OF MTDNA DAMAGE IN PD

C. Montes, I. Barraza, L. Sanders, PhD
Department of Neurology, Duke University; Durham, NC 27710

Parkinson's Disease is the most common neurodegenerative movement disorder, affecting millions worldwide. However, there are no disease-modifying therapies available. Studies from the Sanders laboratory have demonstrated the accumulation of mitochondrial DNA (mtDNA) damage in a brain region-specific manner in PD models in vivo, in vitro, and in human postmortem brain tissue. Given the observed increase in mtDNA damage in PD models and patient tissues, we hypothesize that defective mtDNA repair results in the accumulation of oxidative lesions in PD. The Base Excision Repair (BER) pathway is a mechanism responsible for repairing damaged DNA, specifically addressing lesions such caused by oxidation, alkylation, and base deamination. The overarching goal of this project is to investigate the mechanistic changes in the BER pathway of primary neuronal PD models. The project will employ several molecular biology techniques, including RNA extraction, cDNA synthesis, and RT-qPCR, to analyze changes in gene expression of BER-specific enzymes. This project will produce insights into the processes underlying the accumulation of mtDNA damage in PD and provide a foundation towards the development of targeted therapies aimed at neurodegeneration. Observations could reveal a greater understanding of pathophysiological mechanisms of disease and new strategies for therapeutics.

ABSTRACT NO. 3A

PRENATAL ENVIORNMENTAL TOXIN EXPOSURE ALTERS THE ADOLESCENT BRAIN

E. Rispoli, T. Vaidyanathan, D. Quintero, D. Ngyuen, O. Wirfel, S. Bilbo
Psychology and Neuroscience, Duke University; Durham 27708

The prevalence of neurodevelopmental disorders (NDDs) has increased rapidly in recent decades and epidemiological studies indicate a correlation between prenatal toxin exposure and NDDs . 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 synapse refinement underlie NDD pathology. Sleep, critical to this refinement, is disturbed in nearly 86% of NDD patients. This study used the Diesel Exhaust Particle and Maternal Stress (DEP/MS) paradigm to co-expose pregnant mice to DEP and a maternal stressor. While previous studies have revealed sex-specific social and behavioral changes in DEP/MS adults, we focused on adolescence. Adolescence is a critical developmental period when NDD sleep disturbances are particularly prevalent. This study aims to characterize NDD phenotype of DEP/MS offspring specifically during adolescence. Preliminary RNA sequencing data indicates upregulation of over 450 genes in microglia in DEP/MS adolescents compared to controls. Additionally, preliminary IHC suggests a decreased number of PV interneurons with perineuronal nets (PNNs) in DEP/MS adolescent offspring. Preliminary analysis of sleep data does not suggest changes in overall time spent in REM/NREM and wake. However, analysis of spectral power reveals disrupted high-frequency network dynamics in DEP/MS female adolescents. Additionally, altered network

dynamics were frontal-cortex dependent and sleep state independent. Because the frontal cortex undergoes significant development during adolescence, we hypothesize that changes in network dynamics may have functional consequences contributing to NDD development.

ABSTRACT NO. 3B

ENGINEERING WELL-CHARACTERIZED AND ENVIRONMENTALLY-RELEVANT NANO AND MICRO PLASTICS FOR EXPERIMENTAL MOUSE MODELS

L. Shiell, E. Viverette, A. West
Duke Center for Neurodegeneration and Neurotherapeutics, Department of Pharmacology and Cancer Biology, Duke University; Durham, NC 27710

The ingestion of plastics presents a significant concern for human health as the mass of plastic estimated to be ingested by individuals is increasing every year. Some studies suggest that there is the relative consumption of plastic found in 50 shopping bags per person per year. However, the implications for human health are complex due to the diverse nature of polymer structure and surface charges which could significantly vary biodistribution and interactions with other molecules like proteins, lipids, and nucleic acids. Current studies often rely on pristine engineered nanobeads, usually polystyrene which is relatively rare in the environment, to understand nanoplastic biology. However, these nanobeads do not mimic environmentally relevant particles in both polymer compositions, surface chemistries and morphologies.
To generate particles for research purposes that better mimic what we are exposed to in daily activities, we have developed a methodology for the production of particles with differing surface charges and shapes from the most common types of plastic pollutants. Sourced recycled starting plastics were obtained from different manufacturers and cryomilled to micro and nano mixtures, and exposed to a novel environmental chamber to simulate exposures in the marine environment in years- to decades ranges. Particles are characterized through orthogonal informative suites of approaches that will include empirically measured ZetaPotential for surface charges, and shapes defined by light-scattering and Cryo-EM. Bioavailability of these particles will be studied in young and aged mice, and in mouse models of disease. The goal is to understand the chemical requirements of plastic pollutants to access different compartments in mammals and what their contribution might be to disease risk and progression.

ABSTRACT NO. 4B

EXACT SOLUTIONS OF EINSTEIN'S FIELD EQUATIONS WITH NONZERO MASS AND ZERO MAGNETIC CHARGE

C. Yang
Trinity College of Arts and Sciences; Duke University, Durham, NC 27708

Einstein's field equations (EFE) describe how the distribution of matter and energy distorts the curvature of spacetime. Since their introduction by Einstein in 1915, these equations have been rigorously analyzed for their mathematical and physical implications, providing profound insights into the nature of gravitation. Under extreme conditions, as verified by the LIGO experiment in 2015, the predictions of EFE diverge significantly from the assumptions of classical Newtonian mechanics.
Exact solutions to EFE can be obtained only under certain simplifying assumptions, such as spherical symmetry. This project presents an expository overview of solutions with nonzero

mass and zero magnetic charge. The four metrics discussed are: (1) zero momentum, zero charge (Schwarzschild), (2) non-zero momentum, zero charge (Kerr), (3) zero momentum, non-zero charge (Reissner–Nordström), and (4) non-zero momentum, non-zero charge (Kerr-Newman).

ABSTRACT NO. 5B

HEAT STRESS IS CORRELATED WITH BIOMOLECULAR CONDENSATE FORMATION OF VESICULAR TRAFFICKING PROTEINS

C. Bersche, S. Pathak, L. Strader
Biochemistry, University of Missouri; Columbia, MO 65211; Biology, Duke University; Durham, NC 27710

As global temperatures rise, crops struggle to adapt to the changing climate. A pressing issue is producing enough crops to support the needs of the growing population, as the climate changes. Thus, studying plant model systems is critical to improve crop health. The Strader lab uses the model plant Arabidopsis thaliana ecotype Columbia (Col-0) to gain insight into the formation of temperature dependent protein condensates.

Bimolecular condensates are intracellular aggregates of specific biomolecules, in this case proteins. Specifically, proteins containing a prion-like domain (PLD) have been linked to condensate formation. PLDs are amino acid sequences that can't fold into a single protein structure and exist in an unstructured form. Our lab is specifically interested in understanding condensate formation patterns in vesicular trafficking proteins, which contain PLDs. Vesicular trafficking mediates the transport of cargo materials to their site of function within the cell. Here we focus on condensate formation in clathrin adaptor proteins (CAP6, CAP8, and CAP10) and EPSIN2, a TGN localized clathrin adaptor. Temperature has emerged as a critical regulator of biomolecular condensates formation. Our studies show that under elevated temperatures (37^{o}C) protoplasts enriched for these vesicular trafficking proteins begin forming condensates.

To explore the temperature dependent condensate formation of CAP6, CAP8, CAP10, and EPSIN2, I confirmed overexpression lines. I quantified potential growth and development defects in 4-day-old seedlings under heat stress and temperature shift assays, discovered the timepoint for condensate formation in 7-day-old roots under heat and cold stress, and analyzed condensate formation in protoplasts expressing vesicular trafficking proteins enriched for their PLD or with their PLD removed under heat and cold stress. My data supports the PLD and elevated temperature dependence of condensate formation, namely condensates begin forming after a few hours of incubation at elevated temperature.

ABSTRACT NO. 6A

EFFECTS OF BISMUTH INCORPORATION ON THE ELECTRONIC PROPERTIES OF 2D HYBRID PEROVSKITES

G. Dono, R. Chakraborty, V. Blum
Department of Physics and Astronomy, University of Rochester; Rochester, NY 14627

2D hybrid perovskites are a class of semiconducting materials that combine layers of inorganic metal-halides and organic cations to access a wide range of electronic properties. While lead-based perovskites have become notable for their potential within photovoltaic applications, the toxicity of their composition creates a push for lead-free perovskites. As an alternative, this project investigates the structural stability of bismuth-containing and bismuth-based perovskites, using first principles

methodology and density functional theory to predict the geometry of the structures and to assess ordering preferences associated with compensating vacancies. From this, the electronic band structure of these materials can be calculated and analyzed to better understand the electronic properties. The project first explores different vacancy arrangements of layered (AE2T)Bi2VacI4 compounds, consisting of metal-halide layers with ratios of Bi2 to one site vacancy (Vac). Structure optimization of five different vacancy patterns (each leading to large structure models including 928 atoms) reveals that an arrangement of single next-nearest neighbor vacancy rows on B sites, alternating with two Bi rows, shows the lowest energy among the arrangements probed (FHI-aims code, "light" settings) and also displays an energy band gap consistent with experimental observations. In contrast, nearest-neighbor vacancy rows and zig-zag arrangements of second nearest-neighbor vacancies are higher in energy and, during relaxation calculations, remain metallic in character and present slow, computationally expensive convergence during structure optimization. We next studied a set of (AE2T)PbI4 structures with partial Pb substitution by Bi and vacancies, in which the metal-halide layer was modified to contain Pb5Bi2 and one site vacancy. Band structure calculations for these vacancy arrangements are in progress at the time of writing and are expected to reveal the character of Bi derived energy levels alloyed into a traditional lead halide based layered perovskite.

ABSTRACT NO. 6B

UNDERSTANDING DIMENSIONALITY AND CONNECTIVITY OF MIXED-CATION HYBRID PEROVSKITES

M. Kubovsky, M. Choi, D. B. Mitzi
Physics, University of Florida; Gainesville, FL 32603

Perovskites are being increasingly studied due to their promising applications in solar cells, LEDs, and photodetectors; low-dimensional hybrid perovskites, in particular, exhibit fluorescence and exciton effects, as well as low defect densities. Introducing large cation spacers between the inorganic layers in low-dimensional perovskites plays a pivotal role in determining dimensionality by affecting the degree of connectivity and distortion, influencing bond angles and lengths. Being able to manipulate the dimension and connectivity of perovskites allows for the tuning of the material's properties, aiding in their applications to electronics. Despite the organic cation spacer's importance, there has been limited attention given to investigating how mixing the organic spacers will impact perovskite structure. In this study, we aim to understand the nature of dimensionality and connectivity within hybrid halide perovskites with mixed organic cations.
We chose to mix branched aliphatic cations, that were known to yield one-dimensional face-sharing and one-dimensional corner-sharing structures depending on the cation to lead iodide ratio, to understand if the resulting phases would be altered. The slow evaporation method was used for synthesizing single crystal perovskites with mixed cations, followed by powder x-ray diffraction and single crystal x-ray diffraction to determine the dimension and connectivity the crystals yielded. We observed that the cation that is more favorable than the other to crystalize with the inorganic precursor tends to crystalize

first, determining the crystal's dimension and connectivity. However, when the two cations have similar tendencies to crystalize, we may see cation mixing within the crystals, suggesting that new structures, different from the pure cation structures, can be synthesized.
This study allows us to better understand the impact on the structure choice of dimension and connectivity that organic cations produce in metal-halide perovskites. More informed control of low-dimensional perovskite structures will lead to property tunability of low-dimensional perovskites.

ABSTRACT NO. 7A

INVESTIGATING THE ROLE OF SMC1A IN X CHROMOSOME GENE EXPRESSION AND ACROSS THE ENTIRE GENOME VIA CRISPR/DCAS9-MEDIATED KNOCKDOWN

I. Debayo-Doherty, A. San-Roman
Summer Scholars Program in Genome Sciences & Medicine, Duke University; Durham, NC 27710

Previously we found that X chromosome copy number affects gene expression across the genome. We hypothesize that these effects are due to the SMC1A gene on the X chromosome, a key component of the cohesin complex. The cohesin complex is a protein complex that regulates gene expression through DNA looping by allowing enhancers and promoters to interact, both regions contain binding sites for transcription factors, and RNA polymerase which together initialize the transcription process. The cohesin complex is composed of four core subunits—SMC1A, SMC3, RAD21, and STAG1 or 2, and defects in cohesin components can result in various disorders such as Cornelia de Lange Syndrome (CdLS). Past research has shown that all the subunits are highly dependent on SCM1A. To test our hypothesis, we will employ a lentiviral vector system engineered to carry a deactivated CRISPR/(d)Cas9, a repressive KRAB domain, and a single guide RNA (sgRNA) to target the SMC1A gene. After validating the knockdown using quantitative PCR (qPCR), we will use RNA sequencing to examine the effect of knocking down SCM1A on gene expression genome-wide.

ABSTRACT NO. 7B

IN-VIVO VALIDATION OF EPIGENOMIC THERAPIES FOR PARKINSON'S DISEASE

J. Fraser, D. Hodgson, B. O'Donovan Ph.D, O. Chiba-Falek Ph.D
Summer Scholars Program in Genome Sciences & Medicine, Duke Center for Genomic and Computational Biology and North Carolina Central University; Durham, NC

Parkinson's disease (PD) is a neurodegenerative disease distinguished by the overaccumulation of the protein α-synuclein encoded by the SNCA gene in the substantia nigra (SN). This leads to the degeneration of dopaminergic neurons which interferes with neuronal functions. Today, PD stands as one of the most prominent neurodegenerative diseases as it remains without a definite cure. However, recent studies have suggested that variants within the SNCA gene cause the gene's overexpression which leads to the development to Parkinson's Disease and various other neurodegenerative diseases. Utilizing a PD mouse model induced by the AAV-A53T-human SNCA vector, we will analyze the expression of α-synuclein in the brain and measure the distribution of the vector in several brain regions and the liver. RNA and DNA Extraction techniques were used to extract the vectors and assess its distributions within the specific organ tissue between May-July 2024. After extracting each from the specific tissue, we prepared a polymerase chain reaction protocol to see whether the vector was expressed or not. Our

results demonstrated that when injected with the engineered all-in-one lentiviral vector, the expression of the SNCA gene overall was lowered in most test subjects. The results of this study suggest that utilizing the AAV-A53T-human SNCA vector can lead to a decrease in the expression of the SNCA gene which leads to less α-synuclein accumulating. Further in-vivo studies and research are required to determine if repressing the expression of the SNCA gene will effectively lower the overaccumulation of α-synuclein to hinder or even halt the development of Parkinson's Disease. Additionally, in-vivo studies utilizing varying factors such as subject species and lentiviral vector composition are necessary to discover possible modifications for the potential treatment. Overall, our findings provide in-vivo proof-of-concept for our LV repressor system, advancing the research's potential as treatment for PD.

ABSTRACT NO. 8A

ANTAGONISTIC INTERACTIONS OF MAMMALIAN ODORANT RECEPTORS

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Odorant receptors (ORs), located on the olfactory sensory neurons within the nasal cavity, interact with complex mixtures of volatile molecules from the environment, facilitating animals' discernment of relevant olfactory stimuli. Humans possess approximately 400 ORs, whereas mice have over 1,000 ORs, each activated or antagonized by different odorants. In this study, we aim to identify antagonists for select ORs when mixed with previously established agonists. By utilizing odor mixtures, we identified antagonists for ORs tuned to carboxylic acids. These results suggest a possible link between pharmacological inhibition of ORs at the receptor level and odor mixture suppression at the perceptual level. The identified antagonists will guide our collaborators in testing their effects in in vivo odor stimulation using transgenic mice, in which a specific OR is fluorescently labeled, to elucidate the role of direct pharmacological inhibition on odor sensation. Our study is valuable for understanding the effect of odor mixtures through the pharmacological inhibition of ORs.

ABSTRACT NO. 8B

EFFECT OF ELEVATED CARBON DIOXIDE ON SURVIVAL AND MUTATIONS IN *CRYPTOCOCCUS DENEOFORMANS*, A HUMAN FUNGAL PATHOGEN

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Climate change has caused an increase of extreme weather, allowing fungal species to spread to new regions. Additionally, due to rising global temperatures, environmental fungi that typically thrive in cooler climates (25-30oC) are developing thermotolerance to allow growth at higher temperatures, for example, human body temperature (37oC). If environmental fungi are developing thermotolerance, this may lead to an increase of pathogenicity in humans. To better understand the effects of heat stress and heat adaptation on disease-related traits in fungi, the Gusa lab is studying *Cryptococcus deneoformans*, a species of fungi that can cause infections of the skin, lungs and brain, primarily in those with weakened immune systems. *C. deneoformans* causes fewer invasive infections compared to closely related *Cryptococcus* species and is also less thermotolerant. For my summer project, I

will utilize a prong plating technique growing C. deneoformans cells on RPMI tissue culture medium to investigate the effects of heat stress with the addition of CO2 (5%). The ability for *Cryptococcus* to survive with 5% CO2 as a stressor is advantageous, potentially yielding insights comparable to those found in the human host environment. The natural habitat of *Cryptococcus* in the environment contains low carbon dioxide concentrations (0.04%). In contrast, within mammalian tissues, carbon dioxide concentrations are significantly higher at around 5%. The ability for *Cryptococcus* to survive in 5% CO2 could indicate high virulence. Surviving mutants from the prong plating experiment will be sequenced to identify how the strains have adapted. This work will contribute to our understanding of climate change impacts and fungal threats to human health.

ABSTRACT NO. 9A

TWO-YEAR IN-HOST EVOLUTION OF *CRYPTOCOCCUS*: GENETIC AND PHENOTYPIC FACTORS INFLUENCING ANTIFUNGAL SUSCEPTIBILTY

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Cryptococcus neoformans, an environmental opportunistic fungal pathogen, causes cryptococcal meningitis (CM), a lethal disease in the immunocompromised. This fungus can evade the host's immune system and antifungal drugs through phenotypic and genotypic adaptation, but little is known of its modulation during persistent human infection. Initial analysis of serial strains from a Duke University Health Systems (DUHS) CM patient of over two years revealed in-host evolution with co-infecting lineages, each showing significant genomic changes on chromosomes 1, 6, or 12. These changes are linked to various virulence phenotypes, including growth rate, melanin formation, capsule thickness, cell morphology, and antifungal susceptibility. This study examines whether genomic and phenotypic heterogeneity impacts antifungal susceptibility by comparing in-vitro susceptibility of each distinct strain alone and in co-culture. Our results indicate no significant difference in antifungal susceptibility between individual strains and those in co-culture. However, certain genomic mutations made some strains more susceptible to a specific drug.

Antifungal susceptibility testing (AFST) was performed using E-Tests and microbroth dilution. Both methods showed limited ability to distinguish whether surviving cells were due to specific genotypes or phenotypic heterogeneity in co-cultures, particularly for strains with pseudohyphal morphology. By measuring the optical density (OD) of drug-treated strains, we examined growth and survival dynamics. The OD measurements indicated that survival was influenced by specific genotypes, especially strains with pseudohyphal growth, which altered the expected scaling between absorbance and colony-forming units (CFUs). Thus, antifungal susceptibility in co-infections, such as in human cerebrospinal fluid, may be more influenced by the physical interactions between different genotypic strains.

ABSTRACT NO. 9B

EXPLORING GENE REGULATORY ELEMENTS IN THE HUMAN GENOME

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The human genome consists of many gene regulatory elements, which serve an important role in gene expression and aid in cell differentiation. To explore this, we are targeting gene regulatory elements in the human genome with guide RNAs (gRNAs) using the CRISPR interference (CRISPRi) technique. We chose guides targeting the promoters of GPRIN2, ACTA1, and AURKAIP1. In this study we are specifically interested in understanding if there are differences between the H9 stem cell genome, which is the specific human genome we are experimentally studying, and the human reference genome, hg38, which is what we used for guide RNA design. We will introduce our CRISPRi machinery and guide RNAs to our H9 cells using lentivirus. To measure the gene expression of our target genes, we will harvest the RNA from the cells and then use the RT-qPCR technique to determine the amount of target gene RNA in the cells. We expect there to be less gene expression with the gRNA that targets the specific genes of our choosing than cells that received a non-targeting gRNA. Additionally, we hope to understand how genetic variation that impacts gRNA sequences influences their efficacy. The findings of this project will allow us to determine whether variations in individual human genomes relative to the reference genome are significant for developing more potent therapeutics for the treatment of diseases such as cancer and neurological disorders.

ABSTRACT NO. 10A

EXPLORING THE ROLE OF ARC IN NEURAL CIRCUIT PLASTICITY USING CRISPRi

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Synaptic plasticity, the ability of synapses to strengthen or weaken in response to activity, is essential for learning and memory. Immediate early genes (IEGs) respond rapidly to neuronal activity and are linked to brain regions associated with these processes, thus indicating their importance in regulating synaptic plasticity. Among these IEGs, Activity-regulated cytoskeleton protein (Arc) is particularly relevant because of its unique capacity to function directly on the synapse, where it promotes endocytosis of AMPA-type glutamate receptors (AMPARs) in response to neuronal stimuli. Most of our knowledge about Arc function at the synapses comes from studies involving constitutive Arc deletion. However, the effects of transient changes in Arc expression after synapse formation and the distinct role of Arc when its expression is elevated in response to neuronal activity are less understood. To investigate this point, we used CRISPRi to target different regulatory regions of Arc gene and inhibit Arc expression at different time points in development. First, we assessed how Arc is regulated at seven days in vitro (DIV) prior to synaptic maturity and confirmed that Arc expression levels can be modulated by targeting the promoter and enhancer region. Building on these studies, we are now using these CRISPRi tools to knock down Arc expression at 15 DIV after synaptic connectivity has been established to investigate the consequences of Arc regulation on the synaptic level. To quantify Arc expression levels at 15 DIV after regulation via CRISPRi, we are using western blot and biotinylation

procedures. Using these methods, we aim to ascertain how regulation of Arc's activity-induced expression can alter one of Arc's major functions – receptor internalization – and subsequently synaptic plasticity.

ABSTRACT NO. 10B

INVESTIGATING MUCIN DEGRADATION CAPABILITIES OF THE *AKKERMANSIA MUNICIPHILA* EFFECTOR PROTEIN AMUC_0646.

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Akkermansia muciniphila, discovered in 2004, is a commensal gut bacteria that colonizes and degrades the gastrointestinal (GI) mucin layer. These complex, heavily O-glycosylated mucin glycoproteins form the mucus layer in the GI tract, which acts as a strong protective barrier. This layer is important in protecting the gut epithelial lining from enteric pathogens, and degradation of the mucus layer is a hallmark sign of gut dysbiosis. Higher levels of *Akkermansia muciniphila* in the gut result in increased mucin layer thickness, improving gut protection and barrier function against GI diseases. Therefore, exploring the mechanisms by which *Akkermansia muciniphila* interacts with and degrades mucin provides valuable insight into treatment avenues for mucin-related diseases. Our project aims to investigate the mucin degradation capabilities of the effector protein Amuc_0646 found in the A. muciniphila type strain, BAA-835. Amuc_0646 binds to mucin and bears high structural homology to IdeS, a known IgG-degrading protease, suggesting its potential in degrading similarly glycosylated mucins as well. Using site-directed mutagenesis, we mutated 5 specific amino acids (C46S, H193A, D216A, S217A, and D218A) within the active site of Amuc_0646 to characterize the mucin binding and degradation activity of this protein. We hypothesize that these 5 mutant proteins will no longer degrade mucin when tested using various glycoprotein degradation assays. Our project findings will contribute to the overall understanding of which effectors *Akkermansia muciniphila* uses to thrive in the GI mucin layer which will ultimately further its development as a next-generation probiotic.

ABSTRACT NO. 11A

ELUCIDATING THE MECHANISM OF ABL1 AND MCT1 INHIBITION ON METABOLIC DYSREGULATION IN SMALL CELL LUNG CANCER

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Small Cell Lung Cancer (SCLC) accounts for 15% of lung cancer cases, is highly metastatic, and has limited treatment options. SCLC lacks actionable driver mutations, complicating the process of developing targeted therapies and resulting in a continued reliance on decades-old chemotherapeutic approaches. Stagnated improvement of patient outcomes underscores the dire unmet need for expanding treatment options for patients with SCLC.

The ABL kinases (ABL1/2) are non-receptor tyrosine kinases that play a central role in numerous cellular signaling pathways including tumor progression and metastasis. We have shown that inhibition of the ABL kinases in SCLC induces significant metabolic perturbations, characterized by induction of reactive oxygen species (ROS) and glutaminergic dysregulation which may reveal further druggable vulnerabilities. We performed a whole-genome CRISPR screen to identify sensitizers to ABL kinase inhibition and identified a metabolic axis involving Monocarboxylate Transporter (MCT) 1, a primary efflux transporter of lactate. Inhibition

of MCT1 synergizes with ABL kinase inhibition and further characterization showed that this synergy is agnostic of SCLC transcriptional subtype, but characterization of sensitive and resistant cell lines shows that synergy may be dependent on high MCT1, ABL2, and c-MYC expression. Here, we explore the effects of ABL kinase inhibition on changes in protein expression, phosphorylation, and glycosylation of proteins hypothesized to be implicated in a metabolic axis dependent on the ABL Kinases. We found that ABL directly interacts with MCT1 and Basigin (BSG), a membrane- bound chaperone protein and functional partner of MCT1, responsible for its localization to the plasma membrane. Here, we explore the complexities of ABL's metabolic involvement to reveal targetable metabolic vulnerabilities and novel biology critical to improving ABL kinase-based therapies in cancer.

ABSTRACT NO. 11B

DRINKING IN THE DARK

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Alcohol Use Disorders is a disorder that is most common among young adults. In 2022, 23.5% of people ages 18 and older reported engaging in binge drinking. Binge drinking can lead to liver inflammation, heart complications, and memory problems. Rapastinel, is a drug recently studied in a clinical study as an antidepressant, but failed because it did not differ from placebo in patients with major depressive disoastinel will consume less alcohol and exhibit fewer withdrawal signs compared to those treated with saline treatment.We administered a solution of 20% ethanol and 80% water to a total of 15 mice over the past five weeks, giving them the solution Monday through Thursday each week. In the fifth week, we administered rapastinel and monitored their behavior, with the goal to reduce the receptors. Will present more results of the drug after challenges.

ABSTRACT NO. 12A

KAPOSI SARCOMA HERPESVIRUS REACTIVATION AND CELLULAR STRUCTURE IN THE ABSENCE AND PRESENCE OF ETHANOL

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Kaposi Sarcoma Herpesvirus (KSHV) is a long-term herpesvirus that leads to cancer in a subset of individuals. Our lab studies the reactivation of latent to lytic KSHV cells and its impact on ethanol exposure. During the latent phase, KSHV infected cells express few viral genes. During the lytic phase, KSHV cells are active and create replications of viral genes. Immunofluorescence determines the location of viral or cellular proteins. The purpose of this study is to determine the location of KSHV viral proteins during latent and lytic phases and in the presence of ethanol. Specifically, we studied KSHV proteins: ORF26 and ORF59. ORF26 function is to assemble and stabilize virions. ORF26 ensures that the virion enters the cell, spreads and releases throughout the cell. ORF59 function is to ensure viral genes are replicated in the lytic phase. ORF59 alters DNA by binding the replicates of DNA to the nucleus and cytoplasm. Cells latently infected with KSHV were reactivated for 24, 48, 72 hours in the absence and presence of ethanol [0.4g/dL]. The

localization and abundance of cells expressing ORF59 were compared. The findings of this study determined that the abundance of lytic proteins were increased in the presence of ethanol and the localization of both ORF59 and ORF26 is in the nucleus and cytoplasm, respectively. Future studies will continue to investigate alcohol as a driver of KSHV lytic replication.

ABSTRACT NO. 12B

RAPASTINEL EFFECTS IN MICE ON ALCOHOL CONSUMPTION AND WITHDRAWAL

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The incessant urge to consume alcohol, akin to an insatiable itch in the mind, is a hallmark experience for individuals grappling with alcohol use disorder. Influenced by a complex interplay of genetic predispositions and environmental factors, this condition affects a significant portion of the population, yet effective interventions remain a subject of ongoing investigation and refinement. Rapastinel, a drug initially developed as an antidepressant, acts as a partial agonist in NMDAR activation of glutamate. This mechanism has prompted research into its effects on alcohol consumption and withdrawal. We hypothesized that Rapastinel would reduce alcohol consumption and mitigate withdrawal symptoms due to its unique action on the NMDA receptor. We conducted a six-week study consisting of two experiments centered on generating alcoholism dependency in mice. One experiment used gastric gavage to deliver a 25% ethanol solution to the mice's stomachs to simulate withdrawal. Specifically, withdrawal was measured through this marble burying stress test to elucidate withdrawal behavior in alcohol dependent mice "Stressed behavior" was quantified by measuring the number of marbles buried by each mouse out of a total of 20. The second experiment used a 20% ethanol solution and measured ethanol consumption through tubes during weekdays with a "Drinking in the Dark" (DID) protocol. Results indicate that regarding the withdrawal experiment, mouse behavior was largely reflective of individual behavior rather than differences between experimental groups, though evidence of ethanol dependence was present. Next steps will be to test whether marble burying serves as a better alcohol dependence indicator with the DID protocol which is conducted for longer and may result in more dependence.

ABSTRACT NO. 13A

THE MECHANICALLY ACTIVATED PIEZO1 ION CHANNEL REGULATES INTESTINAL EPITHELIAL HOMEOSTASIS

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Intestinal stem cells (ISCs) maintain intestinal integrity and function in digestion and absorption by replenishing the epithelial lining every 3-5 days from the crypt base. Understanding the mechanisms of ISC homeostasis is thus critical to preventing and treating conditions such as short bowel syndrome, inflammatory bowel disease, irritable bowel syndrome, and colorectal cancer. Previous in vitro studies demonstrated that luminal flow promotes intestinal villus formation, suggesting that mechanical stimulation is important to ISC-regulated intestinal homeostasis. However,

mechanisms behind this relationship remain undefined. Here, we hypothesize that Piezo1, a mechanically activated transmembrane cation channel expressed in crypts, is involved in ISC differentiation and proliferation. First, we identified robust expression of Piezo1 in the mouse intestinal crypt. To evaluate the potential association between mechanical stimulation and Piezo1 in ISC maintenance, wildtype (WT) mice and inducible tamoxifen-treated VillinCreERT2; Piezo1fl/fl knockout (IKO) mice were used to generate 2D and 3D intestinal organoid models of Piezo1 loss of function. We performed an intestinal crypt proliferation assay with crypts isolated from the murine jejunum, and then subjected organoids to static incubation, periodic vibration (5 Hz for 10 min, 2x a day) or constant shaking (150 rpm). After 3 days of treatment, organoids were imaged and collected for proliferation assays and qRT-PCR for intestinal cell markers. Constant shaking increased expression of Piezo1 and secretory lineage markers, including Muc2 (Goblet cells), Dll1 (secretory progenitor) and Alpi (enterocytes) in WT 2D organoid monolayers, more so than in mechanically stimulated WT 3D organoids. Preliminary results have also showed loss of Piezo1 to decrease proliferation, as well as decrease expression of Muc2 and Alpi. This indicates Piezo1 may be required to maintain ISC proliferation and differentiation. Further experiments should continue defining how Piezo1 maintains the intestinal epithelium and subsequently determine how it may be exploited as a therapeutic target for gastrointestinal disorders.

ABSTRACT NO. 13B

INVESTIGATING THE ROLE OF MESODERM SPECIFIC TRANSCRIPT IN FUSION-POSITIVE RHABDOMYOSARCOMA

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Rhabdomosarcoma (RMS), the most common pediatric soft tissue sarcoma, has a 5-year survival of 30% for high risk patients, and with metastasis reduced to <10% in the setting of expressing a PAX/FOXO1 fusion gene. RMS is thought to arise from skeletal muscle precursors that are unable to differentiate. Mutant PAX3/7 fusion genes are found in most alveolar histology RMS tumors. One direct downstream target of PAX3/7 fusion gene is an understudied acyl transferase Mesoderm Specific Transcript (MEST). Since PAX7 orchestrates satellite cell renewal, we hypothesized that inappropriate upregulated PAX7 activity underlies RMS by supporting proliferation and preventing myogenic differentiation. Prior data in our lab verified publicly available data suggesting that MEST has increased expression in PAX7::FOXO1 fusion RMS. Our objective is to identify the role that MEST plays in RMS and to determine the value of MEST as a future therapeutic target. MEST expression was measured in human RMS cell lines through qPCR. Human skeletal muscle myoblasts expressing the PAX3::FOXO1 fusion were analyzed in a microarray for MEST. MEST was suppressed in the PAX7 fusion-positive RMS cell line CW9019 using shRNAs. Knockdown was validated through qPCR and cell growth in vitro and in vivo xenografts was studied. A clonogenic assay was performed to determine the effect of MEST on colony formation behavior of RMS.

Here we show the impact of genetic knockdown of MEST on RMS cells through functional assays, demonstrating its role in promoting the oncogenic phenotype of RMS. Future goals include an in vivo xenograft study with MEST doxycycline-inducible shRNAs, and to perform RNA sequencing on cells transduced with MEST shRNAs. Our data validate previous findings of MEST as a disease promoting factor in fusion-positive RMS and provide a basis for further research on the interaction between the oncoprotein PAX7::FOXO1 and MEST.

ABSTRACT NO. 14A

INFLUENCE OF GUT MICROBIOME COMPOSITION ON ALPHA-SYNUCLEIN PATHOLOGY IN MOUSE MODELS OF PARKINSON'S DISEASE

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Parkinson's disease (PD) is a neurodegenerative disorder primarily associated with motor symptoms such as resting tremors, bradykinesia, and postural instability, as well as non-motor symptoms including cognitive changes and various gastrointestinal symptoms like nausea, constipation, and vomiting. The pathological hallmark of PD is the formation of Lewy Bodies, the aggregation of alpha-synuclein fibrils, and the loss of dopaminergic neurons in the substantia nigra pars compacta. While the disease is traditionally viewed as a central nervous system disorder, Braak's hypothesis proposes that in some subtypes of PD, alpha-synuclein aggregation initiates in peripheral gut epithelial cells and subsequently spreads to the central nervous system via the vagus nerve and the gut-brain axis.

This collaborative study aims to assess the impact of specific microbiome compositions on alpha-synuclein pathology using human-PAC-WT-SNCA+/+ Snca-/- transgenic mice, which over-express wild-type human alpha-synuclein with no interference from mouse alpha-synuclein. Germ-free, gnotobiotic mice with no microbiomes were orally gavaged once with either a *Bifidobacterium* or *Lactobacillus* species, known for their significant health-promoting and immunomodulatory properties. In parallel, conventionally colonized mice with normal microbiomes were routinely gavaged with one of two opportunistic pathogens over a three-week period. The mice were then collected for tissue immunohistochemistry in order to evaluate the pattern and severity of dopaminergic neuron loss and alpha-synuclein pathology in the gut and brain. The ongoing results from this study will provide crucial insights into how changes in the gut microbiome may influence neurodegenerative processes in the brain. Such findings could pave the way for novel therapeutic strategies targeting the gut-brain axis in Parkinson's disease.

ABSTRACT NO. 14B

DEVELOPING AN IN VITRO LIGAND BINDING ASSAY FOR CCR7

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Chemokine Receptor 7 (CCR7) is a G-Protein Coupled Receptor (GPCR) important for leukocyte migration and immune system homeostasis. Activation of CCR7 by its endogenous C-C chemokine ligands CCL19 and CCL21 induces intracellular signaling cascades via G-protein activation and β-arrestin recruitment, promoting chemotaxis of immune cells into Secondary Lymphatic Organs (SLO's). CCR7

upregulation is reported in several types of cancers to enable cancer cell migration into lymph nodes. As a member of the highly druggable GPCR family with significant relevance in cancer progression, CCR7 is a prime candidate for identifying potential cancer therapeutics that modulate its activity. To increase the efficacy of small molecule screening, fluorescence polarization stands as an effective methodology to quantify these biomolecular interactions. Therefore, the objective of this study was to establish a fluorescent polarization assay using a fluorescein labeled CCL19 peptide to pharmacologically characterize CCR7 functionality. To achieve this objective, we generated a modified CCL19 peptide containing an LPETGGH motif at its C-terminus for sortase-mediated installation of fluorescein and a 6x-Histidine tag for purification by affinity chromatography. Following expression and purification of the modified CCL19, we demonstrated similar G-Protein activation by CCR7 by WT and mutant CCL19 using a Bioluminescence Resonance Energy Transfer-based assay. Then, sortase-mediated transpeptidation of Gly-Gly-Gly-fluorescein to CCL19 was performed to generate a working stock of CCL19-fluorescein (fCCL19). The next steps of this project will include assessing the binding of fCCL19 to CCR7-expressing cells by flow cytometry and then testing a broad range of fCCL19 and CCR7 concentrations to further optimize fCCL19 as a reporter peptide in the binding of alternative small molecules to CCR7. Overall, this assay will allow us to functionally characterize CCR7 and enable high throughput screening of mutations in the receptor and/or the effect of other molecules such as nanobodies or small peptides, furthering current efforts in cancer pharmacology.

ABSTRACT NO. 15A

SEX SPECIFIC EFFECTS OF ADOLESCENT INTERMITTENT ETHANOL ON ASTROCYTE-EXCITATORY SYNAPSE INTERACTIONS AND POTENTIAL REVERSAL IN THE DORSAL HIPPOCAMPUS

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Approximately 3.2 million adolescents in the US aged 12-20 have engaged in binge drinking within the past month, with the prevalence among females now matching that of males. Adolescent intermittent ethanol (AIE), a model of binge drinking in rats, decreases astrocyte-excitatory synapse interactions in the dorsal hippocampus (dHPC) and medial prefrontal cortex (mPFC) in adult rats. These deficits were reversed by gabapentin, an FDA-approved anti-epileptic drug, which decreased excitatory postsynaptic current amplitudes. Gabapentin has multiple mechanisms of action, both neuronal and astrocytic. We propose that gabapentin may work directly via astrocytes and will investigate this using astrocytically expressed Designer Receptors Exclusively Activated by Designer Drugs (DREADDs). We will assess the ability of astrocyte-expressed Gq-DREADDs activated by Clozapine-N-Oxide (CNO) to reverse AIE-induced astrocytic-synaptic interaction deficits. Comparisons will include measures of astrocyte morphology (surface area and volume) in astrocytes positive and negative for Gq-DREADD. The ability of Gq-DREADD activation to reverse AIE-induced astrocytic-excitatory synapse proximity will also be assessed. These findings will extend the literature to include AIE-

induced astrocyte morphology and excitatory synaptic proximity in female rats. Male and female adolescent Sprague-Dawley rats (PND 29-51) received 14 doses of intermittent ethanol (AIE, 5 g/kg, 35% Ethanol, intragastric gavage) or isovolumetric water over 22 days (2 days on-1 day off-2 days on-2 days off). Animals were euthanized and brains harvested for immunofluorescent analyses of sex-specific effects of AIE on astrocyte-excitatory synapse colocalization and astrocyte morphology. Analyses are ongoing, and we expect to replicate previous AIE-induced reductions in astrocyte-excitatory synaptic proximity in adult male rats and extend this to adult females. Furthermore, we anticipate that AIE will not affect female astrocyte morphology, as found in males. These results will explore DREADDs as a method of reversing AIE-induced effects. Future studies should extend this investigation into the ventral hippocampus to determine whether results are region-specific.

ABSTRACT NO. 15B

THE SPLICEOSOME PROTEIN PRP38 IS REQUIRED FOR REGENERATION OF THE DROSOPHILA INTESTINE

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Tissues rely on regenerative mechanisms to restore lost cellular mass over an organism's lifetime. The Drosophila intestine is a valuable model for studying these strategies as it faces various environmental insults. The adult hindgut, analogous to the human intestine, lacks stem cells and employs alternative mechanisms. It comprises an anterior pylorus and posterior ileum. The mature adult pylorus exhibits cellular and genomic hypertrophy in response to the proapoptotic gene hid, while the ileum is resistant. Interestingly, the young adult pylorus and ileum are both sensitive to hid, indicating that hid insensitivity develops during maturation.

To understand the mechanisms underlying pyloric and ileal injury responses, we compared RNA expression in mature and young hindguts and conducted a candidate RNAi screen that combined hid expression with knockdown of genes that are unregulated in the mature hindgut. Our first screening focused on genes preventing organismal death with hid overexpression. We identified two RNAi lines of the gene prp38 that enhance survival in mature hindguts expressing hid, highlighting prp38 as a key factor in hindgut regeneration. However, the cellular mechanism remained unknown.

Cell death was next examined to uncover the cellular mechanism of prp38. Preliminary results indicate that prp38 promotes regeneration and cell survival in the mature pylorus. In prp38 RNAi animals with hid expression, nuclear size increases, and cell number decreases. Pyloric chromosome condensation was observed in hid-expressing prp38 RNAi lines, suggesting prp38's role in nuclear integrity. The ileum remained unaffected, indicating a specific role of prp38 in the pylorus. These findings suggest that wild type prp38 protein is crucial for maintaining cellular integrity in the Drosophila intestine. Overall, our findings reveal a new molecular mechanism involved in maintaining intestinal integrity and regulating cellular responses to stress.

ABSTRACT NO. 16A

AIE EXPOSURE INCREASES ASTROCYTE NUMBERS LONG-TERM IN THE AMYGDALA OF AGED MICE

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Binge drinking during adolescence can cause significant damage to the developing brain, persisting well into adulthood; however, less is known about the effects that persist in aging. The primary hypothesis was that the effects of aging on neuroimmune responses would be exacerbated by adolescent binge drinking, together causing a higher increase in neuroimmune reactivity and response than normal. To investigate this, a mouse model of adolescent drinking known as Adolescent Intermittent Ethanol (AIE; 1mos) was utilized, but LPS was administered in later adulthood (18mos) 16 months after the last ethanol exposure. Immunohistochemistry was conducted on extracted brain tissue to highlight GFAP protein, a marker for astrocyte activation, with the results being visualized via image analysis. Whole brain tissue was homogenized and tested using ELISA kits for TNF-α and IL-10. AIE led to a long-term increase in astrocyte numbers in the BLA, CeA, and MeA compared to AIW, but LPS did not enhance this effect. There was no change in immunoreactivity in the MeA or CeA, but surprisingly, in the BLA, immunoreactivity decreased due to adolescent ethanol exposure. In our whole brain samples, AIE increased IL-10, but there was no effect on TNF-α. However, LPS had no effect on either cytokine. These results were unexpected because LPS did not seem to impact immune responses. In conclusion there is evidence that adolescent drinking alters immune response even in aged brains. It is plausible that the increase in IL-10 is an attempt to suppress persisting astrogliosis created by ethanol exposure. Future studies should investigate how adolescent ethanol exposure can cause persisting strain to the neuroimmune response as an individual ages.

ABSTRACT NO. 16B

EFFECTS OF ADOLESCENT INTERMITTENT ETHANOL EXPOSURE-INDUCED DYSREGULATION OF ALZHEIMER'S DISEASE PATHOLOGY IN AGED MICE

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Alcohol use disorders (AUD) are highly prevalent in the United States, and binge drinking among adolescents (ages 10-24) raises the risk for AUD development during both adolescence and adulthood. Excessive alcohol exposure during adolescence has been linked to dysregulation of the neuroimmune system, particularly in the hippocampus. Additionally, aging individuals are at an increased risk of hippocampal neurodegeneration and developing associated diseases such as Alzheimer's Disease (AD). As such, this study tested the hypothesis that adolescent intermittent ethanol (AIE) exposure would exacerbate microglial activation and dementia-associated proteins in the hippocampus of aged mice. Briefly, C57BL/6J mice were administered ethanol or water. Once the mice were aged (18 months), they were treated with lipopolysaccharide (LPS), mimicking an infection to induce immune activation, or saline. To assess immune activation, we measured microglia number and densitometry using immunohistochemistry using Iba-1 in each

of the hippocampal subregions. There were no effects of LPS on immunoreactivity or cell counts; however, ethanol increased microglial immunoreactivity in the CA2/3 but not CA1 or DG subregions. Moreover, ethanol did not directly influence microglial cell numbers. ELISAs were also run to detect Amyloid Beta (Aβ) and phosphorylated-Tau (p-Tau) in the hippocampus, which are proteins highly involved in the pathogenesis of AD. There did not appear to be any effects of LPS or ethanol on Aβ protein concentration in the hippocampus. The results of the p-Tau ELISA, however, suggested that ethanol increases the concentration of p-Tau in the hippocampus and that somehow LPS had a mitigating effect. Overall, these studies imply that ethanol only moderately affects microglia activation, but may contribute to a buildup of p-Tau. Altogether, these findings suggest that adolescent binge drinking has long-term effects that may lead to increased susceptibility for AD development. Future studies should use transgenic mice to further elicit AD effects.

ABSTRACT NO. 17A

DETERMINING WHETHER LONG TERM EXPOSURE TO NICOTINE WHICH INDUCES DESENSITIZING RECEPTOR AFFECTS ATTENTION AND MEMORY

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Nicotine has been smoked for centuries by people seeking feelings of happiness and relief. However, due to negative health detriments arising from smoking, nicotine is often stigmatized and dismissed as a possibly useful substance that may have other isolated positive effects. Nicotine has previously been shown to enhance attention and memory. Whether this is due to its receptor activating or desensitizing effects is unknown. This study aims to investigate whether nicotine enhances these functions through the desensitization effect or the activating effect. In order to mimic the desensitization effect, the study subjects – Sprague Dawley rats – were divided into four groups each receiving the control or escalating doses of nicotine daily: one dose, four doses, or eight doses. Before each attention or memory task, a lower or higher concentration of the antagonists Scopolamine (a competitive muscarinic cholinergic antagonist) or Dizocilpine (a noncompetitive NMDA glutamate antagonist) were administered to the subjects. These antagonists reduce attention and memory when acting alone. Preliminary results indicate the highest doses of daily nicotine appear to reverse the adverse effects of Scopolamine and boost the scores of the subjects in the attention and memory tasks. Subjects who received higher doses of nicotine, developed tolerance and became desensitized to nicotine's long-term effects. Since the highest dosage of nicotine had a positive result, it can be inferred that the desensitizing effect is the reason attention and memory improved. Identifying the mechanism by which nicotine enhances these functions is vital to understanding how different receptors are impacted by desensitizing drugs. Targeting these mechanisms can translate into developing drugs that utilize the desensitizing effect to reverse cognitive deficiency, especially in people who have ADHD or Alzheimer's Disease.

ABSTRACT NO. 17B

PERSISTENT EFFECTS OF ADOLESCENT ETHANOL ON NEUROGENESIS, NEUROIMMUNE, & CHOLINERGIC SYSTEMS IN THE ADULT HIPPOCAMPUS: PREVENTION BY DIETARY CHOLINE

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Adolescence binge drinking is characterized by episodes of high intoxication followed by withdrawal, and as indicated by research in both humans and animals, leads to persistent alterations in learning and memory. The cholinergic system is crucial for memory, movement, and other functions. Adolescent intermittent ethanol (AIE) exposure, a rodent model of adolescent binge drinking, causes deficits in neurogenesis, cholinergic inflammation and increased neuroinflammation in the adult dorsal hippocampus. Choline is a precursor to acetylcholine and the primary neurotransmitter of the cholinergic system and is known to regulate attention, learning, motivation, and memory. Dietary choline supplements decrease neurological deficits associated with prenatal ethanol exposure and may ameliorate the persistent neuroimmune, neurogenetic, and cholinergic alterations in the adult dorsal hippocampus following AIE exposure.
Male and female Sprague-Dawley rats received choline supplementation (100 mg/kg, 6% choline chloride in sweetened condensed milk, PND 24) and AIE dosing (5 g/kg, 35% ethanol, PND 29) during adolescence via oral gavage. Upon adulthood (PND 70), animals underwent behavioral testing. AIE reduced male locomotion and increased risk-taking, both prevented by choline. Effects of AIE were less pronounced in females. After testing, animals were sacrificed, and brain tissues were collected for immunohistochemistry analysis of neurogenesis, neuroinflammation, and cholinergic markers using DCX, VAChT, and RAGE as proxies. Imaging was done with a fluorescent scope and analysis in QuPath-0.5.1 focused on the granular cell layer, reporting results as percent positive staining within the ROI.
Analysis is still underway; however, we anticipate that dietary choline will ameliorate persistent AIE deficits in the adult dorsal hippocampus, increasing neurogenesis (DCX), decreasing neuroinflammation (RAGE), and maintaining cholinergic projection levels (VAChT). These findings could inform therapeutic strategies for addressing neurocognitive deficits resulting from adolescent alcohol usage.

ABSTRACT NO. 18A

WI-FI MONITORING USING LOW SAMPLING RATE RADIOS RECEIVERS

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The next generation of Wi-Fi evolves large bandwidth to meet the demands of high data rates, posing challenges for passively detecting Wi-Fi packets and extracting unencrypted information, or termed as Wi-Fi monitoring, for spectrum sharing network security and network diagnostics applications. This research project explores the use of radio receivers operating at low sampling rate for low-cost and energy-efficient Wi-Fi monitoring.
Compared to traditional Wi-Fi monitoring approaches that rely on spectrum analyzers and Wi-Fi sniffers operating at the full sampling rates,

our method leverages sub-Nyquist radio receivers in assistance of machine learning to extract packet properties to improve performance under low sampling rates. The significance of our work lies in its ability to utilize machine learning to provide insights into network usage patterns, which can lead to more efficient Wi-Fi networks. This integration is pivotal for ensuring efficient resource management, and smarter communication systems.

In this study, we use one PlutoSDR to capture Wi-Fi packets from commodity Wi-Fi access points (APs) and clients (e.g., laptops, smartphones) at a selectable low sampling rate; we employ another auxiliary PlutoSDR operating at the full sampling rate to decode the ground truth information, which serves as the labels for our data. By analyzing the correlation of the received signals and leveraging the repetitive legacy preambles, our system is able to extract the data rate, bandwidth, and other Wi-Fi properties from the legacy signal field (L-SIG) as part of the Wi-Fi packet preambles. The captured packets waveform in low sampling rate (as the inputs) and information extracted from the full sampling rate packets (as the labels) form our dataset, which is used to train machine learning models.

ABSTRACT NO. 18B

ETHANOL EXPOSURE ENHANCES KHSV VIRAL REACTIVATION AND PROTEIN EXPRESSION

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Kaposi's sacoma-associated herpesvirus (KSHV), fomally known as human herpesvirus 8 (HHV8), belongs to the lymphotropic gamma herpesvirus subfamily. KSHV is implicated in several malignancies, notably, it causes Kaposi's sarcoma (KS), primary effusion lymphoma (PEL), multicentric Castleman's disease, and KSHV inflammatory cytokine syndrome (Damania and Cesarman, 2013). Despite being one of the seven recognized human cancer viruses (oncoviruses), there is no known cure for KSHV. KSHV has a broad tropism in adherent cell lines, where the default pathway following primary infection is the establishment of viral latency (Bechtel et al., 2003). While latency allows persistent infection, lytic replication is crucial for viral dissemination. Lytic reactivation results in a cascade-like expression of viral immediate-early (IE), early (E), and late (L) genes in a highly regulated temporal manner. The spontaneous lytic reactivation of the virus in these cells is not well understood but human environment and behavior, including alcohol exposure, are of primary interest to our research. To determine the expression pattern and localization of viral lytic proteins during reactivation we seek to assess how viral and cellular proteins in latently infected ISLK.219 cells change during KSHV reactivation in the presence and absence of ethanol. We propose that ethanol exposure at the onset of KSHV reactivation enhances viral lytic protein expression. Specifically, we hypothesize that during KSHV reactivation, increased ethanol

exposure leads to a more rapid expression of specific viral proteins involved in viral replication. This effect may involve modulation of key viral proteins, such as glycoprotein, gB (ORF 8), tegument protein (ORF 45), and polymerase processivity factor, PF–8 (ORF 59) Immunofluorescence assays (IFA) time course experiments at 24hr,48hr, and 72hrs following lytic reactivation tracked KSHV protein movement/localization within cells during infection both with and without exposure to ethanol. The results from our study demonstrate that ethanol exposure contributes to greater production of lytic proteins and quicker maturation of viral protein expression throughout a time-course manner of reactivation. Previous studies in our lab have utilized Western blot techniques and quantitative PCR to confirm an increase in lytic protein and lytic transcripts respectively. Using this data we aim to unravel the molecular mechanisms underlying viral pathogenesis and disease progression. Future direction for this project is to examine if exposure to an environmental stressor, such as ethanol, increases the total number of viruses produced. Further research may potentially indicate that alcohol is risk factor for human herpesvirus infections.

ABSTRACT NO. 19A

OPTIMIZING STACKING OF VAN DER WAALS HETEROSTRUCTURES

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Van der Waals heterostructures are devices cosisting of stacked 2D crystals held together by Van der Waals forces. The combination of these atomically thin materials allows for the creation of new properties that do not occur naturally, allowing for research into quantum effects and applications in electronic devices and sensors. However, unreliability in the fabrication process of Van der Waals heterostructures induces significant inefficiencies in the research process. This presentation examines a current fabrication procedure, demonstrates modifications to the procedure that seek to increase fabrication reliability, and explores potential mechanisms from which such improvements may result. Various procedures for component exfoliation are compared and significant differences in the resulting component size, quality, and yield are observed. Additionally, different designs for the stacking apparatus are presented, demonstrating tradeoffs between reusability, reliability, and precision. Furthermore, effects of various stacking parameters—such as temperature and speed—on the stacking process are determined to perform optimization of parameter values.

ABSTRACT NO. 19B

TRANSITION METAL CARBIDES: FROM MULTI-RESPONSIVE ACTUATION TO CHEMICAL VAPOR DEPOSITION AUTOMATION

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The combination of transition metal carbides (TMC), also known as MXenes, with cellulose composites has shown to be advantageous in soft robotics. Soft robotics has the potential to transform applications in minimally invasive surgeries, environmental monitoring, and human-robot interaction. The TMC-cellulose robotic actuators exhibit improved characteristics and capabilities compared to their non-2D material counterparts. This research focuses on continuously enhancing the properties of the TMC actuators by modifying their surface terminations, specifically in response to near-infrared (NIR) light and electrical stimuli. The actuators demonstrate fast actuation response, high robustness, strength, and energy efficiency. To achieve better results with higher-quality TMC and higher yields, we investigated chemical vapor deposition (CVD) as a growth technique. Our preliminary results demonstrate the successful growth of molybdenum disulfide (MoS2), a crucial step in optimizing TMC production. We developed an automated CVD system that remotely controls the fabrication processes for more precise results. By utilizing this autonomous system, we aim to enhance the material properties, leading to more efficient and reliable soft robotics.

ABSTRACT NO. 20A

PAYING ATTENTION: THE EFFECT OF DISTRACTIONS ON ATTENTIONAL STATES IN AUGMENTED REALITY

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Augmented Reality (AR) overlays digital information, such as images and videos, onto the real-world environment. With its applications increasingly prevalent in educational, professional, and entertainment contexts, evaluating Quality of Experience (QoE) within these virtual environments is crucial. While most AR content is intended to enhance user experience, certain types of virtual stimuli may impair perception. As such, this research project seeks to better assess how AR applications affect users' QoE, specifically by investigating the impact of distractors on user attention within the augmented scene.

This project centers around the development of a multi-part AR-guided Sudoku app, which employs a variety of theoretically-grounded distractions to gauge their effects on task performance. Participants were recruited to engage with the app, solving printed Sudoku puzzles with overlaid AR hints while maintaining focus amidst visual and auditory distractions. Data collected included self-reported task load (using the NASA Task Load Index), task completion times, error rates, and eye gaze metrics to analyze fixation patterns. Preliminary findings suggest that AR environments with dynamic and contextually relevant distractors significantly challenge participants' ability to maintain attention, compared to static or irrelevant distractions.

This research informs the field of AR development by highlighting the effects of

human attentional demands and the need to consider potential for distraction. The outcomes have implications for the design of AR systems in education, training, and other fields where attention is critical.

ABSTRACT NO. 20B

PRINTED ELECTRONICS TECHNOLOGY FOR INFRARED-POWERED MICROBOTICS

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Microrobotics have been investigated for environmental, biomedical, and imaging applications, making use of materials that respond to external stimuli to perform precise functions. Previous work has studied self-folding polymers, for which the 3D structures created were utilized to package and transport materials for drug delivery applications. This work investigates aerosol jet printing capabilities with MXene material inks for the formation of a thin film that will respond to infrared light, folding the substrate into 3D shapes. Previous studies have shown that MXene films used as electrodes in supercapacitors can withstand mechanical manipulation such as twisting and folding. Flexible MXene films can be prepared through vacuum filtration, printing, coating, and other methods. The advantages of printed electronics technologies for the formation of the MXene films include design versatility through computer-aided design, quick fabrication process, and low cost compared to conventional microscale electronic fabrication techniques. In this work, a pure aqueous MXene ink and a MXene ink mixed with nanocellulose (CNF) at 3% were evaluated after printing on a hydrophilic polycarbonate membrane. This flexible substrate bends with the MXene film as it responds to light stimuli. Print process parameters including atomizer flow, sheath flow, and print speed were optimized to maximize the bending angle when exposed to infrared light. The optimization reduced the bending angle 3-5% by increasing area coverage (ratio of MXene film area to total substrate area) from 9% to 23% and reduced the bending angle by 11-16% by decreasing the print speed from 3 mm/s to 0.5 mm/s. Future work with printed light-responsive MXene films can incorporate additive manufacturing techniques to fabricate self-actuating devices for more complex microrobotics.

ABSTRACT NO. 21A

CELL BARCODING AND PANEL DEVELOPMENT FOR MULTIPLEXED CD8+ T CELL PHENOTYPING

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CD8+ cytotoxic T cells have immense therapeutic potential due to their ability to target and kill infected or cancerous cells, and many novel cancer immunotherapies focus on the engineering of these cells toward specified targets. However, the dynamism of these cells and their regulatory networks in vivo gives rise to significant heterogeneity in both cell subtype and anti-tumor efficacy among activated T cell populations. This project aims to use multiplexed T cell stimulation conditions alongside novel spatial-omics tools to elucidate potential design targets for more precise cellular immunotherapy. Differential activation of CD8+ T cells using artificial antigen-presenting cells (aAPCs) conjugated to an array of co-stimulatory signals results in subpopulations with distinct phenotypic, metabolic, and epigenetic markers. With CODEX multiplexed imaging, over 50 of these markers can be probed in parallel. Early stages of this project have included development and validation of a multicycle marker panel that

will capture the broad heterogeneity of the CD8+ T cell subpopulations, alongside investigation of cell barcoding strategies that allow for pooled readouts of the multiplexed stimulation conditions. Preliminary results suggest success with CD45/CD90 paired-oligonucleotide barcoding of distinct cell subpopulations.

ABSTRACT NO. 21B

USING IMPORTANCE SAMPLING TO MODEL THE PERFORMANCE OF QUANTUM ERROR CORRECTION CODES

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Quantum computing algorithms promise to revolutionize many fields including chemistry, physics, biology, and finance by leveraging quantum mechanics to run calculations and simulations which are far too complex for classical computers. However, due to noise within modern quantum computers destroying information, many potential applications cannot be realized. Quantum Error Correction (QEC) addresses this problem by encoding quantum information in QEC codes, which allows the original information to be retrieved via decoding in the presence of noise. The likelihood of the decoding successfully retrieving the original information is dependent on both the intensity of the noise and the properties of the specific QEC code. There are many families of QEC codes and simulations are crucial for comparing their performance. Monte Carlo algorithms are a common approach for simulation and the standard method for studying QEC randomly samples the noise on each qubit. This method requires very large sample sizes to simulate very rare events such as the likelihood of decoding failure in a low noise environment. Here we show the use of a variant Monte Carlo algorithm called importance sampling to model the performance of rotated surface codes at varying noise levels. We find that, compared to the standard Monte Carlo method, importance sampling is able to provide a lower margin of error measurement of the performance of these codes for low noise levels with significantly fewer samples. This decrease in the number of samples results in a decrease in the time and compute resources required to perform accurate simulations. By extending these techniques to other QEC codes, we expect importance sampling to become an important tool in analysing the performance of a wide range of codes.

ABSTRACT NO. 22A

BIOPHYSICAL CHARACTERISTICS AND IMMUNOSTIMULATORY EFFECT OF DNA-NANOPARTICLE INTERACTIONS WITH APPLICATIONS IN AUTOIMMUNE DISEASE

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Autoimmune diseases are complex conditions in which the host immune system attacks healthy cells and tissues. Due to the diverse manifestations and limited understanding of autoimmune disease pathogenesis, developing treatments to combat illness remains a challenge. Systemic lupus erythematosus is an autoimmune condition involving cell-free DNA as a key antigen. Clinical studies have shown that cell-free DNA binds to the surface of biological microparticles. However, the heterogeneity of DNA-bound microparticles makes them challenging to characterize and study. This work employs a synthetic particle system offering increased tunability and control to understand the

immunostimulatory effects of DNA-particle complexes. We stimulated human macrophage cells with the model particle system and analyzed RNA sequencing data to identify biochemical pathways involved in DNA-particle-macrophage interactions. DNA bound to particles resulted in significant upregulation of cytokine activity and interferon signaling compared to free DNA. We characterized DNA adsorption to polystyrene particles (50 nm, 200 nm, 1 µm, 2 µm) incubated with varied amounts of DNA relative to particle surface area. Smaller particle sizes (50 nm, 200 nm) exhibited higher DNA adsorption with a larger percent degradation of excess DNA following DNase exposure. We then sought to determine the structural characteristics of DNA adsorption to particles using transmission electron microscopy and small-angle X-ray scattering. We observed that DNA forms a corona on the particle surface with greater aggregation for smaller particle sizes. These results supply mechanistic insight for DNA-nanoparticle interactions that could translate to future investigations of therapeutic opportunities in autoimmune diseases.

ABSTRACT NO. 22B

PERFORMANCE AND RELIABILITY OF INDIUM TIN OXIDE FIELD EFFECTIVE TRANSISTORS

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This work focused on the performance and reliability of dual gate Indium Tin Oxide (ITO) field effective transistors. Samples of transistors with an ITO channel, and top/bottom gates were fabricated with varying channel lengths. Different samples also had varying thicknesses of the top gate dielectric. The performance of the devices, and device to device variability was investigated by performing IV characteristic measurements. The reliability of these devices was investigated through observing Positive and Negative Bias Temperature Instability (PBTI/NBTI) effects on these devices. Using common stress measurement techniques for amorphous oxide channel transistors, such as the Measurement Stress Measurement (MSM) method and the Fast ID method, PBTI and NBTI were measured. Also, using a newly proposed Modified Gate Pulse Voltage (GPV) method for amorphous oxide channel transistors, PBTI and NBTI were measured. These methods showed that under the effect of PBTI and NBTI, a threshold shift occurred for the transistor under operational stress. The results of the modified GPV method were also compared to that of the other methods. From our results it was shown that the MSM method and Fast ID method provided under reported values of threshold shift for the devices under stress, while our modified GPV method reported a greater threshold shift. The findings of these experiments were collected and organized into a paper which was submitted for publication in the IEEE International Electron Devices Meeting (IEDM) conference.

ABSTRACT NO. 23A

ASSESSING REGIONAL LUNG VENTILATION DISTRIBUTION IN INDIVIDUALS WITH NORMAL LUNG FUNCTION COMPARED TO ILD WITH 129XE MRI

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Pulmonary ventilation is not homogeneous, even in healthy individuals, due to gravitational and structural factors. Few clinical tools can quantify ventilation inhomogeneity with high spatial resolution non-invasively. Hyperpolarized 129Xe MRI provides

high-resolution ventilation images and has shown differences between young and old healthy subjects. However, most work has involved 2D imaging and bias field correction approaches that remove true physiological gradients.Ventilation heterogeneity is likely influenced by age-related changes in chest wall compliance, small airway dysfunction, and enlargement of alveolar spaces without tissue destruction.

We used randomized 3D radial MRI with physics-based bias field correction (called RF-Depolarization) to preserve physiological gradients. This quantified the ventilation distribution in healthy young and older subjects with normal lung function in a supine position. Ventilation gradients were compared in the apical-basal and anterior-posterior directions.

Participants include 9 older (age: 62 ± 6.9 years) and 10 younger (age: 23 ± 2.7 years) healthy individuals with normal spirometry and 30 older individuals with IPF.

Hyperpolarized 129Xe was inhaled from dosage bag, and MRI ventilation images were acquired during a 10-second breath hold. Images were bias-field corrected by RF depolarization mapping. Anterior-posterior and apical-basal ventilation gradients were calculated as percentage change in relative signal intensity.

Older subjects exhibited a significantly greater anterior-posterior ventilation gradient than younger subjects due to decreased ventilation in the anterior regions. The apical-basal ventilation gradient was larger and had greater variability in both young and older subjects. Ventilation defects were larger in older healthy subjects but did not reach statistical significance. Significant differences ($p<0.05$) were found for average regional relative intensity in the basal and anterior lung regions between young and older healthy subjects. Significant differences ($p<0.05$) also found for percent regional ventilation in the anterior region between young and older healthy subjects.

Decreased ventilation in the anterior regions of older subjects may be due to reduced chest wall compliance, small airway dysfunction, and enlargement of alveolar spaces. Ventilation gradients may be useful for diagnosing lung diseases and monitoring therapeutic effects.

ABSTRACT NO. 23B

INTRAOPERATIVE APPLICATION OF THETA BURST DBS IN PARTICIPANTS WITH ESSENTIAL TREMOR AND PARKINSON'S DISEASE

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Deep brain stimulation (DBS) is the primary surgical intervention to manage motor symptoms of Parkinson's disease (PD) and essential tremor (ET). To reduce tremor, electrical pulses are delivered to the subthalamic nucleus (STN) or ventral intermediate nucleus of the thalamus (VIM) with a pulse repetition frequency of at least 100 Hz. However continuous high-frequency DBS can cause side effects and deplete the implanted battery. Conversely, DBS with a frequency in the theta band (4 – 8 Hz) has proven ineffective. Bursts of high-frequency pulses gated by a slower theta frequency (theta burst) may manage symptoms with fewer side effects and reduced battery drain. When applied as transcranial magnetic stimulation or STN DBS, this pattern was shown to improve motor symptoms in patients with PD. To our knowledge, subcortical theta burst stimulation has not been evaluated in patients with ET. Therefore, we recorded local field potentials and hand acceleration from 12 participants (8 with ET and VIM DBS, 4 with PD and STN DBS) during DBS surgery. All participants provided written informed consent. Four

stimulation patterns were tested; continuous high frequency (> 100 Hz), theta burst, continuous 4.5 Hz, and DBS off. We analyzed tremor power (2 – 20 Hz) to determine differences in motor symptom between conditions. With 12 participants, there were no significant differences in tremor power between stimulation patterns (repeated measures ANOVA with participant and stimulation pattern as factors). Indeed, even high-frequency DBS, which is known to be therapeutic, did not reduce tremor compared to DBS off ($p = 0.0751$). A greater sample size is required before drawing conclusions from this study.

ABSTRACT NO. 24A

ISOLATING NITRITE-OXIDIZING BACTERIA TARGETING PHAGES FROM ACTIVATED SLUDGE

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A major pollutant wastewater treatment plants (WWTPs) are tasked with removing is fixed nitrogen. Nitrogen in the environment can expedite eutrophication in natural water bodies, and if found in drinking water can cause “blue baby syndrome.” Nitrogen removal occurs through two major biochemical processes, nitrification, and denitrification, facilitated by bacteria (ammonia-oxidizing, nitrite-oxidizing, and denitrifying), oxygen, and electron donors. In traditional WWTPs nitrification and denitrification incur heavy energy and monetary costs, due to the need for aeration and carbon that acts as an electron donor. Studies have shown that nitrite-oxidizing bacteria (NOB) suppression can reduce oxygen and carbon demands by about 25% and 40%.[1] However, there is still a gap in knowledge about biological techniques and tools that can facilitate stable NOB inhibition. Researchers have found that bacteriophages/phages (viruses that target bacteria) can be used to control microbial communities. We hypothesize that NOB-targeting phages can be isolated from activated sludge samples. A protocol was developed using common methods for isolating phages from complex matrices and tested on activated sludge samples. Multiple spot and plaque assays were performed to test for NOB-targeting phages, conducted with nitrite-oxidizing media/agar, LB media/agar, and two incubation temperatures of 25°C and 37°C. The plaque assays and spot tests did not indicate a positive presence of NOB-targeting phages, and when tested on heterotrophic bacteria no plaques formed as well. Further troubleshooting and testing of the protocol may be necessary to isolate phage from activated sludge. Particularly, focusing on the impact of temperature, incubation time, light, and nutrients on bacteria growth and plaque formation.

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ABSTRACT NO. 24B

SONIC ATOMIZATION ENHANCED SMALL EXTRACELLULAR VESICLE PURIFICATION

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Small Extracellular Vesicles (sEVs) are small, lipid-enclosed particles released by cells. They are often associated with various diseases, and their identification from biological fluids can be used for clinical detection and monitoring. However, this process poses many challenges including high expense, time-consuming procedures, low yield, and low purity of sEVs. We developed a filter that allows for the inexpensive, high-yield separation of sEVs from biological fluids. The device contains a filter membrane that is located directly above a circular interdigitial transducer (IDT) that is attached to a thin ring of piezoelectric substrate. The IDT produces oscillating acoustic pressure on the membrane, which prevents particles, such as sEVs, from clogging the membrane while also driving fluid through microscopic holes in the IDT. The movement of fluid through the microscopic holes atomizes the fluid on the outside of the device, allowing easy filtration of large volumes of biological fluid. The device's functionality was validated by using Western Blot and Total Protein Analysis (BCA) to determine the amounts of protein removed. For clinical validation, RT-qPCR was used to measure expression levels of microRNAs found inside the exosomes of pre-eclampsia patients that were isolated by the filtration device.

ABSTRACT NO. 25A

EFFECTS OF BACKGROUND PRESSURE DURING RESONANT INFRARED MATRIX-ASSISTED PULSED LASER EVAPORATION (RIR-MAPLE) DEPOSITION OF THIN FILM HYBRID PEROVSKITES

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Hybrid organic-inorganic perovskites (HOIPs) are a class of materials with highly tunable electrical properties that are excellent candidates for novel optoelectronic technologies such as photovoltaics and light emitting diodes. Resonant Infrared Matrix-Assisted Pulsed Laser Evaporation (RIR-MAPLE) is a physical vapor deposition technique that reduces the limitations of traditional solution processing methods. During RIR-MAPLE deposition, the frozen precursor solution is placed in the vacuum chamber, where the hydroxyl bonds of the matrix solvent resonantly absorb energy from the laser, producing a vapor plume that propels the desired precursor materials up to the substrate. However, previous studies of RIR-MAPLE deposition for HOIPs have been conducted under high-vacuum conditions, which are a substantial obstacle to the use of RIR-MAPLE for HOIP manufacturing on an industrial scale. 2D samples of phenylethylene lead iodide, (PEA)2PbI4, and 3D samples of methyl ammonium lead iodide, MAPbI3, were grown at pressures from 10-5 mTorr to 500 mTorr and were analyzed using atomic force microscopy and optical spectroscopy methods. Raman spectroscopy indicated a correlation between background pressure (BGP) during deposition and photoluminescence peaks, where films grown at higher pressures had narrower, blue-shifted

peaks. This suggests that films grown at higher BGP absorb and emit higher-energy wavelengths, and that these higher BGP films have fewer defects that cause PL peak widening. In addition, atomic force microscopy showed that while an increase of BGP from 10-5 mTorr to 100 mTorr was associated with an increase in film roughness of approximately 60%, further increase of BGP up to 500 mTorr did not significantly affect film roughness. These results show that perovskite films of comparable quality can be produced under higher BGP, demonstrating the continuing potential of RIR-MAPLE as a large-scale HOIP deposition technique.

ABSTRACT NO. 25B

Sustainable Eradication of Plant-Parasitic Nematodes Using Energy-Efficient Electromagnetic Technology.

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This research project focuses on developing a sustainable and novel approach to eradicate plant-parasitic nematodes (PPN) using electromagnetic technology. Our method leverages electromagnetic pulses to inhibit weed growth and target the eggs and infectious juveniles of PPN, aiming to offer an energy-efficient alternative to traditional chemical and mechanical control methods. In collaboration with North Carolina State University (NCSU), we are advancing the next-generation prototype of this system, designed for practical application in sweet potato and tomato fields. The primary innovation, microwave heating, consists of an automated cart, reminiscent of a Roomba, which integrates optimally designed lensing antennas and a solid-state source. The microwave heating approach involves heating the soil to a temperature that effectively eliminates nematodes and has shown promise in preliminary trials on sweet potato plots. However, it requires significant energy input. To address the energy demands, we have embarked on an alternative method using electromagnetic pulses. This technique requires less energy compared to microwave heating and offers a targeted approach to disrupt the biological functioning of the PPNs, effectively eradicating them. The development and optimization of this method involved comprehensive Multiphysics modeling to ensure energy efficiency. This project, therefore, represents a significant step toward sustainable agricultural practices by providing a viable, energy-efficient alternative for weed and nematode management. Future work will focus on further refining the technology and scaling up field applications to broader agricultural contexts.

ABSTRACT NO. 26A

EVALUATING THE PERSISTANCE OF OVERLOOKED PATHOGENS IN WATER TREATMENT SETTINGS

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Surveillance efforts frequently detect elevated nucleic acid levels of respiratory viruses, including SARS-CoV-2, influenza virus, and rhinovirus, in domestic wastewater. However, this detection fails to provide information regarding viral infectivity. As water scarcity worsens in many parts of the world due to climate change and population growth, communities use wastewater as the source water for drinking through a process termed water reuse. Historically, when wastewater is treated for reuse, enteric viruses are the major concern; respiratory viruses are not usually

considered a microbial risk in this setting. However, the presence of infectious respiratory viruses in wastewater is important to consider in planned water reuse settings, because viruses can be aerosolized during showering, drinking, or recreational activities. There is currently minimal research investigating the infectivity of nonenveloped respiratory viruses, such as rhinovirus and adenovirus, in wastewater matrices. We hypothesize nonenveloped respiratory viruses can be released as infectious viruses in human waste and persist in wastewater for extended periods. To investigate this, influent wastewater was collected and concentrated for detection of infectious respiratory viruses. Concentration via two methods, namely ultrafiltration and ultracentrifugation, was conducted using wastewater spiked with adenovirus to assess the most effective method for recovering infectious viruses. Adenovirus quantification in pre- and post-concentrated samples revealed that ultracentrifugation concentrated infectious virus by 6.318-log10, while ultrafiltration was less effective, only 5.262-log10. An integrated cell culture assay was then performed with wastewater concentrated using the optimal method, ultracentrifugation, by applying the samples to A549 cells and harvesting wells for extraction and qPCR after incubation for up to six days to detect infectious adenovirus growth. These results will allow us to establish whether infectious nonenveloped respiratory viruses are indeed found in wastewater. This work has implications for informing overlooked risks of virus exposure in reuse settings.

ABSTRACT NO. 26B

IMPACT OF AR CONTENT OBSTRUCTIONS ON OBJECT DETECTION PERFORMANCE

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Augmented reality uses technology to create an interactive experience by implementing computer generated content into real-world environments. The innovation of AR technology has conjoined many technological advancements such as Artificial Intelligence (AI) and Machine Learning. However, the rapid rise of AR prompts serious security concerns, in that hackers could potentially adjust the properties of virtual content to obstruct a users' view of the real world, compromising task performance and even safety. In the case of an attack like this, we want to automatically detect any signs of foreign obstructions. Specifically we want to use object detection models to determine whether important objects are obstructed. This begs the question, how is the performance of an object detection model affected when an image has been manipulated?

My project focuses on the concept of object detection, which is a computer vision technique that uses machine learning models to identify key objects in images and videos. I performed experiments using two different models, a traditional model (SSD MobileNet) and a state-of-the-art model (Grounding DINO). Using these object detection models, I studied how simulated obstructions on AR camera images affected their confidence scores, which represents the model's certainty in identifying objects. The two main experiments focused on the placement and color of the obstructions. By generating a heat map of the average confidence scores, I visually depicted the areas where obstructions on the image predominantly

influenced the score, therefore exposing the most critical part of the image that helps the model identify what the object is. With this data, we are able to help further detect when an image is being obstructed and how we can identify potential cyber attacks for AR systems.

ABSTRACT NO. 27A

CONTROLLABLE CARBON NANOTUBE DENSITY FOR THIN FILM TRANSISTORS VIA LATHE-BASED AEROSOL JET PRINTING

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Printed electronics is a growing field that uses low-cost environmentally friendly manufacturing options as opposed to traditional vacuum processing methods. Additive manufacturing methods such as screen printing, inkjet printing, aerosol jet printing (AJP) can be used to fabricate printed electronic devices and sensors. These electronics can be utilized in applications like wearable electronics, in which flexible on-body sensing capabilities are valuable. AJP is an emerging technique for printed electronics that involves using a wide range of nanomaterial-based electronic inks, which are aerosolized into microdroplets and jetted by nitrogen gas flows onto a substrate. By spraying aerosolized material, AJP can form thin films on a variety of substrates with resolutions down to the micron scale. Despite these benefits, AJP still possesses challenges in scalable manufacturing of electronics due to issues in achieving consistent device performance. Device-to-device variation can occur during AJP due to ink processing variability, substrate surface morphology, and fluctuations in deposition volume. Our study explores the benefits of using a rotating lathe tool for obtaining more consistent thin film formation from AJP regardless of erroneous conditions, thus decreasing device-to-device variation while achieving desired electrical performance. The lathe tool provides high rpm spinning of target substrates below the AJP nozzle, which results in printed devices with more consistently repeatable electrical performance because film uniformity and thickness is enhanced. By varying the number of print passes and linear speed we show control over the density of printed carbon nanotubes (CNTs), which we confirm via scanning electron microscopy (SEM). Then, we present fully-printed thin film transistors (TFTs) utilizing CNTs for a semiconducting channel, silver nanowires (AgNWs) for contacts, and ion gel for a gate insulator. Through our lathe-based AJP method, we demonstrate control of printed CNT density, resulting in CNT-TFTs with reduced device-to-device variation compared to regular printed devices.

ABSTRACT NO. 27B

METAL/INSULATOR/GRAPHENE-BASED INTERFACIAL ANALOG MEMRISTORS AND 1R CROSSBAR ARRAY FOR IN-MEMORY COMPUTING

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As complementary metal-oxide semiconductor (CMOS) technology reaches fundamental scaling limits and the performance gap between memory and processing increases, i.e., a memory wall, a novel architecture is evidently necessary to overcome these limitations inherent in the current design. Recent breakthroughs in deep learning have garnered attention in search of a computing paradigm that combines analog in-memory computing (IMC) as artificial intelligence tasks performed on digital computers are energy exhausting due to von

Neumann architecture. IMC hardware based on memristor-based crossbar arrays is a potential candidate to solve this energy and data latency. Current filamentary memristors suffer from high noise, poor cycle-to-cycle variation, and non-scalable energy consumption. To improve on the current design, we have fabricated an interfacial metal-insulator-graphene (MIG) memristor. We optimized the MIG structure by engineering the stack of insulators, including the types of insulators and their sequences. We finalize the insulator stack to be TiO_x/Al_2 O_3/ TiO_2, in which the TiO_x serves as the reservoir of oxygen vacancies, Al_2 O_3 serves as the tunnel barrier, while TiO_2 serves as the layer to prevent the memristor from forming. The optimized device shows nonlinear IV characteristics, which enables its application in 1-resistor (1R) crossbar array. The utilization of graphene as the top electrode enables ultra-low write energy consumption at around 10 pJ level. The device also shows an endurance of 10^3 cycles and a retention of 10^5 s at room temperature, which highlights its reliability. To validate its applicability in 1R crossbar array, 2x2 1R crossbar arrays were fabricated and measured to ensure independent programmability.

ABSTRACT NO. 28A

AUTONOMOUS ORTHOPEDIC IMPLANT DESIGN: A CT DERIVED SOLUTION

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The idea of creating a perfect orthopedic implant solution can be viewed as inherently flawed as no patient is identical, neither are their circumstances. We worked to narrow the gap between native patient anatomy and implant design focusing on the Total Knee Arthroplasty (TKA) system. Creating an autonomous system that produces a patient specific tibial tray component of the TKA system, our project aims to bridge the gap between personalized care, knee arthroplasty, and optimal surgical outcomes. Emphasis was placed on the engineering principles that these devices are dependent on to succeed. Beginning with a CT scan, collecting Hounsfield Units from the cancellous bone present in the proximal tibia. From here, we can derive the elastic modulus of the native bone in the axial plane, through bone density relationships present in existing scientific literature. Once the native modulus is obtained, our system, using machine learning, can output the necessary cell wall thickness and porosity of the gyroid lattice structure present in the stem of our tibial tray. This inherently can provide us with a graded structure, with elastic modulus idealized between implant and native bone. Our system resulted in a CT derived, elastic modulus dependent, autonomous solution for implant design containing a gyroid lattice-based structure in the stem of the tibial tray. This solution was created with the intent of providing an idealized component for osseointegration, minimizing the risk of tibial component subsidence, component loosening, and stress shielding, which are common complications associated with the TKA system. Our solution depends on the integration of multiple software applications, collaborating and providing accurate data to create a product idealized for a specific patient. Although the principle behind this solution can be applied in theory, several tests would have to be performed before this product could be introduced in the TKA space.

ABSTRACT NO. 28B

APPLICATION OF INJECTABLE SCAFFOLDS FOR PERIPHERAL NERVE REPAIR

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Peripheral nerve injuries (PNIs) affect millions of individuals, leading to sensorimotor dysfunction and lifelong disability. The gold standard for PNI treatment, tension-free primary repair, involves direct suturing of divided nerves, which remains invasive and possesses limited regenerative capacity. Consequently, innovative, therapeutic options are urgently needed.

Partially ordered polypeptides (POPs) are recombinant proteins that combine intrinsically disordered proteins such as elastin-like polypeptides (ELPs) with ordered domains (α-helices). The molecular tunability of these sequences allows control over stimuli-responsiveness and protein interactions. POPs mimic elastin's reversible, thermoresponsive lower critical solution temperature (LCST) behavior, functioning as an injectable liquid at lower temperatures and transitioning to porous viscoelastic networks past a transition temperature, holding potential for tissue healing. We can fine-tune a scaffold through sequence-specific modification of these recombinants, enabling controlled delivery of biologically active proteins such as growth factors.

Vascular endothelial growth factor (VEGF) promotes angiogenesis, a crucial process in the regeneration of peripheral nerves, by encouraging formation of new blood vessels to support axonal growth. We hypothesize that when fused to POPs and a matrix metalloproteinase (MMP) site to form a scaffold, VEGF-MMP-POPs can encourage neovascularization within PNIs, promoting nutrient supply.

We demonstrate that VEGF-MMP-POPs can be expressed and purified by leveraging its phase transition behavior through an inverse transition cycling (ITC) protocol. Characterization of the protein shows that it retains LCST behavior and can form a scaffold, highlighting its potential for injectable, therapeutic delivery for nerve repair. In an in vitro assay, the scaffold promotes tube formation of capillary-like networks in endothelial cells, indicating successful relay of angiogenic signals.

Future work is required in optimizing the purification protocol to achieve greater yield and purity, as well as further characterizing the biological activity of the scaffold. Experimentation can advance to in vivo models to more accurately assess its potential in peripheral nerve repair.

ABSTRACT NO. 29A

THE USE OF CARTILAGE THICKNESS MODELS TO ANALYZE KNEE MECHANICAL PROPERTIES

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Introduction: In many imaging-based orthopaedic laboratories, attempts have been made to analyze joint mechanical properties in vivo. Computed topography (CT) has become increasingly popular due to well-defined cortical bone that allows simple segmentation and manipulation. However, CT is incapable of viewing soft tissue structures, such as the anterior cruciate ligament or cartilage. Therefore, magnetic resonance (MR) imaging is still considered the gold standard image modality when assessing soft tissue structures. The primary objective of this project was to understand the innerworkings of a knee cartilage

thickness model, as previously developed by Dr. DeFrate. From this, a cohort of bed rest participants may be analyzed to understand the impact of long-term bed rest on knee health.

Methods: A thorough literature search was performed to understand the various methodologies to measure cartilage thickness. Using Rhinoceros3D, sagittal MR scans were manually segmented to isolate the femur, tibia, tibial and femoral cartilage. Scans were verified by an expert in the field. Next, the segmented MR scan was converted to a three-dimensional model and registered to scans from the same subject. Methodology beyond this point is still in consideration.

Results: From a literature search, it was concluded that cartilage thickness is best measured by sampling distinct regions of the tibia and femoral cartilage with small circles. In an effort to prevent edge effects and variability between people, this semi-automated method seemed the most robust and comprehensive for measuring knee cartilage thickness in vivo. A total of 10 bed rest scans were manually segmented and will be used in future studies.

Discussion: Significant time was spent learning the innerworkings of a new imaging analysis mechanism. Future directions include utilizing this mechanism to study bed rest patients. However, with a short amount of time, development of the algorithm was the only completed task.

ABSTRACT NO. 29B

EXAMINING THE IMPACT OF PROTEIN MOTION ON THE ELECTRON BIFURCATION SYTEM HYDABC

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Bifurcation is a ubiquitous mechanism throughout microbial life. Electron Bifurcation involves the coupling of an endergonic reduction pathway to an exergonic pathway. HydABC is a protein with the ability to bifurcate; it oxidizes hydrogen gas, using the products to reduce CO2 to acetate. The desired product of this enzyme is reduced low potential ferredoxin. This endergonic reaction is coupled to the reduction of the high potential NADP. Previous experimental work indicated that protein motion is necessary to electron bifurcation in HydABC. We simulate the enzyme in python using a modified master equation approach incorporating protein motion. We measured electron transfer efficiency by determining how many electrons are transferred from initial cofactors 2Fe-2S (C1 and B2) to the ferredoxin sink in 2 cycles of the protein motion, where the maximum value is 2 electrons. We will vary model parameters related to the cofactor's potential energy landscape and the time scale of the protein motion and analyze the impact of these changes on the electron transfer efficiency. We find that electron transfer to ferredoxin is maximized when the C1 midpoint potential is higher than B2 enabling reduction of C1 prior to the second conformational change. We also find that the electron transfer efficiency increases with slower protein motion, although the real system is constrained by the need to move electrons to the ferredoxin quickly for function. We compare our results with the real system for insight into the role of protein motion.

ABSTRACT NO. 30A

MITIGATING REVERBERATION IN COCHLEAR IMPLANT STIMULUS USING PHONEME-BASED TRANSFORMATIONS AND TIME-FREQUENCY MASK ESTIMATION

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Cochlear implants (CIs) can restore hearing sensation to Deaf/Hard-of-Hearing people. However, CI users struggle to interpret speech in reverberant environments due to signal distortion introduced under those conditions. Time-Frequency (TF) masking is a method used to mitigate these distortions by multiplying a matrix of gain values called a mask with the time-frequency decomposed signal. Chu et al. [Proceedings of Meetings on Acoustics, 50, 1 (2022)] showed that a mask estimation algorithm using multiple phoneme-dependent models generally performs better than a mask estimation algorithm using a single phoneme-independent model in increasing intelligibility of speech under reverberant conditions. This current work aims to extend those results by reducing the number of models needed to generate phoneme-dependent TF masks. We propose an algorithm that generates phoneme-dependent transformation matrixes for input signal features, then generates TF masks with a single mask estimation model that uses the images of the features under phoneme-dependent transformations as its input. We evaluate the performance of this algorithm in the ideal case where the phoneme is known using objective speech intelligibility measures.

ABSTRACT NO. 30B

USING LARGE LANGUAGE MODELS (LLMS) AND MACHINE LEARNING TO CHARACTERIZE CHEMICAL VAPOR DEPOSITION (CVD) SYNTHESIZED MOS2

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Two-dimensional (2D) materials, such as transition metal dichalcogenides (TMDCs), have attracted significant attention due to their unique atomic thickness. These materials exhibit a range of characteristics, including high carrier mobilities, mechanical flexibility, high optical absorption, and photothermal effects. Consequently, 2D materials hold promise for a wide array of applications, including electronics, soft robotics, catalysis, and biosensing. Synthesis and analysis are pivotal areas of research for 2D materials. In our lab, we synthesized monolayer molybdenum disulfide (MoS2) flakes using chemical vapor deposition (CVD). By optimizing the growth parameters, we achieved various sizes and structures of MoS2 flakes, with the largest flake measuring approximately 100 µm. Image processing and identification techniques powered by machine learning were employed to distinguish the domain and layer numbers. To achieve more automation of optical microscopy and accelerate the identification process, I use large language models (LLMs) to assist with unsupervised learning to quickly identify the features of MoS2.

ABSTRACT NO. 31A

AN ASSESSMENT OF REAL-WORLD EVIDENCE ON THE IMPACT OF PHARMACOGENOMIC BIOMARKER CYP2D6: A SYSTEMATIC REVIEW

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Background: The highly polymorphic gene CYP2D6 is involved in 20 – 25% of all drug metabolism and, consequently, is extensively studied in pharmacogenomics (PGx). Despite growing research, PGx remains under-utilized in clinical decision making and workflow. This systematic review explores real-world data/evidence (RWD/E) literature on CYP2D6 and assesses current strengths, challenges, and opportunities for clinical PGx implementation.
Methods: The authors employed PRISMA methodology in this systematic literature review, conducted through two separate search strings in Fall 2023 and Summer 2024. Data analysis consisted of four stages: filtering out duplicate results and broken links, title/abstract screening, full text review, and qualitative analysis. Peer-reviewed articles were included if they utilized data from electronic health records (EHR) or insurance claims, centered on PGx, and contained pertinent CYP2D6 findings.
Findings: Our search identified 218 articles across four databases (Google Scholar, PubMed, Semantic Scholar, and Scopus). After applying our inclusion/exclusion study criteria, 38 articles were included in the final review. Qualitative analysis resulted in eight themes across two domains—CYP2D6-specific and General PGx and RWD/E—covering areas such as PGx methodologies and classifications, patient demographic and sub-group trends, and PGx implementation impacts. Both clinician and patient outcomes were reviewed. CYP2D6 had major implications in analgesia (pain management), psychiatry, and cardiology.
Conclusion: This review raises ethical and policy considerations, including ensuring RWD is representative of diverse patient sub-groups and implementing inclusive research methodologies. Additionally, there is a need for greater pediatric PGx research accounting for that population's unique considerations. Major challenges with implementation of PGx test results and related guidelines into EHRs and clinical decision making were data inoperability, cost barriers, and inadequate clinician familiarity with PGx. However, when PGx was successfully implemented, most clinicians followed PGx-based recommendations. Finally, multi-disciplinary teams are crucial for integrating PGx into clinical workflows to enhance patient care.

ABSTRACT NO. 31B

IDENTIFYING BARRIERS TO CLINICAL TRIAL ACCESS AND PARTICIPATION IN RURAL NORTH CAROLINA

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Clinical trial participation among cancer patients has remained relatively low with less than 10% of patients participating. Furthermore, participation is even lower among underrepresented populations and residents in rural communities who face a greater burden with cancer morbidity and mortality. Despite attempted interventions to increase participation, there has been little to no progress in increasing clinical trial access. We

hypothesized that a rural community with significant percentages of minorities will face notable barriers to clinical trial access that result in significantly lower participation in comparison to other populations. One such community is exemplified by Robeson County in Southeastern North Carolina. Robeson stands as the county in North Carolina with the worst health outcomes with increased rates of cancer mortality and chronic disease. In addition to this, Robeson County is located over 100 miles away from the nearest National Cancer Institute-Designated Cancer Center, focusing most of their cancer care within the community health environment. We conducted a pilot qualitative study to determine barriers to clinical trial access. By interviewing providers at community hospitals in Robeson County, we determined several barriers. Health care providers identified lack of awareness and infrastructure, such as space and administrative support, and clinical trials expertise as barriers to clinical trial access in their communities. With the identification of these barriers, we hope to bring in stakeholders to mediate the barriers to access, and to create an academic/community partnership that will allow patients to have access to lifesaving care and enable clinical investigators to have representative data of the population.

ABSTRACT NO. 32A

Standardizing Local CAR-T Manufacturing and AI-Driven Personalized Diagnosis to Enhance Therapy Access

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Chimeric Antigen Receptor T-cell (CAR-T) therapy has emerged as a groundbreaking treatment for certain cancer types, offering hope to patients who have exhausted traditional options. However, the complex manufacturing process and high costs associated with centralized production have restricted widespread access to this potentially life-saving therapy. This study aims to address these challenges through two key approaches: standardization of local manufacturing protocols and development of AI-driven personalized diagnosis tools.

To investigate local CAR-T manufacturing standardization, we conducted a comprehensive survey of academic institutions worldwide, covering key aspects such as cell sourcing, genetic modification methods, culture conditions, quality control measures, and regulatory compliance. Additionally, semi-structured interviews were performed with key personnel from selected institutions to gain deeper insights into specific manufacturing challenges and innovative solutions.

Preliminary results indicate limited standardization efforts, with most protocols being institution-specific. Commercial partnerships face challenges in collaboration and differing focuses. Patient access is hampered by cost, limited availability, and the need for

specialized infrastructure. Regulatory aspects, including FDA regulations and GMP facilities, remain significant considerations. Cost factors include high development and clinical trial expenses, although local manufacturing shows potential for cost-effectiveness.

The second arm of our research focuses on developing an artificial intelligence model to enhance CAR-T diagnosis, potentially improving treatment efficacy and patient outcomes. Utilizing data from Duke's Functional Cellular Analysis Platform (FCAP), we aim to train an AI-driven diagnostic tool. This probabilistic graphical model will incorporate various clinical and biological parameters.

This research has significant implications for expanding access to CAR-T therapies, particularly in regions distant from centralized production facilities. By standardizing local manufacturing protocols and leveraging AI for personalized diagnosis, we anticipate improving the efficiency, accessibility, and efficacy of CAR-T treatments. Future directions include refining the AI model and conducting external validation studies to ensure its robustness and clinical applicability.

ABSTRACT NO. 32B

A NATIONAL SURVEY OF TRAUMA-INFORMED CARE IN U.S. ADULT ICUS

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Psychological trauma affects many adults and can be triggered or worsened in healthcare settings, especially in ICUs. Trauma-informed care acknowledges the prevalence and impact of trauma on health and strives to deliver care that promotes healing and avoids re-traumatization. Despite the highly traumatic nature of ICU care, there is a largely untapped opportunity to apply trauma-informed approaches in the ICU. This study aimed to examine the current state of trauma-informed care practices in adult ICUs across the United States, identifying areas for improvement and best practices.

A cross-sectional survey study was conducted using a stratified random sample of 25% of U.S. hospitals with adult ICUs. Stratification was based on hospital type (community, university, federal/VA) and geographic region to ensure national representation. The Trauma-Informed Organizational Assessment (TIOA), adapted for adult ICU settings, was utilized as the survey instrument. ICU nurse managers were recruited as primary respondents to complete the survey for their respective units. Survey responses were analyzed to evaluate the prevalence and types of trauma-informed policies and practices in various hospital settings nationwide, offering a comprehensive overview of trauma-informed care implementation in U.S. adult ICUs.

This study offers the first comprehensive assessment of trauma-informed care practices in U.S. ICUs. The findings will guide future interventions, policy development, and resource allocation to improve trauma-informed care in critical care settings.

ABSTRACT NO. 33A

CLOSING THE GAP ON HEALTH DISPARITIES AND OUTCOMES IN HYPERTENSION: USING QI TO IMPROVE HYPERTENSION MANAGEMENT

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It is estimated that Black Americans are 30 percent more likely than White Americans to have high blood pressure and more likely to die from hypertension-related conditions. Given the high proportion of people identifying as Black with hypertension in Durham County and the evidence that self-monitoring blood pressure helps to lower blood pressure in community-dwelling adults, providing education and resources for Black Durham community members is critical in reducing the racial disparities in hypertension and hypertension-related conditions. Therefore, providing education and resources for Durham community members to record SMBP is critical in achieving this goal of reducing hypertension. Our objective was to address hypertension disparities amongst the population of patients at the Lincoln Community Health Center through "Hypertension Hero" classes that focused on managing hypertension and healthy living habits. We used a pre-post single cohort design to identify minoritized patients with uncontrolled hypertension (systolic > 160 mmHg and/or diastolic > 100 mmHg). Trained Ambassadors conducted telephone outreach to 291 patients to engage them in the program. In-person hypertension education classes provided education and skill-based blood pressure (BP) monitoring. Patient engagement, interest in classes, BP recordings before and after telephone outreach, and in-person class attendance were tracked. Among 291 patients contacted, 149 (51.2%) picked up the call during telephone outreach. Of those reached, 71 (77.2%) expressed interest in attending classes. Significant reductions (in systolic BP (170.47 mmHg to 139.94 mmHg, $p < 0.001$) and diastolic BP (97.15 mmHg to 83.21 mmHg, $p < 0.001$) were observed post-outreach. Out of the 24 patients who attended the in-person hypertension classes, 12 (50%) attended because of the phone call outreach. In the first class, 18 patients (75%) did not own a blood pressure cuff, while 6 patients (25%) owned a cuff.

ABSTRACT NO. 33B

EVALUATING THE INTERACTION OF IMMIGRATION STATUS AND HEALTH CARE PAYMENT MODELS IN MEDICAID: IMPACTS ON HEALTH

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North Carolina's (NC) population has grown 1.6 times the amount it was in 1990. As of 2022, NC's immigrant population alone has increased nearly eightfold. Immigrant and foreign-born populations in NC have historically faced distinct barriers to attaining good health (e.g., language barriers, confusion about coverage eligibility, cultural differences, and fear). With NC Medicaid expansion in 2023 and the transition to Medicaid Managed Care and Value-Based Payment (VBP) models in 2021, NC aims to close coverage gaps and ensure equitable

care. It is necessary to assess how these reforms impact immigrant populations. To achieve equity in health care, all populations, including immigrants, must receive equitable care. NC's evolving health policy landscape presents a unique opportunity to evaluate the intersection of immigration and health care payment models. This study compares NC with California (CA) and Texas (TX) to understand the impacts of coverage and payment models on health care access, utilization, and outcomes for immigrants. In CA, Medicaid coverage has been expanded to all regardless of immigration status, while in TX, coverage is limited to children, pregnant people, and emergencies for undocumented immigrants. This study uses data from qualitative interviews with stakeholders, state and national surveys on population demographics, health coverage, and outcomes, and policy analysis of coverage and payment models to compare how states fund and provide care for immigrant populations.

Findings illustrate the presence of prominent disparities in health coverage and outcomes between immigrant and native-born populations. When assessing payment models for immigrant coverage, variability in types of payment models used and in eligibility criteria was recognized between states. This reinforces the necessity of targeted policy action to advance health equity within NC.

In designing payment and care models within Medicaid, needs of immigrants in NC should be addressed, offering opportunities to promote health equity and ameliorate health outcomes.

ABSTRACT NO. 34A

ASSESSING CONTRACEPTIVE USE IN VIRGINIA USING ALL-PAYER CLAIMS DATA

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We are using the Virginia All-Payer Claims Data (APCD) for 2018 and 2019 to characterize the prevalence of contraceptive use and method mix of Virginia publicly and privately insured women ages 15 to 49. The National Survey of Family Growth (NSFG) 2017-2019 suggest 65.3% of women aged 15 to 49 use contraception and provides information about contraceptive methods. There are limited data available at the state-level outside of a survey of the postpartum period, so the APCD can provide useful information about actual contraceptive utilization for a large population.

ABSTRACT NO. 34B

BRIDGING HEALTH CARE AND SOCIAL SERVICES TO ADDRESS HEALTH-RELATED SOCIAL NEEDS: INSIGHTS FOR COMMUNITY CARE HUBS

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North Carolina's Healthy Opportunities Pilots ("Pilots") program works to address health-related social needs (HRSNs) through non-clinical interventions across the domains of

housing, transportation, food, and interpersonal violence and toxic stress. Community care hubs (CCHs) play a central role in the Pilots and comparable work in other states by providing infrastructure to link the health care sector with community-based organizations. The Community Action and Analysis Plan synthesizes practical insights from stakeholders involved in the Pilots and similar initiatives to highlight key data, resources, and partnerships that can support the efforts of CCHs nationwide.

We studied the implementation of this work to address HRSNs using a multimethod qualitative approach. Through previous research and community engagement, we identified six overarching themes related to the functions of a CCH. We conducted 16 interviews with 27 informants from different sectors involved in addressing HRSNs, using a semi-structured guide that was organized by the six themes. We used consensual, team-based qualitative methods to analyze content and synthesize ideas and recommendations across interviews. Key takeaways from each interview were compiled into a matrix organized by the themes. Thematic memos were drafted for each interview and subsequently debriefed with a multi-disciplinary team to reflect on the findings.

We identified essential steps and resources for the work of a CCH within the six themes of 1) building organizational capacity; 2) assessing local needs and resources to address them; 3) supporting financial sustainability; 4) ensuring equitable access and participation; 5) coordinating across different initiatives; 6) developing a monitoring and evaluation plan. Across these themes, we highlight key considerations for the delivery of HRSN services. As the Pilots program looks to expand statewide and similar programs emerge, the Community Action and Analysis Plan offers practical guidance for how CCHs can connect the health care and social sectors to address HRSNs.

ABSTRACT NO. 35A

STEPS TOWARDS ACCOUNTABLE CARE: IMPLICATIONS OF THE 2024 MEDICAID MANAGED CARE FINAL RULE ON THE SAFETY-NET

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Safety-net providers – such as community health centers, rural health clinics, and public and critical access hospitals – are a critical component of the U.S. health care system and are responsible for the care of millions of Americans who are uninsured, underinsured, and who receive public insurance through Medicaid. Safety-net providers rely heavily on Medicaid as a primary source of funding, and the Medicaid managed care program plays an outsized role in orchestrating the flow of dollars to these organizations. It is therefore critical to ensure that the Medicaid managed care program is designed to support providers in delivering comprehensive and longitudinal care for the communities they serve. Value-based payment (VBP) models are promising tools to improve care coordination and financial sustainability, but adoption of value-based care remains limited in the safety-net compared to other types of providers.

The Centers for Medicare and Medicaid Services (CMS) issued a new Medicaid Managed Care Final Rule in April 2024. This rule is a significant development in Medicaid managed care policy, with new provisions that bolster regulatory oversight across six domains. We focus on three components that have particular relevance to advancing accountable care practices in the Medicaid managed care program: state-directed

payments, medical loss ratio reporting, and broader reporting and administrative requirements. Building on a landscape review and stakeholder interviews, we examine how the final rule can promote value-based care initiatives, reduce administrative barriers to reform, and increase transparency and fiscal accountability. We provide insights into how states and plans can leverage the new managed care provisions to support safety-net providers, and explore additional opportunities for advancing accountable care at the state and federal levels.

ABSTRACT NO. 35B

IMPROVING HCAHPS SCORES THROUGH PATIENT-CENTERED INITIATIVES AT A COMMUNITY HOSPITAL

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This project investigates the impact of unit leadership and patient population characteristics on HCAHPS scores at a community hospital in North Carolina. It highlights differences between surgical and medicine units by evaluating HCAHPS trends, focusing on race and age disparities. Surgical units typically achieve higher scores due to shorter, predictable stays and less complex cases. In contrast, medicine units, dealing with chronic conditions and longer stays, face greater challenges in maintaining high patient satisfaction.

Key factors influencing HCAHPS scores include unit leadership, patient population, and length of stay (LOS). Effective leadership and tailored initiatives are crucial in addressing these disparities. Nurse manager interviews revealed that strong communication, shared governance, and staff involvement are vital for improving patient satisfaction. Units that implemented mental health support during the COVID-19 pandemic, such as the Medicine unit, highlighted the importance of staff well-being in maintaining a positive work culture.

Recommendations for improving HCAHPS scores include developing leadership training specific to the challenges faced by different units, encouraging cross-unit collaboration, and implementing targeted strategies to address patient needs. The findings suggest that tailored leadership strategies and cross-unit collaboration are essential for improving patient experience and satisfaction in diverse hospital environments.

ABSTRACT NO. 36A

IMPROVING EFFECTIVENESS OF A COMMUNITY HOSPITAL OUTPATIENT PHARMACY

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Hospital-based retail outpatient pharmacies are an increasingly common way to provide a variety of pharmaceutical services to patients and the community. These pharmacies, located in the hospital setting, are ideal for patients due to the ease of communication between pharmacists, providers, and patients. These pharmacies face unique and specific challenges in a community hospital. This project aimed to observe the role and effectiveness of a community hospital outpatient pharmacy through the perspective of various stakeholders involved in the patient discharge process.

Through literature review, process mapping, and shadowing stakeholders, the goal of this project was to review current data, identify any process

limitations, and explore the most effective utilization of a hospital-based retail outpatient pharmacy. The poster presents multiple root causes and barriers to access which inhibit a hospital outpatient pharmacy's ability to best serve the hospital and community. Interventions and possible next steps are proposed to eliminate root causes in order to improve utilization of the hospital outpatient pharmacy. These next steps have the potential to improve patient outcomes overall.

ABSTRACT NO. 36B

DISAGGREGATED HEALTH EQUITY DATA: CASE STUDY AND ANALYSIS OF CURRENT LANDSCAPE

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Disaggregated health equity data is broken down sociodemographic information, such as race, ethnicity, and language (REL), that can identify and address health disparities between populations. REL data is critical to understanding the unique health risks and healthcare needs of individuals and communities. When leveraged properly, disaggregated REL data informs targeted health interventions by revealing differences in health outcomes that are obscured in aggregated data.
A case study of COVID-19 data in Hawaii helped visualize the importance of disaggregated REL data when developing health interventions. Hawaii was chosen for this case study for its successful collaboration with community partners, the Hawaii State Health Department, and CDC scientists to disaggregate COVID-19 data into more detailed race categories. Comparisons of racially aggregated COVID-19 data revealed elevated mortality among the Asian population and heightened case incidence among the Native Hawaiian and Pacific Islanders. A closer look into disaggregated racial data revealed that Pacific Islanders accounted for 22% of all COVID-19 cases and deaths in Hawaii over a yearlong period, despite comprising 5% of the total population. With data highlighting this health disparity, the Hawaii State Department of Health created a task force to address these disparities among Pacific Islanders using culturally-focused interventions.
The case study demonstrates how disaggregated REL data is critical to advancing health equity. However, this method comes with challenges. A landscape review of federal and state reports, journal articles, and other policy reports revealed current limitations of collecting and using disaggregated health equity data. Limitations include small sample sizes leading to privacy concerns and reduced statistical reliability, inconsistent data collection methods, and siloed data-sharing infrastructure. Policy recommendations to address these limitations include strategies to increase survey sample sizes and implementation of a national standardized data collection model and data interoperability standards to improve data collection and sharing.

ABSTRACT NO. 37A

BIOCHEMICAL CHARACTERIZATION OF *CRYPTOCOCCUS DENEOFORMANS* HEXOKINASE 1 (HXK1)

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The trehalose biosynthesis pathway is essential in maintaining homeostasis in fungi, plants, and some bacteria. In fungi, trehalose biosynthesis contributes to the organism's metabolism and membrane formation. The enzymes responsible for catalyzing the reactions in this pathway, trehalose synthase (Tps1) and trehalose phosphatase (Tps2) have been rigorously studied for their potential as drug targets in the fungal pathogen, *Cryptococcus*. Cryptococcal infections are especially a threat to immunocompromised people. An important aspect of the trehalose pathway is that it allows pathogens to survive at 37 degrees—body temperature. Cryptococcal strains in which the gene encoding Tps1 has been deleted are unable to survive at 37 ºC. To understand the mechanism by which Tps1 contributes to thermotolerance, we performed a suppressor screen. The *Cryptococcus deneoformans* tps1Δ strain was grown at 37 ºC. Suppressor strains that did not have the temperature-sensitive phenotype associated with *Cryptococcus deneoformans* tps1Δ were isolated. Whole genome sequencing of these strains showed that most have a variety of mutations in the gene encoding hexokinase 1 (Hxk1), a protein crucial to the first step of glycolysis. Interestingly, Hxk1 is inhibited by trehalose-6-phosphate, an intermediate in the trehalose pathway. The hypothesis explored in this project is that the Hxk1 mutations lead to the inactivity of the hexokinase protein, which may explain the loss of the temperature sensitive phenotype. Therefore, our goal was to purify recombinant *C. deneoformans* wild-type Hxk1 protein and measure Hxk1 activity in vitro. To this end, we successfully purified C. deneoformans Hxk1 and determined its activity in vitro. Future work will include determining if the mutations identified in the suppressor strains affect the function of Hxk1. As a result of this work, we will have learned more about the potential involvement of hexokinase proteins in the temperature regulation, and therefore infectivity, of fungal pathogens.

ABSTRACT NO. 37B

Evaluating the role of NAUK2 in Neuroendocrine Prostate Cancer

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Prostate Cancer (PC) accounts for roughly one third of cancer diagnosis and is the second leading cause of cancer specific mortality in men. Neuroendocrine prostate cancer (NEPC) is a highly aggressive advanced form of prostate cancer that develops as a treatment resistance response. NEPC has an unfavorable prognosis largely due to a lack of targeted treatment options. Thus, there is an unmet need for molecular targeted therapies in NEPC. Our preliminary studies suggest the AMPK protein kinase family member NUAK family kinase 2 (NUAK2) is a high value target in NEPC. Though understudied, NUAK2 is a highly druggable protein, and therefore merits further research. The goal of this study was to evaluate NUAK2

mechanisms of action in NEPC and evaluate the role of NUAK2 in NEPC cell line xenograft tumors.

Methods: NUAK2 dependent genes were validated by RT-qPCR from total RNA extracted from NCI-H660 cells with shRNAs targeting NUAK2 or non-targeting control. For in vivo studies, NUAK2 was targeted using a doxycycline inducible Cas9 system. At endpoint tumors were flash frozen and pulverized using LN2 for protein extractions. Protein lysates were analyzed by western blot.

Results: RT-qPCR analysis showed that loss of NUAK2 significantly altered expression of PRKAA1, PROM1, ASCL1, NRDG1, NRP2. ASCL1, NRDG1 and NPR2 are neuronal specific gene and PROM1 is a cancer stem cell marker (aka CD133). Targeting NUAk2 in vivo slowed NCI-H660 xenograft tumor growth. Western blot analysis tumor lysates confirmed genetic deletion of NUAK2 in vivo.

Conclusions: Loss of NUAK2 alters expression of neuronal related genes and cancer stem cell markers which could impact neuroendocrine differentiation and therapeutic response. Genetically targeting NUAK2 in vivo slowed NEPC tumor growth. Future studies should evaluate the therapeutic potential of targeting NUAK2 pharmacologically

ABSTRACT NO. 38A

USING COMPUTATIONAL SIMULATIONS TO INFORM MUTAGENESIS IN CONNEXIN PROTEINS

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Electrical synapses play a crucial role in neurotransmission, by synchronizing the activity of neuronal networks. They are formed by transmembrane proteins called connexins that form hexameric hemichannels called connexons. When compatible, connexons at the plasma membrane of two adjacent cells can dock to form a functional gap junction channel that allows for molecules to selectively flow through when the pore is open. Differences in connexin identities within the hexamers can lead to differential selectivity of certain molecules to pass through the channel. Excitingly, computational models of protein dynamics have proven to be useful in predicting and simulating protein interactions to guide future experimentation with high accuracy and utility. Combining these models with the known data on gap junction functionality, this project aims to simulate the docking and interaction energy between two hemichannel pairs. The simulation contains connexons that are placed in an environment with two lipid bilayers and water molecules surrounding the gap junction to closely match their natural environment. Using this molecular dynamics simulation, predicted residue-wise interaction energies are measured for the amino acids at the connexon docking interface. This approach helps form a hypothesis about the residue-wise interaction pattern between connexons, such that those residues can be subsequently manipulated to achieve desired docking selectivity patterns. Three homomeric connexons (Cx34.7, Cx35, and Cx31.3) were simulated to dock homotypically and heterotypically using Visual and Nanoscale Molecular Dynamics software. Analysis of the simulation outputs includes creating contact plots for the interaction energy calculations that are generated during the process. Future aims are to assess which residues are predicted to form strong interactions at a specific docking site, which will inform the mutagenesis that will make a mutant connexon that selectively docks in certain arrangements.

ABSTRACT NO. 38B

CILIARY SIGNALING IN NEURONS IN THE BRAIN: A NEW FAMILY OF CILIARY KINASES

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Primary cilia are organelles that project from most types of mammalian cells, featuring a hair-like structure similar to their close relatives, flagella and motile cilia. Primary cilia are required for key developmental signaling pathways. Previous studies have shown that primary cilia mediate the Hedgehog and WNT signaling pathways, which are crucial for the development of various organs and tissues, particularly the brain and spinal cord. Consequently, primary cilia have gained increasing importance as dysfunctions in these structures are linked to neurodevelopmental and neuropsychiatric disorders. Despite this, there remains a significant gap in understanding the different signaling pathways and protein functions in the cilia of cells and neurons. Our preliminary study, utilizing a biotin-based proximity labeling strategy, identified two casein kinase 1 family members localized to the cilia: casein kinase 1 gamma 1 (CSNK1G1) and casein kinase 1 gamma 3 (CSNK1G3). Although these proteins are understudied, emerging literature suggests their involvement in WNT signaling, another crucial developmental pathway. Interestingly, the other member of this protein family, casein kinase 1 gamma 2 (CSNK1G2), was not identified but will also be examined. In this study, we will build upon these findings and test the requirements for the casein kinase 1 gamma family members in cilia structure and function, and/or ciliary WNT signaling. Thus, we will employ a multifaceted approach in Lund Human Mesencephalic cells (LUHMES), Retinal Pigment Epithelium cells (RPE), and other cell lines through antibody staining, selective inhibition, expression of GFP and/or mCherry-tagged proteins, and gene knockout techniques. By contributing to the existing knowledge of ciliary signaling and protein expression, we aim to catalyze the development of therapeutic measures to treat and prevent diseases related to cilia dysfunction, which have high rates of lethality.

ABSTRACT NO. 39A

THE UBIQUITIN CONJUGATING ENZYME UBE2L3 REGULATES RNF213-MEDIATED UBIQUITYLATION AND DESTRUCTION OF *CHLAMYDIA TRACHOMATIS* INCLUSIONS

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Chlamydia trachomatis is the most prevalent sexually transmitted infection (STI) in humans and can cause permanent damage to women's reproductive systems in particular. *C. trachomatis* is an obligate intracellular pathogen that replicates in a vacuolar compartment termed an inclusion upon entering the host cell and has evolved various strategies to evade the cell-autonomous immune response. We recently identified that a *C. trachomatis* bacterial effector, garD, shields the pathogen from ubiquitylation and clearance mediated by the E3 ubiquitin ligase RNF213. However, where the ubiquitin chain is assembled and what E2 ubiquitin conjugating enzyme works with RNF213 for the ubiquitylation of garD-null *C.trachomatis* inclusions remain unknown. Here, we identify UBE2L3 as the main E2 ubiquitin conjugating enzyme for RNF213-dependent ubiquitylation of

C. trachomatis inclusions. We demonstrate UBE2L3 facilitates the recruitment of RNF213 and the ubiquitylation of garD-deficient inclusions. This study highlights UBE2L3 contribution to RNF213-orchestrated antibacterial response during Chlamydia infection.

ABSTRACT NO. 39B

TREHALOSE-6-PHOSPHATE SYNTHASE, TPS1, AS AN ANTI-FUNGAL DRUG TARGET

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Candida albicans and *Cryptococcus neoformans* are wide-spread fungal pathogens that disproportionately affect the immunocompromised population. *C. albicans* causes both superficial and invasive infections due to disruption in healthy bacteria and overgrowth of yeast in the body. *C. neoformans* is typically inhaled and is responsible for cryptococcal meningitis. Due to the increase in toxic effects and resistance to current antifungal drugs, novel fungal targets must be explored. One such target for therapeutic intervention is the trehalose biosynthesis pathway. The trehalose biosynthesis pathway is essential for the survival of pathogenic fungi yet does not exist in humans, which potentially limits possible off-target effects. The biosynthesis of trehalose is a two-step process. In the first step, trehalose-6-phosphate synthase (Tps1) converts UDP-glucose and glucose-6-phosphate to trehalose-6-phosphate (T6P). In the second critical step, trehalose-6-phosphate phosphatase (Tps2) converts T6P to trehalose. Our hypothesis is that only UDP-glucose is utilized by Tps1. Here, we aim to determine the dissociation constant (Kd) of Tps1 and UDPG in both *Candida* and *Cryptococcus* spp., with the goal of further investigating the potential of this protein as a drug target. As part of this work, we shall determine the Kd of Tps1 and UPDG-galactose, galactose being the epimer of glucose, to test the specificity of binding. To do so, we have expressed and purified the proteins and carried out enzyme activity assays to confirm their activity. Isothermal titration calorimetry will be used to determine the Kd for UDPG, UDP-galactose, and glucose-6-phosphate. The results of this work will contribute significantly to our understanding of stress-tolerance in *Candida albicans* and *Cryptococcus neoformans* and lead to the discovery of new antifungal therapeutics.

ABSTRACT NO. 40A

Optimization of long-read RT-PCR-seq to Quantify Pathogenic Pseudoexon Inclusion in Glycogen Storage Disease IX

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Glycogen Storage Disease type IX γ2 (GSD IX γ2) is a genetic disorder caused by pathogenic variants in PHKG2, a subunit of glycogen phosphorylase kinase. The resulting phosphorylase kinase deficiency leads to inefficient glycogenolysis and toxic glycogen accumulation in the liver. Without intervention, this can lead to liver failure, demonstrating the need for timely development of a therapeutic.
In two siblings with GSD IX γ2 showing signs of progressive liver damage, our team discovered a potential pathogenic variant (c.556+1069T>G) in intron 6 of PHKG2. That variant causes a 76 bp

pseudoexon to be included in the transcript, resulting in frameshift and a premature stop codon that is predicted to cause nonsense-mediated decay. The pseudoexon inclusion causes very low levels of phosphorylase kinase as evidenced by enzyme activity testing in a personalized cell culture model containing c.556+1069T>G. By studying the rate of pseudoexon inclusion in the cell model, we will have a comparable baseline when measuring the efficacy of potential therapeutics to correct splicing. Short-read RNA-seq of the cell model has previously led to inconsistent alignment of the pseudoexon, prompting us to investigate targeted long-read sequencing to improve pseudoexon quantification.

We performed RT-PCR amplification of a 304 bp region for high-throughput short-read sequencing, in addition to a 454 bp region surrounding the pseudoexon and an 806 bp region containing most of PHKG2 for long-read sequencing. We successfully amplified all of these regions of the PHKG2 transcript and are optimizing the reactions for high-throughput sequencing. Together, these efforts will determine the most accurate and cost-effective methods for quantifying pseudoexon inclusion and splicing of the whole transcript. This will contribute to a more complete understanding of PHKG2, the patients' genetic variant, and the resulting pseudoexon, and will have a continued impact on research of targeted RNA therapeutics.

ABSTRACT NO. 40B

INTERACTIVE VISUALIZATION OF MULTI-REGIONAL OPTOGENETIC STIMULATION

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Complex behaviors and mood-related brain states require coordination across multiple brain regions. Designing therapies that target these states could optimize their modulation. However, the effects of techniques like pharmaceuticals or neural stimulation on multiregional brain activity are not well understood. Optogenetic stimulation is effective for altering neural activity in a cell-specific manner. To understand its effect across different brain regions, our lab conducted an experiment on mice with soma-targeted channelrhodopsin expressed in six mood-regulating brain regions. We implanted optical stimulating fibers and recording microelectrodes to simultaneously stimulate and record in these regions. Mice were stimulated in a single region using a laser connected to a single port, with different regions stimulated on different days. Stimulation frequencies varied up to 30 Hz over 288 randomized trials. We previously developed a model representing brain changes from various frequency and region-specific optogenetic stimulations. To make this data more accessible, I created an interactive bokeh-based app hosted online. Users can select their region of interest from a dropdown menu and adjust the frequency using a sliding scale with a 0.01 Hz step size. The app visualizes the model's output based on these inputs, displaying the results on a plot. This interactive tool helps researchers understand the multi-regional perturbation caused by single-region stimulation in rodent models, improving our understanding of brain region interactions.

This tool enhances research on neural connectivity, brain function, and therapeutic development for neurological disorders.

ABSTRACT NO. 41A

ELUCIDATING THE MORPHOLOGICAL CHANGES IN PERICYTES IN RESPONSE TO LUNG INJURY

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Pericytes exhibit extensive branched cytoplasmic extensions embedded in the basement layer on the exterior surface of microvessels such as capillaries. They interact with endothelial cells and other cell types to maintain homeostasis of the vessels. Pericytes main functions are generally considered to be providing and maintaining structural integrity for the microcapillaries and supporting the formation and development of the vascular network. In the lung, several reports suggested that pericytes can differentiate into multiple kinds of cells including myofibroblasts in response to lung injury. However, the exact mechanisms through which pericytes are activated and involved in tissue repair have not yet been fully understood, especially in the lungs where pericytes have seldom been researched. In this study, I assessed the morphological changes of pericytes and their potential to renew in response to lung injury induced by butylated hydroxytoluene (BHT)s. I used lung samples collected from NG2-creER;R26R-tdTomato that received tamoxifen (to induce lineage labeling) followed by BHT administration (to cause lung damage). Through analysis of images produced by immunofluorescence, confocal microscopy, and image analyses on lung sections collected on day-3 and 6 post BHT injury to assess, the structural differences between pericytes from uninjured and BHT-injured lungs collected at different time points I found that pericytes undergo extensive morphological changes. Further, my work found no evidence of pericytes proliferation after lung injury. My findings provide some insights into pericyte dynamics and are a step toward future possibilities to improve injury repair.

ABSTRACT NO. 41B

Investigating the role of a novel TrkB Y782 signaling in status-epilepticus induced neuronal death

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Temporal lobe epilepsy (TLE) is one of the most common types of epilepsy, affecting approximately fifty million people worldwide. It causes unprovoked seizures that originate from the medial or lateral temporal lobe and hippocampal sclerosis due to neuronal death, thereby resulting in impaired cognitive functions such as speech, memory, and learning ability. Previous research suggests that an episode of de novo prolonged seizures, known as status epilepticus (SE), is one of the main causes of TLE. Understanding the molecular and cellular mechanisms by which SE transforms a normal brain into an epileptic, namely epileptogenesis will provide insight into therapeutics of TLE. Previous studies in animal models implicate that brain-derived neurotrophic factor/TrkB receptor tyrosine kinase signaling is one of the molecular mechanisms critical for epileptogenesis. We recently discovered a novel signaling pathway through TrkB-Y782 following SE. We hypothesize that the TrkB-Y782 signaling pathway, when activated by SE, contributes to neuronal degeneration. To investigate the functional consequences of TrkB-Y782 signaling, we

generated a genetic knockin mutant mouse line (Y782F) in which tyrosine 782 is substituted with phenylalanine (Y782→F). Using Fluoro-Jade C (FJC) staining to detect degenerating neurons, we aim to examine SE-induced FJC-positive cells in the neocortex and hippocampus between wild-type and Y782F mutant mice. The FJC-positive cells were identified by epifluorescent microscope and imaged with Keyence microscopy. Our preliminary results revealed a reduction of FJC-positive cells in these regions in Y782F mutant mice 48 hr following SE. These results are consistent with the idea that signaling from TrkB-Y782 promotes neuronal death following SE. To confirm these results, we conducted additional experiments comparing wild-type (WT) and Y782F mutant mice following SE. The data analysis is ongoing. The discovery of TrkB Y782 signaling contributing to neuronal cell death will provide insight into developing novel therapeutics for TLE and neurodegenerative diseases.

ABSTRACT NO. 42A

EXAMINATION OF SERVICES & UNMET NEEDS AMONG THE INTELLECTUAL AND OTHER DEVELOPMENTAL DISABILITIES COMMUNITY IN NORTH CAROLINA: A DATA INITIATIVE

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North Carolina has nearly 200,000 individuals with intellectual and other developmental disabilities (I/DD) living in the state. The Innovations Waiver is the Home and Community-Based Services (HCBS) Medicaid program that provides individuals with the support and services needed to live in a community instead of an institutional setting. Receiving the Innovations Waiver reduces the risk of future institutionalization, minimizes the use of crisis services such as the emergency department, and facilitates self-determination. Currently, 14,138 people are receiving the Innovations Waiver, but an additional 17,902 individuals are on the waitlist. The average time to receive a waiver is nine years, yet some have waited up to 17 years, while others have died while waiting.

The purpose of this initiative was to collect, analyze, and create an inventory of state and national I/DD data in order to propose recommendations to advocate for necessary policy change. The method taken was twofold. First, a review of academic literature, government websites, policy briefs, and other published and unpublished sources was conducted. This aimed to identify what is known and what is needed but not currently available. Next, stakeholder convenings were conducted with a diverse set of participants to contextualize the data collected and provide key recommendations. Convenings included people with lived experience, family caregivers, community organization representatives, and leaders from the NC Department of Health & Human Services, the NC Council of Developmental Disabilities, and managed care organizations.

Recommendations for future research efforts, including data collection, were made according to the following themes: the needs and service utilization of people with I/DD, the needs and experiences of family and other caregivers, integrating physical and behavioral healthcare support, planning and long-term support needs, costs associated with care, and state comparisons.

ABSTRACT NO. 42B

EVALUATION OF CLINICAL DECISION SUPPORT TOOLS AT DUKE HEALTH

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Introduction: FDA guidance includes algorithm-based tools, and Duke Health has pioneered Clinical Decision Support (CDS) software governance amid evolving regulations.

Methods: This project aims to assess the variety of tools registered with Duke Health and their respective characteristics to provide insight into the types of CDS tools utilized in one health system and to anticipate future internal and federal-level needs.

Results: To date, there are approximately 53 total registered tools with the ABCDS Oversight Committee and of these tools, 49 unique tools have consented to sharing their data. Overall, 17 supporting departments were represented. Most tools were data-driven (n = 39), some were considered a standard of care model (n = 9), and other tools were derived based on knowledge (n = 3). Most tools were part of full review (n = 35), but some tools were part of fast-track review (n = 9). Overall, models were approximately evenly distributed across the lifecycle phases: Model development (n = 10), silent evaluation (n = 11), effectiveness evaluation (n = 6), and general deployment (n = 12). Most of the model owners (n =16), clinical owners (n = 36), and executive sponsors were physicians (n = 19).

Conclusion: Consistent oversight across different lifecycle phases of registered CDS tools submitted to the ABCDS Oversight Committee is necessary. This study identifies significant growth potential in both tools and tool owners. Scalable management strategies to streamline developmental efforts are crucial given the physician-driven growth in CDS tools and the fact that there are over 2,000 faculty physicians and researchers at Duke University School of Medicine. Future directions should focus on continuous standardization and bias mitigation in CDS development to maintain regulatory and ethical standards while fostering innovation and patient care improvements. Standardization efforts are essential for clarity and consistency, optimizing the benefits of innovative technologies.

ABSTRACT NO. 43A

TAXOL TREATMENT INDUCES MORPHOLOGICAL CHANGES IN KERATINOCYTES LEADING TO LOSS OF NERVE INNERVATION

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Chemotherapy patients often experience peripheral neuropathy, or nerve damage, during or after the onset of treatment. Taxol is a chemotherapy drug that induces the death of highly mitotic cells by stabilizing microtubules. The stabilization of microtubules removes the dynamic, polymerizing nature of microtubules, preventing the formation of spindle fibers and the separation of chromosomes, which pauses cells in the metaphase stage of mitosis. Nerve fibers are also rich in microtubules and it has been assumed that peripheral neuropathy from Taxol treatment is likely due to direct effects on neurons. However, Taxol treatment has also been shown to increase contractility of epidermal keratinocytes in vitro, and increased epidermal contractility is sufficient to cause denervation of

this tissue. We hypothesized that Taxol treatment in mice would increase the contractility of epidermal keratinocytes, leading to damaged nerve innervation of the epidermis. We injected Taxol into mice and collected glabrous skin (non-hairy skin) and back skin to determine the effect of Taxol on keratinocytes and ultimately nerve innervation of the epidermis. We used a variety of markers to demonstrate the impact of Taxol treatment. We found that Taxol was able to induce focal morphological changes in the epidermis that corresponded with local loss of neurons. Future goals are to better characterize Taxol's effects over time and to determine whether blocking epidermal contractility rescues denervation.

ABSTRACT NO. 43B

RECOVERING HRTF FEATURES AFTER BLIND SOURCE SEPARATION

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HRTFs (Head Related Transfer Functions) are functions encoding how sound is filtered from a specific position to an individual's ears, accounting for sound source location, head shape, and ear & pinnae shape. They are currently difficult to measure for any individual human, requiring an anechoic chamber and measurements in all directions around the head. HRTFs are often used for synthesizing binaural audio, where the left and right ears have different mixtures of the same speech signal, creating the effect of sound coming from specific directions. In this project, we attempt to localize binaural audio after blind source separation. Blind source separation (BSS) is a method of "blindly" separating n unknown sources from a mixture of those sources, where the n sources and the mixing matrix creating the n observations are both unknown. BSS requires that there be n distinct "observations" of the mixed sources, and usually relies on certain characteristics of the signals, such as being non-Gaussian, non-stationary, or non-white. It will separate the speech signals and provide an estimate of the mixing matrix that was used to create the n observations. We first artificially synthesize binaural noise with two speech signals from different locations using measured HRTFs. We then separate them with blind source separation, which returns the estimated speech signals, and the estimated mixing matrix, the columns of which are an estimate of the HRTFs. We then attempt to recover the spatial cues of the HRTF using the BSS-estimated HRTF.

ABSTRACT NO. 44A

WDR5 REVEALED AS PUTATIVE GLIOBLASTOMA RADIOSENSITIZER IN ORGANOTYPIC BRAIN SLICE CULTURE CRISPR SCREEN

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Glioblastoma (GBM) comprises 49% of malignant brain tumors with a 5-year survival rate of less than 10%. Current treatment strategies involve a multimodal approach, combining surgical resection with radiotherapy (RT) and alkylating chemotherapy agents. However, the radioresistance of GBM tumors amplifies the non-specific effects of RT on surrounding healthy cells, demonstrating the need for more effective strategies to improve tumor response and increase overall patient survival. Previous studies in this field have been limited to deciding between in vivo mouse models that more accurately assimilate the tumor microenvironment and in vitro cell culture

models which are more time efficient and cost-effective. In this study, we performed a genome-wide CRISPR knock-out radiosensitizing screen across the two aforementioned model systems along with a novel mediating model: organotypic brain slice cultures (OBSC). We hypothesized that radiosensitizers discovered through only the in vivo and OBSC conditions may uncover tumor microenvironment-specific factors otherwise inaccessible via in vitro methods. One such candidate radiosensitizing factor we identified is WDR5, a chromatin remodeler which interacts with various complexes to trimethylate H3K4 and has been shown to promote malignant characteristics in colon cancer models. We demonstrate that shRNA-mediated knockdown and inhibition of WDR5 with a novel small-molecule, OICR-9429, both cause a reduction in H3K4me3. Furthermore, our results denote decreased survivability when cells are treated with inhibitor on OBSC, but not in vitro. Future work will validate these findings within in vivo models, expand to CRISPR Cas9-mediated WDR5 knockout in all models, and explore potential mechanisms of radiosensitization via WDR5 inexpression.

ABSTRACT NO. 44B

INVESTIGATING THE ROLE OF ZEB2 AND THE BONE MORPHOGENETIC PATHWAY IN RHABDOMYOSARCOMA NEUROGENIC DIFFERENTIATION

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Rhabdomyosarcoma, the most common pediatric soft tissue cancer, is classified according to fusion status into two subtypes: fusion-positive and fusion-negative. Fusion-positive rhabdomyosarcoma (FP-RMS) has a grim survival rate of less than 30% when high-risk. It is characterized by the presence of a fusion gene, most commonly PAX3::FOXO1. Both PAX3 and FOXO1 are transcription factors, resulting in the fusion protein activating many downstream targets and being highly oncogenic. Currently, direct targeting of PAX3::FOXO1 is not feasible, making other approaches necessary. Unbiased proximity labelling assays nominated the TGFβ pathway transcription factor ZEB2, which is a top common protein found in the interactome of all seven fusion proteins present in RMS. Previous experiments in our lab found that the knockdown of ZEB2, with the addition of retinoic acid, alters the phenotype of FP-RMS tumor cells, which are myoblast in origin, into neuronal-like cells. Moreover, the TGFβ pathway involves the translocation of SMAD protein complexes from the cytoplasm into the nucleus, where they interact with ZEB2. Thus, we hypothesize that the bone morphogenetic pathway (BMP), which is a part of the TGFβ superfamily, is the driver of ZEB2's neurogenic effect. Preliminary data of protein and mRNA expression indicates that knocking down ZEB2 alters SMADs phosphorylation and the expression of neuronal targets downstream of BMP, pointing to a possible mechanism of action of ZEB2 in RMS differentiation. Our long-term goals for this project are to contribute to the development of innovative therapies that can mitigate the oncogenic activity driven by oncofusions in FP-RMS.

ABSTRACT NO. 45A

CONSTRUCTING TISSUE MIMICKING PHANTOMS FOR THE VALIDATION OF SIMULTANEOUS IMAGING OF 3 FLUOROPHORES REPORTING ON METABOLIC PATHWAYS RELEVANT TO AGGRESSIVE BREAST CANCER

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Tumors are highly adaptable, often shifting metabolism to glycolysis or oxidative phosphorylation (OXPHOS) and relying on glucose, lipids, or amino acids throughout disease progression and treatment. Developing tools to track tumor metabolism may lead to targeted therapies leveraging metabolic vulnerabilities.

Fluorophores 2-NBDG, Bodipy, and TMRE have been validated to report on glucose uptake, fatty acid uptake, and OXPHOS respectively, individually and pairwise. We aim to combine these fluorophores for in vivo concurrent use.

We imaged human breast tissue mimicking liquid phantoms made of 1 µm monodisperse polystyrene spheres for scattering, bovine serum albumin in PBS for protein binding, and the three fluorophores using fluorescent microscopy. The three fluorophores were imaged either mixed in the same phantom solution or individually at varying concentrations (Bodipy: 0-1 µM, 2-NBDG: 0-10 µM, TMRE: 0-15 nM).

For the mixed phantoms, a linear spectral unmixing strategy was employed to distinguish 2-NBDG and Bodipy, which have overlapping excitation and emission peaks. The mixed spectrum is a linear combination of individual 2-NBDG and Bodipy. The unmixing determined the individual contributions of Bodipy and 2-NBDG, using their known linear relationship and reference spectra.

We observed a linear relationship of increasing intensity with increasing concentration for both mixed (R2=0.9908) and individual (R2=0.9896) TMRE, which were not significantly different from each other, indicating its ability to produce accurate measurements when combined with other fluorophores. After unmixing, the R2 value for the relationship between intensity and concentration for both Bodipy and 2-NBDG was >0.98, and not significantly different from individual phantoms.

Developing a spectral unmixing strategy to mitigate optical crosstalk between fluorophores and confirming the ability to use multiple fluorophores simultaneously paves the way for in vivo studies of breast cancer metabolism. Understand tumor metabolism of specific patients is crucial to creating a specialized therapy to best treat aggressive tumors.

ABSTRACT NO. 45B

THE NON-CANONICAL HISTONE VARIANT H3.3 IS INVOLVED IN ECDNA FORMATION IN CANCER CELLS

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Extrachromosomal circular DNA (ecDNA) has been found in most cancer types and has been recognized as a major driver of cancer cell evolution and progression through the generation of genetic heterogeneity. Although this connection has been made, factors involved in the biogenesis and maintenance of ecDNA remain largely unknown. H3.3 is a non-canonical histone variant that has been previously linked to the non-homologous end joining (NHEJ) DNA repair pathway during double-stranded DNA

breaks, but its involvement in the ecDNA life cycle has not been recognized. In our study, we employed CRISPR-Cas9 technology and a molecular biology-based reporter system to investigate the role of H3.3 in ecDNA formation within cancer cells. Our findings demonstrate that H3.3 is indeed involved in the formation of ecDNA. This novel insight into the function of H3.3 not only expands our understanding of the mechanisms driving ecDNA dynamics in cancer cells but also showcases a potential therapeutic target for cancer evolution.

ABSTRACT NO. 46A

INVESTIGATING THE ALTERNATIVE SPLICING OF PARP2 IN INFLUENZA A INFECTION

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Influenza A virus (IAV) infection has caused seasonal and pandemic influenza outbreaks, posing a serious concern to global health. Various clinical outcomes including hospitalization and death can result from infection, though many patients remain asymptomatic. A breadth of factors can influence IAV susceptibility, such as previous exposures, vaccinations, comorbidities, viral genetic variation, and host genetic variation. Here, we leverage a cellular genome-wide association study method called scHi-HOST (single cell High-throughput Human in vitrO Susceptibility Testing), to identify genetic variants that impact viral burden. Using pooled, single-cell RNA sequencing of 96 IAV-infected lymphoblastoid cell lines, we identified a splicing quantitative trait locus (sQTL) in Poly (ADP-Ribose) polymerase 2 (PARP2) that confers susceptibility to IAV. This sQTL governs an alternative 5' splice site, resulting in two PARP2 isoforms distinguished by a length of 13 amino acids depending on sQTL genotype. This genotype-dependent difference in PARP2 isoform length has been confirmed by western blot. Additionally, the longer PARP2 protein isoform is associated with greater IAV burden. Knockdown of PARP2 in vitro resulted in significantly lower IAV burden, indicating a pro-viral role during infection. We then discovered that inhibition of PARP2 had no effect on IAV infection across either sQTL genotype, suggesting that PARP2 promotes IAV infection in a catalytic independent manner. Comparison of ADP-ribosylation across sQTL genotype with IAV infection via western blot revealed IAV strain specific effects. Infection with pandemic influenza, A/California/04/09 (H1N1), resulted in induction of ADP-ribosylation, though specific targets remain unclear. Alternatively, we discovered that infection with IAV strain A/Hawaii/70/2019 (H1N1) led to induction of ADP-ribosylation across both homozygous sQTL genotypes. Together our findings highlight how host genetic variation impacts disease susceptibility and represent the beginnings of an investigation into an unknown mechanism in IAV infection.

ABSTRACT NO. 46B

EVALUATING THE IMPACT OF DISSOLUTION TIME ON A PHASE-CHANGING POLYMER

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Ethyl cellulose-ethanol (ECE) is a novel method for ablating tumors and shows promise as a method intratumoral delivery of immunotherapies or chemotherapies to increase the efficacy of treatments. To effectively deliver these drugs, it is necessary to develop a reliable method for mixing ECE to produce consistent results. The purpose of this study is to investigate if mixing time has an impact on the release rate of ECE. This knowledge would allow ECE mixtures to have consistent rates of drug delivery. In past experiments, researchers mixed ECE at least 24 hours before the experiment and visually checked for issues such as clumps. The experiments performed in this study look at how the mixing time impacts the kinematic viscosity of ECE and the rate at which the ethanol diffuses. The viscosity measurements were taken at varying time intervals using a Ubbelohde viscometer. The second experiment was a release into sink study where ECE was combined with small amounts of fluorescein. This ECE solution is placed in a dialysis tube in water, and by measuring the levels of fluorescein with a spectrophotometer, the ethanol release rate is recorded. In these experiments, the mixing time did not influence the viscosity of the ECE. The variations in the viscosities could be due to differences in the mixing process or the dispersity of the ethyl-cellulose polymer. The release into sink study displayed that ECE had quicker release rates when mixed for 1 hour and slower rates when mixed for 12 hrs. Further studies looking at longer time points would be necessary to determine how long it takes ECE to completely diffuse. Overall, the results of the study indicate that kinematic viscosity is not impact by the mixing time of ECE, but the release rates of the ECE solutions are impacted by the mixing times.

ABSTRACT NO. 47A

KRT13 MARKS A NEW HILLOCK-LIKE CELL STATE IN SQUAMOUS CELL LUNG CANCER

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Squamous cell lung cancer (LUSC) is a subset of non-small cell lung cancer with poor survival outcomes due to a lack of targeted therapies. A previous study identified tumor-propagating cells (TPCs) in LUSC, which resemble normal basal cells, are highly proliferative, and are able to serially transplant the disease. We hypothesized that additional cancer cell types may exist in squamous tumors and that this heterogeneity can impact response to therapy. Utilizing single-cell RNA sequencing, we identified another distinct cell population marked by keratin-13 (Krt13). These Krt13+ tumor cells transcriptionally resemble the recently discovered Krt13+ hillock cells of the normal lung. Normal lung hillock cells are derived from basal cells and known to be resistant to multiple forms of injury. We hypothesize that the Krt13+ hillock-like cells would act as an injury resistant subpopulation of the tumor and therefore may survive chemotherapy better than the TPC population. Additionally, we identified KLF4 as a predicted regulator of the Krt13+ hillock-like state. Given that basal cells are regarded as the cell of origin for squamous tumors in the lung and that our tumor populations transcriptionally resemble

normal lung cells, we tested if KLF4 regulates a KRT13+ state in normal lung basal cells. To determine if KLF4 is sufficient to drive a KRT13+ state, KLF4 was overexpressed in a human basal cell line, BEAS-2B. Overexpression of KLF4 increased KRT13 expression and led to morphological changes in 2D cell culture. Next, to determine if KLF4 is necessary to drive this KRT13+ state, we utilized a CRISPR/Cas9 mediated knockout of KLF4 and hypothesize that these basal cells lacking KLF4 will not be able to give rise to a KRT13+ state. Together, we identified intra-tumoral heterogeneity that may be driven by KLF4, support chemotherapy resistance in LUSC, and be a new target for LUSC treatment.

ABSTRACT NO. 47B

MEASURING ENTEROENDOCRINE CELL LIFESPAN IN THE ZEBRAFISH INTESTINE WITH KAEDE PHOTOCONVERSION

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Enteroendocrine cells (EECs) are sensory cells in the intestinal epithelium that detect nutrients and other chemicals in the gut and relay that information to the rest of the body through regulated release of hormones and neurotransmitters. Zebrafish serve as a powerful model for studying intestinal development in vertebrates because they are highly amenable to live imaging, allowing for the probing of longitudinal questions about EEC renewal and division. However, the lifespan of zebrafish EECs during embryonic development, as well as the correlation between EEC lifespan and subtype or intestinal region, is poorly understood. To probe this question, we created a transgenic line of zebrafish whose pan-EEC marker, NeuroD1, was tagged with the photoconvertible protein Kaede. Embryos of this Tg(neurod1:Kaede) line were then subjected to photoconversion at various days of development and imaged using stereoscopy and confocal microscopy. By calculating ratios of red and green wavelengths emitted by individual EECs at different timepoints, we were able to look at the number and location of converted (red) and non-converted (green) cells 24, 48, and 72 hours post-conversion to give us a readout of how many new cells arose at each day of development. Understanding the points in development at which EECs divide and replenish themselves throughout the intestinal epithelium may allow for improved understanding of the dynamics of EEC subtypes, including their lifespan, their segregation to particular gut regions, and their turnover rate.

ABSTRACT NO. 48A

INVESTIGATING THE EFFECT OF ELASTIN-LIKE POLYPEPTIDE SEQUENCE ON MULTICOMPONENT CONDENSATE FORMATION IN VITRO

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Biomolecular condensates are membrane-less liquid-like compartments in eukaryotic cells that are rich in proteins and nucleic acids. They are involved in spatiotemporal regulation of various cellular functions. Investigating the molecular factors that influence condensate formation could improve our understanding of how such processes are regulated, and provide insights on engineering condensates for applications like protein purification and the development of synthetic biology tools. Elastin-like polypeptides (ELPs) are a class of synthetic intrinsically disordered proteins that exhibit sequence,

length, temperature and concentration-dependent phase transition behavior, making them useful tools to systematically model condensate formation. ELPs are composed of (VPGXG)n, where X is any amino acid except proline and n denotes the number of repeats. In this study, we investigate co-expression of ELPs with different guest residues with an aim to develop multicomponent condensates. Based on previously reported in vitro experiments, we cloned four sequences of interest: (VPGIG)80, (VPGVG)80, (VPGSG)80, and (VPGVGVPGAG)40, referred to as E1-4 hereafter. ELPs 1-3 were cloned in a pET-derived vector as a sfGFP fusion while E4 was cloned in a pBAD vector with mCherry fusion. We co-expressed E4 with E1 or E2 or E3 in E.coli strain BL21, and used confocal microscopy to visualize protein localization at several time points post-induction. Green puncta were observed for ELPs carrying relatively hydrophobic guest residues (E1 and E2), suggesting their ability to form distinct intracellular condensates at each time point, whereas the more hydrophilic E3 do not form puncta. We note that co-expression of E4 with the condensate-forming E1 or E2 did not alter the phase behavior of E4, suggesting no interaction between these proteins. At the 8hr time point, most of the cells expressed only E4-mCherry while few showed co-expression of the puncta-forming sfGFP partner. In future experiments, we plan to improve E4 condensate formation by increasing its length. We also plan to express E4 with ELPs containing amino acids of varying hydropathy, to further characterize multicomponent condensate formation in vivo.

ABSTRACT NO. 48B

USING PCR TO EXAMINE CRISPR/Cas9 EDITING OF A MOUSE MODEL OF A DIFFUSE MIDLINE GLIOMA

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Diffuse midline gliomas (DMGs) are brain tumors that arise in the brainstem of children and young adults, resulting in a median survival of less than two years. Studying DMG-specific tumorigenesis and tumor-immune interactions via genetically engineered mouse models (GEMMs) may inform the design of new urgently-needed treatment approaches. The Reitman Lab is developing a new approach to generating DMG GEMMs that involve the combination of RCAS/tv-a, an avian retrovirus gene delivery system to express transgenes in specific brain cell lineages in the mouse brain, and the CRISPR/Cas9 gene editing technology. To develop this method, we sought to confirm that CRISPR/Cas9 could disrupt specific DMG-relevant genes in our mouse DMG model. To do so, we examined a panel of n=7 mouse DMGs generated via CRISPR/Cas9 disruption of DMG-associated genes (p53, Pten, Atm, PPm1d and Cdkn2a). We first microdissected formalin-fixed, parrafin-embedded (FFPE) DMGs from the whole mouse brain and extracted genomic DNA. We then designed PCR primers to specifically amplify the genomic locus that we predicted to be targeted by Cas9 for each gene using Primer3. We found that the development of primers targeting shorter amplicons (bp < 225) was

needed to PCR-amplify the target sites, indicating that genomic DNA in the FFPE samples may be fragmented. The samples are currently undergoing next generation sequencing to confirm CRISPR/Cas9 gene disruption. We also amplified CRISPR guide RNA barcodes to confirm the presence of CRISPR guide RNA constructs present in the mouse tumors. Our results demonstrate that RCAS/tv-a and CRISPR/Cas9 can be used as an accurate tool to model DMG tumorigenesis in the mouse brainstem. Confirming the effectiveness of this mouse model will streamline future GEMM DMG research by allowing genes of interest to be rapidly perturbed by generating new RCAS retrovirus constructs.

ABSTRACT NO. 49A

INVESTIGATING MEAK-7 RNA SPLICING IN LUNG CANCER: ADDRESSING RACIAL DISPARIES IN ONCOLOGY

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Disparities in cancer widely impact the prevention, diagnosis, and treatment of disease and patient outcomes. Despite healthcare equity efforts, Black lung cancer (LC) patients suffer disproportionately compared to their White counterparts. LC disparities can exist genetically at an individual level resulting from ancestry-related factors. Many current oncology investigations focus on cancer among White patients and their respective genetic mutations. Consequentially, cancer among patients of other races and ethnicities are less understood, and additional molecular mechanisms driving cancer heterogeneity, such as RNA splicing, are less investigated. Our lab has identified race-related RNA splicing events in lung cancer in exon 2 of mEAK-7, located in the 5' untranslated region (UTR). Mammalian MTOR-associated protein, eak-7 homolog (mEAK-7) is a lysosomal membrane protein that activates the mTOR pathway, a cell growth and mobility regulator. Increased mEAK-7 expression is associated with decreased patient survival in LC. Gene expression can be regulated by upstream open reading frames (uORFs) in the 5'UTR. An uORF is hypothesized to be present in mEAK-7 and may be impacted by race-related exon 2 splicing in LC patients. To assess the functionality of the uORF, we are currently transfecting LC cell lines derived from Black or White patients with antisense oligonucleotides (ASOs) targeting the 5' UTR at the hypothesized uORF location to determine effects on mEAK-7 RNA expression and mEAK-7 protein expression. If a targetable uORF exists in mEAK-7, this has the potential to inform therapeutic developments to modulate mEAK-7 expression in LC and create individualized patient therapies. Through investigating population-related RNA splicing events in cancer, scientists and clinicians can identify unique molecular mechanisms contributing to disease progression, which can aid in development of novel biomarkers and therapies to lessen disparities in cancer.

ABSTRACT NO. 49B

MITOCHONDRIAL REMODELING DURING EARLY DEVELOPMENT IN C. ELEGANS

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Organelle remodeling, the change in organelle structure, is an essential event in embryogenesis. Mitochondria are essential organelles in development as they produce ATP through the electron transport chain (ETC). During embryonic development, the structure of the mitochondrial cristae and cristae organizing proteins undergo a dynamic reorganization in response to developmental signals. In C. elegans, IMMT-1 and IMMT-2 are proteins that control cristae formation, and when mutated cause defects in germ-line development and egg-laying. We have shown that the expression of ETC complexes increases over developmental time and differs between the developing primordial tissues. However, how mitochondrial structure is remodeled to support ETC expansion is unknown. In this study, we utilized microscopy of endogenously tagged fluorescent IMMT-1 and IMMT-2 in two-cell to two-fold stage embryos. Through whole embryo analysis of fluorescent intensity, we show that IMMT-1 and IMMT-2 increase in expression over developmental time. Furthermore, IMMT-1 and IMMT-2 show differential expression in differentiating tissues. Our results demonstrate how mitochondrial morphology is altered in development, and provide evidence for developmental organelle remodeling. Future research will investigate mechanisms of mitochondrial and organelle remodeling and their roles in embryonic development and metabolism.

ABSTRACT NO. 50A

INVESTIGATING THE NF-KB SIGNALING INHIBITOR, IKK-16, AS A NOVEL TREATMENT FOR CHONDROSARCOMA METASTASIS

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Chondrosarcoma (CSA) is the second most common type of bone cancer. Due to its resistance to chemotherapies and radiation, treatment for this malignancy relies on surgical resection alone, without effective options for patients with metastatic disease. Published literature supports NF-κB signaling as an integral pathway for cancer metastasis progression. IKK-16 inhibits IκB kinase, reducing NF-κB signaling, and thus may be used as a therapeutic target for treatment of advanced chondrosarcoma. Our lab has previously demonstrated the relevance of IKK-16 in chondrosarcoma, thus deciding to portray the efficacy of IKK-16 against chondrosarcoma in vitro. We hypothesize that IKK-16 can inhibit metastatic potential of CSA cells, minimizing tumor formation in vivo. To evaluate this hypothesis, we used the cell line 725, derived from human chondrosarcoma with known metastatic potential, in our metastatic mouse model. Luciferase labeled 725 cells were injected via tail vein with 150,000cells/animal. Mice were treated in two groups with intraperitoneal dosing of either 0.03mg/g of IKK-16 or vehicle control, three times a week. In Vivo Imaging System 200 (IVIS) was utilized at bi-weekly intervals to analyze pulmonary metastatic disease development until the study was terminated or humane endpoints arose. Data comparison involved IVIS fluorescence values at 7-8 weeks and a histological analysis of the lungs at the study endpoint. Statistical

significance was evaluated using unpaired t-test with Welch's correction. Results support our hypothesis that IKK-16 decreases CSA metastasis in vivo. Figure 1 shows the 7–8-week endpoint with the Average Maximum Radiance in the control being 5.67 x 10^4 photons/second, and 1.69 x 10^4 γ/sec in the treatment group (p=0.027). Figure 2 portrays a histological analysis with decreased tumor formation. No mice in the treatment group presented metastatic disease at the studies' final endpoint. In summary, NF-κB can be targeted using IKK-16 to inhibit metastatic disease. Future directions include pre-clinical testing for future development of clinical trials.

ABSTRACT NO. 50B

IDENTIFYING AND CHARACTERIZING CLINICALLY RELEVANT BREAST CANCER MODELS OF TUMOR DORMANCY

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Although outcomes have improved for breast cancer (BC) survivors, approximately 30% will eventually succumb to the disease upon locoregional or metastatic recurrence. For estrogen receptor (ER) positive patients, this can occur as many as 30 years post diagnosis with the likelihood of metastatic relapse remaining consistent each year. We previously demonstrated that certain dormant tumor cells maintain both epithelial and mesenchymal features, and can evade the adaptive immune system via induction of Tregs within the microenvironment. Thus, the aim of this study is to determine the universality of these findings and develop reliable models to further study dormant tumor-immune interactions. Syngeneic mouse breast cancer cell lines (D2.OR, TSAE1) were sorted to enrich for epithelial (CD104+) or mesenchymal (CD44+) phenotypes, confirmed via qRT-PCR and RNAseq. A dormancy reporter with non-functional p27 fused to mVenus was added by lentiviral transduction and 3D culture assays were performed by seeding tumor cells on a basement membrane extract. ER activity was assessed in 2D culture by qRT-PCR for ER response gene Greb1 after treatment with 4-hydroxytamoxifen (4-OHT); 3D culture cells were plated with increasing doses of 4-OHT or Fulvestrant. For in vivo studies, 500k cells were implanted into the mammary fat pad of female syngeneic Balb/c mice. In vitro 3D cultures and in vivo implantation demonstrated that the hybrid epithelial/mesenchymal tumor population was less proliferative than more mesenchymal cells from the same tumor. Treatment with 4-OHT reduced Greb1 mRNA expression, and 3D culture assays revealed that ER antagonism could inhibit colony growth. Finally, immunohistochemistry of tumors confirmed ER protein expression in vivo. Our studies suggest that dormancy-competent tumor cells indeed exist as an independent population with classical epithelial and mesenchymal expression patterns. Importantly, these cells respond to ER antagonism, which supports their usefulness as clinically-relevant models of tumor dormancy and delayed relapse.

ABSTRACT NO. 51A

INTEGRIN ALPHA 6 EXPRESSION AIDS BREAST CANCER ADAPTATION TO METABOLIC STRESS

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Metastasis to the leptomeninges, which can occur in multiple cancer types including breast and lung cancer, is highly lethal and has few treatment options. Previously, our lab discovered that bone-metastatic breast cancer (BC) cells that express the laminin receptor, integrin alpha 6, can metastasize to the leptomeninges by interacting with laminin on the abluminal surface of emissary vessels that stretch from the calvarial bone marrow down to the leptomeninges. In the leptomeninges, resident macrophages promote BC survival, but additional factors that support BC growth in the nutrient-poor microenvironment which is low in glucose but sufficient in oxygen remain to be elucidated. We hypothesize that BC in the hypoglycemic leptomeninges will shift from glycolytic to mitochondrial metabolic pathways to meet their energy demand for proliferation, and that integrin alpha 6 plays a role in this process.

We tested our hypothesis by culturing leptomeninges-homing 1833 parental and alpha6 knockout (KO) BC cells in high (serum level) or low (leptomeningeal level) glucose conditions. Although no differences are observed in the high glucose condition, Mitotracker staining shows that 1833 alpha6 KO cells had lower mitochondrial mass than 1833 parental cells in the low glucose condition. Coincidently, DilC1(5) staining shows that the mitochondrial membrane potential of 1833 alpha 6 KO cells decreases in the low glucose condition. Mitotracker confocal imaging and seahorse data consistently demonstrate that integrin alpha 6 KO increases mitochondrial fragmentation and decreases mitochondrial respiration. The parental cells showed no change in mitochondrial mass or membrane potential in high vs. low glucose. These results point to the importance of integrin alpha 6 expression in breast cancer adaption to the metabolic stress induced by the glucose-poor environment of the leptomeninges.

ABSTRACT NO. 51B

TLR7-ACTIVATED B CELLS PROMOTE LUNG FIBROBLAST ACTIVATION

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Background: Chronic graft-versus-host disease (cGVHD) is an autoimmune-like syndrome that occurs following hematopoietic stem cell transplantation. We have previously shown that allo-/autoreactive B-cells from patients with cGVHD are aberrantly activated through the B-cell receptor and through synergistic pathways including Toll-like receptor 7 (TLR7)1. In cGVHD B-cells, TLR7 hyperresponsiveness is mediated by increased expression and activation of the downstream transcription factor Interferon Regulatory Factor 5 (IRF5). In patients with cGVHD, TLR7-hyperactivated B-cells secrete increased amounts of IL-6 and TNFα, which we postulate may contribute to the development of cGVHD manifestations including fibrotic airway disease. Using a cGVHD mouse model, we have found IRF5+ B-cell aggregates clustered near collagen deposits around airways. Thus, we hypothesize that the TLR7-IRF5 axis promotes B-cell-mediated fibroblast activation and subsequent fibrosis through the secretion of soluble cytokine

mediators in cGVHD. The aim of this project was to elucidate the role of the TLR7 signaling axis in healthy B-cells on fibroblast activation.

Methods: Healthy B-cell receptor (BCR)-activated B-cells were stimulated through TLRs (R848; TLR7, CpG; TLR9, LPS; TLR4) and cultured in a transwell system with primary lung fibroblasts. After 72 hours, we examined IL-6 gene expression in fibroblasts (marker of fibroblast activation). In separate experiments, neutralizing antibodies against IL-6 and/or TNFα were added to transwells. To determine the effects of inhibiting B-cell IRF5 activity on fibroblast activation, B-cells were pre-incubated with the oligodeoxynucleotide MS19 prior to culture.

Results: Relative to unstimulated, TLR4-stimulated, or TLR9-stimulated B-cells, TLR7-stimulated B-cells promoted significantly increased expression of IL-6 in lung fibroblasts. Neutralizing antibodies to both IL-6 and TNFα attenuated fibroblast activation. Additionally, inhibition of B-cell IRF5 activation attenuated fibroblast activation after TLR7 but not TLR9 stimulation.

Conclusion: Our findings demonstrate that the TLR7-IRF5 axis promotes B-cell-mediated activation of lung fibroblasts.

ABSTRACT NO. 52A

INVESTIGATING THE EFFECTIVENESS OF DRUG CANDIDATES TARGETING SCHLAP1 IN BLADDER CANCER CELL LINES

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Metastasis is a major cause of cancer-related deaths. Metastatic spread is mediated by gene expression programs that promote migration and invasion. Among these pro-metastasis genes, Second Chromosome Locus Associated with Prostate 1 (SChLAP1) is a long non-coding RNA that is frequently overexpressed in prostate and bladder cancer and involved in tumor invasion and metastasis. As a result, SChLAP1 inhibition is a promising approach to prevent or delay metastasis of these cancers. To this end, we have identified a series of candidate RNA-targeting agents that selectively bind the 3D structure of SChLAP1. We evaluated the efficacy of these drug candidates at inhibiting migratory and invasive potential using scratch wound assays and invasion assays. The assay was imaged for 24 hours, every hour, to study the effectiveness of each drug therapy. An invasion assay kit was used to check the ability of drug candidates in preventing invasion. The expression levels of invasion related proteins, such as MMP-2 and MMP-9 were quantified through reverse transcription polymerase chain reaction (RT-PCR). Of the 3 lead compounds, one of the candidates demonstrated significant inhibition of wound closure speed in SChLAP1-expressing bladder cancer cells. Additional studies will include analysis of these lead compounds in invasion assays and in vivo models to support future clinical trials aimed at reducing or eliminating metastasis in SChLAP1-expressing cancers.

ABSTRACT NO. 52B

UTILIZING PROTEOMIC LOCALIZATION TO CHARACTERIZE SYNERGY OF XPO1 AND PROTEASOME INHIBITION IN OSTEOSARCOMA

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Osteosarcoma (OS) is a rare bone cancer affecting children and young adults that is often associated with a poor prognosis. Relapsed OS tumors are difficult to treat due to their ability to resist chemotherapy, driving a need to identify novel effective therapies. Using high throughput drug screening, our lab has identified the combination of exportin 1 (XPO1) and proteasome inhibition to be effective in chemotherapy-naive and -resistant OS, which has since been validated in cell line, organoid, and ex vivo pulmonary metastatic models. XPO1 shuttles cargo proteins, including tumor suppressor proteins (TSPs), from the nucleus into the cytoplasm and has been found to be upregulated in OS as well as negatively correlated with metastasis free and overall survival. Our goal is to characterize the mechanism by which combined XPO1 and proteasome inhibition synergize in OS. We hypothesize that combined XPO1 and proteasome inhibition enhances nuclear localization of key TSPs that would otherwise be degraded by the proteasome in the cytoplasm, thereby promoting apoptosis.

Proteomic assays, including western blotting and mass spectrometry, will be performed on nuclear and cytoplasmic fractions of 143b and 173x chemotherapy-naive and -resistant OS cell lines to determine localization of key TSPs following treatment with the XPO1 inhibitor, selinexor (SEL) and proteasome inhibitor, bortezomib (BRT) compared to non-treated cells and cells treated with each single agent. Protein abundance will be compared across nuclear and cytoplasmic fractions in triplicate to determine significant differential localization of proteins. Localization of established key TSPs, including p27 and IkB, will be validated by western blot. Understanding where these TSPs are localized post combination treatment can provide insight on the mechanism of treatment synergy as well as potential mechanism of resistance to dual XPO1 and proteasome inhibition in chemotherapy- naive and -resistant OS.

ABSTRACT NO. 53A

DEFINING THE ROLE OF POLIO-SPECIFIC T CELLS IN CLINICAL POLIO VIROTHERAPY

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Glioblastoma is the most lethal brain tumor in adults. Immunotherapy, whereby a patient's own immune system is leveraged to target malignant cells, offers potential to target highly heterogenous and refractory gliomas. One emerging approach to engage antitumor immune responses comprehensively is that of attenuated virotherapy. PVSRIPO is a recombinant polio:rhinovirus chimera that infects cells within the tumor microenvironment to engage innate and adaptive inflammation. Prior clinical trials demonstrated feasibility and safety of PVSRIPO, with a subset of patients with recurrent glioblastoma surviving >24-36 months. Importantly, pre-treatment polio-specific antibody titers (due to childhood vaccination against polio) were higher in long-term survivors of polio virotherapy. Moreover, pre-treatment herpes virus type I (HSV1) titers were higher in patients with glioblastoma treated with a

recombinant Herpes virus. Indeed, mice vaccinated against polio mount stronger antitumor responses to polio virotherapy. These observations indicate a critical role for pre-existing immunity in the antitumor efficacy of clinical virotherapy and support the use of 'recall' or reactivation of intratumor memory T-cell responses of pre-existing virus specific T-cell populations.

The goal of this study was to develop a protocol for measuring T-cell responses after stimulation with polio antigen to define their potential antitumor activities and determine whether polio-specific T-cell immunity associates with clinical outcomes after PVSRIPO therapy. To this end, in vitro T-cell stimulation assays were performed against polio antigens and relevant controls. Flow cytometry was used to assess positivity/reactivity to polio antigen and assessments of longitudinal cytokine secretion were used to determine the pattern and intensity of responses to polio antigen versus relevant controls. After optimization, this assay will be used to trace polio-specific T-cells pre- versus post-treatment, and to isolate polio-reactive T-cells for TCR sequencing to track their intratumor presence in pre- versus post-tumor tissue.

ABSTRACT NO. 53B

DEVELOPING AN IL-33 TOOLKIT TO EXPLORE INTRINSIC AND EXTRINSIC REGULATION OF TUMORIGENESIS IN MAMMARY GLAND

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Stromal-derived Interleukin 33 (IL33) acts as a nuclear alarmin, mediating both innate and adaptive immune responses while regulating tissue homeostasis, development, and tumorigenesis. IL33 is also a marker of epithelial cell plasticity suggesting non-canonical roles for IL33 driven by its nuclear localization and independent of its cytokine function. A major challenge has been the absence of suitable fluorescently traceable IL33 constructs for accurately analyzing cell behavior. Here, we report on the development of IL33 constructs that co-express the fluorescent protein LSSmOrange for visualizing Il33 expression and lineage tracing. Using SnapGene, we designed IL33 constructs, ordered synthesized fragments, and utilized In-Fusion and Gateway cloning techniques to generate recombinant plasmids. These constructs, full-length IL33, IL33 fused with a secretion signal (IL33-Sec), nuclear domain-only IL33, and cytokine domain-only IL33, were lipofectamine transfected into MM3MG cells and HEK Cells, then transfection efficiency was assessed via confocal microscopy. Transfected cells were fixed and stained on MatTek plates to first confirm IL33 subcellular distribution. Preliminary data demonstrate that full length IL33 is nuclear localized, and further data regarding different IL33 domains is currently under investigation. Currently, single cell cloning, and proliferation assays for MM3MG cells are being conducted to evaluate their effects. HEK cells will be used for ELISA and HEK Blue assay to analyze expression levels, stability, and biological activity. We aim to investigate IL33's impact on cellular senescence, proliferation, apoptosis, and other cancer hallmarks. Future directions include in vivo tracking of cells expressing different IL33 domains throughout mammary gland development and tumor progression. Understanding these mechanisms may clarify how IL33 influences the tumor-immune relationship and potentially enhance treatment strategies for breast cancer patients.

ABSTRACT NO. 54A

STRUCTURAL INVESTIGATIONS INTO THE DRUGGABILITY OF PLASMODIUM FALCIPARUM UBC13

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Plasmodium falciparum, the most lethal malaria parasite, continues to pose a significant threat to human health, despite advancements in treatment and mitigation strategies. Currently, artemisinin-based combination treatments (ACTs) are widely used to treat P. falciparum malaria; however, with rising cases of drug resistance, new treatment methods are urgently needed. Knockdown of PfUbc13 has been shown to sensitize the parasite to ACTs and significantly reduce parasite proliferation, suggesting that PfUbc13 is a potential drug target. PfUbc13, a ubiquitin-conjugating enzyme, functions in essential cellular processes, including protein degradation, cell cycle progression, and DNA repair. Subsequent disruption of these critical parasite pathways through chemical inhibition of Ubc13 shows promise for the development of new antimalarial therapies. The small molecule NSC697923 has previously been shown to inhibit PfUbc13 activity via binding at the catalytic cysteine; thus, we sought to solve the cocrystal structure using protein NMR. We expressed and purified recombinant N15-labeled PfUbc13, validated by mass spectrometry, and are optimizing production protocols for future studies. To identify novel inhibitors, we conducted in silico molecular docking studies in Schrödinger Maestro to assess potential inhibitors with varying chemotypes for selectivity of PfUbc13 over the human homolog by calculating binding affinity values. Additionally, we sought to determine druggable PfUbc13 lysine residues by employing assays with 2,4,6-Trinitrobenzene sulfonic acid, which quantifies reactive free amines in solution by monitoring products at absorbance 340 nm. Preliminary results from assays using lysine and proline as positive and negative controls, respectively, suggest that PfUbc13 contains several druggable lysine residues. Continued investigation into the nucleophilic sites of PfUbc13 and small molecules that covalently bind to them will provide critical insight into drug discovery efforts to combat malaria disease.

ABSTRACT NO. 55A

ELUCIDATING THE CONTRIBUTION OF HYPOXIA/HIF SIGNALING FOR SENSORY NEURON INNERVATION IN THE BONE AFTER RADIATION EXPOSURE

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Radiation therapy is a mainstay of treatment for multiple types of cancer. In patients receiving treatment to decrease tumor burden, radiation is especially effective due to its potential to alleviate debilitating bone pain from cancer. However, some patients fail to respond to radiation treatments and continue to suffer from bone pain, underscoring the need for improved options for these patients. Pain is detected by sensory neurons within the bone. The bone microenvironment is composed of a landscape with steep oxygen gradients in which tensions decrease from peripheral endosteal regions towards the central medullary cavity. Interestingly, hypoxia and active HIF signaling have been shown to promote nerve innervation. For these reasons, we hypothesized that hypoxia/HIF signaling will promote sensory neuron function in the bone after radiation exposure. We irradiated 11-week-old wild-type mice at various doses including total body and

single limb irradiation. Micro CT and histological analysis of the hind limbs revealed a reduction in trabecular bone volume and trabecular number, along with an increase in trabecular separation and deterioration compared to nonirradiated controls. Confocal analysis of the hypoxia marker pimonidazole revealed a conversion of homeostatic bone microenvironment to a more hypoxic niche. Collectively, our preliminary data has confirmed that irradiation causes a decrease in bone density and volume to bone. Intriguingly, we also demonstrated that radiation exposure results in changes to the homeostatic oxygen tensions and enhances the hypoxic bone microenvironment. These dynamic changes in the hypoxic bone niche may thus be associated with altered sensory axon distribution and function in the bone to regulate pain. In summary, these data suggests that radiation causes significant changes within the hypoxic gradients in the bone microenvironment, which decreases bone integrity, thus causing an increase in the likeliness of pain experienced by patients.

ABSTRACT NO. 55B

INVESTIGATING THE ROLE OF TOLEROGENIC DENDRITIC CELL PRODUCED PCSK9 ON T CELL CROSS-PRIMING AND ANTI-TUMOR IMMUNITY

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Dendritic cells (DCs) are antigen-presenting cells that play a crucial role in cancer immunity. Type 1 conventional dendritic cells (cDC1s) are particularly important for supporting anti-tumor immune responses. cDC1s migrate from the tumor to tumor draining lymph nodes where they recruit and activate cytotoxic T cells. However, DCs within the tumor microenvironment can become dysfunctional, resulting in immunosuppression and tumor progression. For example, tumor-released lactate can promote a mature regulatory DC (mregDC) transcriptional state with immunosuppressive qualities. mregDCs have increased SREBP2 activation, which leads to increased PCSK9 expression. In previous studies, genetically silencing tumor-expressed PCSK9 was shown to suppress tumor growth in a cytotoxic T cell-dependent manner. However, it is unclear whether mregDC produced PCSK9 contributes to their tolerogenic effects.

In this current study, we utilize an enzyme-linked immunosorbent assay (ELISA) to demonstrate that mregDCs express elevated levels of PCSK9 relative to other conventional DC populations. Flow cytometry further revealed that cDC1s treated with recombinant PCSK9 exhibit decreased activation markers, reducing their ability to stimulate cytotoxic T cells.

Our results demonstrate a potential mechanism by which tumor-associated mregDCs suppress immune function via PCSK9 expression. This research provides the foundation to further explore the mechanisms behind the recent success of anti-PCSK9 in oncology clinical trials. Future experiments aim to determine whether PCSK9 produced by the tumor or mregDCs has a greater impact on regulating anti-tumor immunity. Findings from these upcoming experiments may allow for the selection of patients expected to derive more benefit from anti-PCSK9 therapy.

ABSTRACT NO. 56A

EVALUATING RABL6 AS A DOWNSTREAM TARGET OF TTK IN NEUROENDOCRINE PROSTATE CANCER

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Neuroendocrine Prostate Cancer (NEPC) is one of the most lethal types of prostate cancer (PC) due to its occurrence after resistance to previous androgen receptor (AR) treatments. Since NEPC is AR-independent, there are no targeted therapies to treat NEPC. Our preliminary data suggest Threonine Tyrosine Kinases (TTK), is a potential target NEPC. Our preliminary data shows TTK expression is increased in NEPC and targeting TTK with small molecule inhibitors or genetically slows NEPC tumor cell growth. To identify TTK mechanisms, we conducted a phospho-proteomic study of NEPC cells targeted with two clinical grade TTK kinase inhibitors. Among the top differentially expressed phospho-peptides we found RABL6. Rab proteins are guanosine triphosphatases (GTPases) that function as molecular switches and regulate cellular trafficking. We found RABL6 is enriched in NEPC tumor cells and implicated in other neuroendocrine cancers. The goal of this study was to evaluate the role of RABL6 in NEPC and validate RABL6 as a TTK phospho-target.

Methods: We utilized PC cell lines LNCaP, DU145 and NCI-H660 cells. RABL6 expression was assessed across a panel of PC cell lines by western blot analysis. For genetic knockdown studies shRNA targeting RABL6 were utilized, and knockdown validated by western blot analysis. The effect of RABL6 on cell proliferation was evaluated by shRNA knockdown and Incucyte live cell imaging.

Results: We found RABL6 expression varies across PC cell lines and analysis from publicly available single cell-RNA-Seq show RABL6 is enriched in neuroendocrine cells. Western blot analysis shows we effectively knockdown RABL6 protein levels by shRNA. Reduced RABL6 expression coincided with reduced proliferation rates in DU-145 cells.

Conclusions and Future Directions: RABL6 is expressed in NEPC cells and is essential for NEPC cell proliferation. Further studies are needed to determine if TTK phosphorylates RABL6 and the consequence(s) of this post-translation modification is on RABL6.

ABSTRACT NO. 56B

OBJECTIVE REALITY STUDY: TESTING CHILDREN'S CAPACITY TO UNDERSTAND DIFFERENT PERSPECTIVES

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The ability to understand that different people hold perspectives different from our own is something humans develop, a concept known as theory of mind, is studied in the false belief task. By 4 years-of-age, children are able to pass the false belief task, but are they able to differentiate that other people's subjective realities might not align with their "objective" reality? Prior literature suggests children can understand and hold different perspectives, however, there is a gap in the literature of children's conceptualization of objective and subjective realities. The present study is a novel approach in the development of an understanding of objectivity naturalistically. This study aims to understand whether 3- to 5-year-old children can conceptualize the beliefs of others that contradict objective reality and how

these findings compare to the false belief task. In this study, children will be presented 6 different object related stories with 6 different conditions of beliefs (e.g., to dream, to imagine, to hope, having reason to, the false belief task and a control). We anticipate that 3-year-old children will be more likely to fail the false belief and objective reality tasks in comparison to older children meaning that we expect children will improve with development. The present study will make important contributions to understanding children's perspective taking in the field of developmental psychology which could benefit parents and educators in better approaching an array of situations such as conflict resolution and social situational awareness. It will also give researchers in the field more insight into theory of mind, an ability that is significant to the development of children.

ABSTRACT NO. 57A

EXPLORING THE ROLE OF INTERNEURONAL CALBINDIN IN HIPPOCAMPAL SEIZURE SUPPRESSION

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Current surgical and pharmacological therapies for epilepsy remain insufficient in fully correcting circuit abnormalities displayed in many epileptic patients. More recent alternatives have proposed transplantation of cortical inhibitory interneurons to combat uncontrollable excitation often displayed during seizures. Experiments using multi-electrode array have shown that mouse organotypic hippocampal slice cultures (mOHSCs) will exhibit seizure like activity by DIV 14. Interneuron transplants from the medial ganglionic eminence (MGE) have reduced seizure-like activity in mOHSCs by DIV 28. The mechanism driving this result remains unknown. One hypothesis proposes the upregulation and overexpression of calbindin. Calbindin is a calcium binding protein that buffers intracellular calcium levels. In neurons, calcium not only plays a role in neurotransmission, but it acts as a secondary messenger in many signaling pathways. Excess intra and extracellular calcium can disturb neuronal signaling as well as lead to mitochondrial death and neural apoptosis. Excessive apoptosis in inhibitory interneuron populations can cause excitatory-inhibitory imbalance and lead to seizures. Upregulation of calbindin in native interneurons may keep interneuron populations healthy, preventing seizure activity and excitatory-inhibitory imbalance. Experiments using mOHSCs are being developed to determine whether transplantation is driving calbindin upregulation and overexpression within native interneurons. Additionally, a strategy for inducing calbindin expression in mOHSCs without transplants involving a Cre-dependent virus with calbindin is being explored to further substantiate the role of calbindin in modifying epileptogenic circuits. Jointly, this exploration will help advance a mechanistic understanding of interneuron transplantation in animal models as well as illuminate calbindin's role in preventing seizure-like events to together aid the development of future therapeutic tools for seizures.

ABSTRACT NO. 57B

A SPATIOTEMPORAL ANALYSIS OF ENVIRONMENTAL FACTORS AMONG CONCURRENT DENGUE, ZIKA, AND CHIKUNGUNYA DISEASE OUTBREAKS IN 2016 CAMPINAS, BRAZIL

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In 2015-2016, Brazil experienced an outbreak of Dengue, Zika, and Chikungunya, three viruses spread by the yellow fever mosquito, Aedes aegypti. Like all mosquitos, Aedes aegypti's biologic development is mediated by environmental factors and geospatial variance, especially temperature and water sources. Additionally, Aedes aegypti are anthropophilic and highly adaptive to living in and near human dwellings; therefore, human-population density and behavior can affect transmission rates.

To further explore these relationships, Campinas, Brazil's third largest city, was examined for the first six months of 2016. Human case data for all three diseases were provided. Using ARCGIS Pro (ESRI, 2024), we overlaid a 400 meter hexagonal grid and aggregated all cases within. We then imported, converted, and aggregated environmental, climatic, and geographic layers. Analysis using the statistical program JMP (SAS, 2024) was performed to determine the importance of each variable to the spread of all three Aedes aegypti diseases and each one independently.

Preliminary results indicated that precipitation weeks before case documentation, area population, and urban land coverage were significant factors when looking at total disease transmission. Low temperatures combined with low precipitation tended to decrease the rate of all three diseases. Initially, cases appeared in the city center and reached more rural districts as time progressed. Dengue cases decreased as Zika cases increased, a trend documented in other outbreaks of these flaviviruses. Chikungunya less closely followed the patterns of Zika and Dengue, which could be due to fewer Chikungunya cases or differences between the types of viruses. Previous Chikungunya infection likely provides lifelong immunity, unlike Dengue and Zika, which can reinfect individuals.

Vector-borne disease outbreaks are heavily influenced by their environment. Temperature and precipitation significantly affect mosquito populations and therefore disease transmission. Understanding these relationships is crucial as weather patterns change globally, impacting disease ecology.

ABSTRACT NO. 58A

Understanding Complex Disease Genetics using Next-Generation CRISPR Tools

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Despite increasing diagnoses of schizophrenia (SCZ), the functional mechanisms of the disorder remain unsolved. Schizophrenia risk is influenced by many genetic factors that remain largely unknown. Through genome-wide association studies (GWAS), researchers have identified 287 genomic loci where common variation influences an individual's risk of developing schizophrenia. However, due to linkage disequilibrium, where variants in proximity are more often inherited together, GWAS can only pinpoint regions of relevant variants and not causal variants. Using prime editing—a technique able to install disease associated variants—we aim to characterize common variants in SCZ-associated GWAS loci. Our goal is to show prime editing's capabilities to

induce and characterize SCZ-associated variants in disease relevant cell lines, iPSCs and iNeurons, and develop an increased understanding of the role of common variation in schizophrenia risk. This study will showcase the effectiveness of this newfound technique and provide analysis that will lead to the development of superior medication and improved treatments for schizophrenia.

ABSTRACT NO. 58B

FROM DROPOUT TO RETURN: A MODEL OF TRANSFORMATIONAL RESILIENCE IN EDUCATION

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In American society, the term "high school dropout" carries negative assumptions about a person's character; namely, they left high school because they do not recognize the value of education. Yet, the reality, for many students, is that the decision to leave high school is the product of external circumstances, not a disregard for education. Of the students who leave school before graduation, about 50% eventually earn an equivalent diploma by completing a General Education Development (GED) program. It is those students' active decision to return to schooling that forms the basis of this study. To identify their reasoning, this study will employ focus group discussions with students in a local GED program. Our questions will center on the complex metacognitive processes that facilitate students' returns, while simultaneously exploring participants' memories of their high school education. Based on our pilot study findings, we expect a universal commonality to be the emergence of a newfound resilience that we have aptly named transformational resilience. Transformational resilience occurs when a person undergoes adversity, and, as a result, reflects on life, reconnects with primary values, and ultimately develops a more nuanced identity and a greater sense of self-efficacy. If our hypotheses for this theoretical model hold, findings will underscore the importance of recognizing personal values and exhibiting compassion towards past selves, which together prove the need for values-based goal-setting reflection and we suspect were absent in the participants' high school education. Ultimately, this study hopes to improve high school retention rates by promoting the integration of resilience-building strategies into the public education curriculum. If schools can successfully educate and eventually graduate their vulnerable students, social mobility within underprivileged communities becomes increasingly attainable.

ABSTRACT NO. 59A

IS THERE HYPERPHOSPHORYLATED TAU IN THE LOCUS CORULEUS OF RHESUS MONKEYS?

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Alzheimer's disease (AD) is the sixth leading cause of death in the US, with number of cases projected to triple by 2060. Current drugs aim to clear beta-amyloid plaques in the brain but are ineffective at stopping disease pathology. Thus, research is pivoting to focus on hyperphosphorylated tau (pTau), another hallmark of AD that may also be amplifying beta-amyloid plaques. pTau is first seen in the locus coeruleus (LC), a small structure in the brainstem, during early adulthood decades before AD symptoms arise. The LC innervates brain regions critical for memory, attention, and

higher cognition. These are also where the first cognitive deficits are witnessed in AD. Could the LC be responsible for spreading pTau and initiating AD? To answer this question, we use rhesus monkeys because they spontaneously develop tau pathology, amyloidosis, and cognitive decline consistent with early-stage AD in humans. However, it is not yet known whether rhesus monkeys have pTau in the LC, so we must first address this gap. Brainstem blocks containing the LC of two females and one male, ranging from early to late adulthood, were sectioned into 50 microns. Subsequently, immunohistochemical staining was conducted to tag for phosphorylation sites on tau seen in AD (threonine 181, serine 202, and serine 214) to visualize pTau. If pTau is found in the LC, we can corroborate that rhesus monkeys are a reliable model for studying AD, and explore whether the LC is responsible for spreading pTau. If there is no pTau, we can investigate possible mechanisms preventing pTau which can lead to potential treatment implications for AD.

ABSTRACT NO. 59B

EXPLORING THE RELATIONSHIP OF RELIGIOSITY AND COMPASSION AMONG BUDDHIST AND CHRISTIAN POPULATIONS IN THE U.S.

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Whether one is religious or not, compassion, the desire to care for others and alleviate their suffering, remains central to the human experience. Compassion can manifest in many ways, including donating, volunteering, and praying for sufferers in the world. Prior research has explored compassionate responses within religious groups. Most of this literature, however, has focused primarily on Abrahamic religions. By surveying Christians in addition to Buddhists, this study aims to extend research beyond Abrahamic faiths. We hypothesize Christians and Buddhists may vary in the ways they conceptualize, cultivate, and show compassion, specifically to different targets. In addition, we expect a positive correlation between religiosity and compassion. Christian and Buddhist participants (N=400) were recruited through an online platform. Participants completed a survey comprised of open-response questions and other self-reported measures on their perceptions of compassion, religiosity, and targets of compassion. The tendency to engage in compassion was measured by a behavioral task, where participants completed 9 trials of deciding between objectively describing victims of war or generating feelings of compassion for them. In previous studies, participants with higher religiosity were more likely to engage in compassion, confirming a positive link between religiosity and compassion. We are interested in investigating whether this association differs between Christians and Buddhists. Ultimately, by studying the association between religiosity and compassion, we can extract findings and apply them to our world today.

ABSTRACT NO. 60A

INVESTIGATING THE ROLE OF GERMLINE-SOMA HETEROCHRONY IN *CAENORHABDITIS ELEGANS* STARVATION-INDUCED TUMOR FORMATION

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Stress in early life can predispose humans and other organisms to disease. The nematode *Caenorhabditis elegans* enters larval arrest to survive early-life starvation when hatched in the absence of food and returns to normal development once food is provided. In recovered adults, extended larval arrest leads to the development of gonad tumors and other reproductive abnormalities. Several critical genetic pathways regulate the formation of this phenotype, including insulin signaling, Hh signaling, and lipid metabolism. However, the direct cause of starvation-induced reproductive abnormalities is unknown. Previous research has demonstrated that early-life starvation can disrupt developmental synchrony between the soma and the germline. Germline-soma heterochrony can contribute to tumor formation and abnormalities in cell division through disruption of GLP-1/Notch signaling that drives germ cell proliferation. We hypothesize that germline-soma heterochrony during development following prolonged larval arrest causes aberrant germline-soma signaling that generates gonad tumors. We therefore chart the rate of somatic and germ cell divisions in both starved and fed larvae and identify whether those with germline-soma heterochrony have an increased risk of developing gonad tumors. We expect that starved animals will exhibit a greater delay than fed animals in germline development relative to somatic development and that animals with heterochrony will develop more reproductive abnormalities. Following this stage of the project, we will explore whether relevant signaling networks decrease the prevalence of heterochrony and reproductive abnormalities. Our results will highlight the role of starvation in inducing germline-soma heterochrony. Overall, we hope to illuminate the mechanism of extended starvation and subsequent larval arrest resulting in germline tumor formation in *C. elegans*, expanding understanding of the consequences of early-life stress.

ABSTRACT NO. 60B

READING THE RIPPLES: AN ENVIRONMENTAL HISTORY APPROACH TO BALANCING ACCESS AND CONSERVATION IN THE NATIONAL PARKS

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Visited by hundreds of millions every year, America's National Parks System is a much-beloved project closely tied to our national character and collective appreciation of nature. However, when the Organic Act of 1916 first established the National Parks Service (NPS), it contained a contradiction; the NPS was created "to provide for the enjoyment of [national parks, monuments, and reservations] in such manner and by such means as [would] leave them unimpaired for the enjoyment of future generations," a paradox encouraging both preservation and widespread use. Now, as many National Parks experience overcrowding and conflicting policy priorities, we must acknowledge the shortcomings of the agency in meeting those stated aims. Early Park management prioritized access and visitation as essential components of democratic participation in nature, often without adequate consideration for ecological consequences or long-term sustainability. Since then, both internal debate and external pressure have caused significant changes to the structure,

management, and overall objectives of the Parks Service, calling into question if current NPS policy aligns with its original ambitions. Using the lens of environmental history, this research will contrast founding documents and legislation from the NPS with visitation records and economic impact datasets to interrogate how successfully it has pursued its goals. By understanding the ideological, political, and managerial decisions that shaped the parks, we seek to uncover the root causes of overcrowding and identify effective solutions. In doing so, this research will offer insights into how past decisions continue to influence overcrowding issues today and underscore the importance of adaptive management strategies that balance visitor experience with conservation imperatives. We hope that by learning from historical successes and failures, policymakers and NPS officials will be better equipped to navigate the complex challenges of overcrowding while safeguarding the ecological integrity and cultural value of the National Parks for future generations.

ABSTRACT NO. 61A

THE EFFECT OF CONCEALED FIREARMS PERMITS ON GUN DEATHS IN UTAH

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Firearm prevalence and its impact on social harm remains a critical public health issue. This research investigates how firearm availability affects mortality in Utah, using concealed handgun permit counts to measure gun prevalence. We hypothesize that county-level increases in permits issued lead to more gun deaths, through a greater supply of guns in circulation and not securely stored so readily available for use by owners and subject to theft or loss. We collected data on concealed firearms permits issued, population demographics, and economic conditions in Utah counties. Our main analysis sample consisted of annual data from 2001–2020 for the 12 largest counties, comprising 93.7% of Utah residents. The relationship between gun deaths and permits issued was estimated using two-way fixed effects linear regression, which adjusts for the influences of factors that are invariant within counties or years along with variables such as population size, concentrations by race, ethnicity, gender, and age, and economic indicators. The estimated relationships between gun deaths and permits issued are positive and statistically significant, corresponding to elasticities of 0.43 overall, 0.37 for suicides, 0.64 for homicides, and 0.42 for accidents. Comparable elasticities for non-gun deaths, overall and separately by cause, are much smaller and highly insignificant. These results held true controlling for linear, quadratic, or cubic county-specific gun death trends, omitting demographic and economic controls, altering the sample to include only the six counties with populations above 1 million or all 15 counties with median or above population, and controlling for gun sales proxied by federal firearm background checks submitted in conjunction with gun purchases. The findings support our hypothesis, indicating that greater gun availability contributes to increased social harm from gun mortality. These insights are crucial for policymakers aiming to develop effective strategies to enhance public safety and reduce gun violence.

ABSTRACT NO. 61B

SHADES OF LATINO IDENTITY: ETHNICITY VS. RACE, SKIN COLOR, AND DISCRIMINATION

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When asked, "What is your race?" many Latinos face a dilemma: is Latino a race or an ethnicity? Despite the lack of consensus, current demographic forms list Latino only as an ethnicity, which creates an institutional form of social exclusion and threatens one's sense of belonging. This study explores how Latinos perceive their identity in the context of demographic forms, skin tone, and experiences of discrimination. Participants, both children (N=72) and their parents (N=43), were asked to state their preference for a demographic form that listed being Hispanic/Latino as a race versus an ethnicity. Participants then self-reported their skin tone based on a range of Crayola Multicultural Crayons and answered questions about past experiences with discrimination. Results showed that participants overall had a slight preference for forms listing Hispanic/Latino as a race, especially among parents with more experiences of discrimination. However, there were no significant differences in skin tone among children and parents who chose the race vs ethnicity form. This is possibly due either to the lack of color variability in the Crayola stimuli or to difficulties children have in assessing their own skin tone. To address this limitation, using the recorded video sessions, we are reanalyzing skin tone using a wider range of shades. In sum, providing evidence to support the use of more inclusive demographic forms is critical for groups like Hispanic/Latino individuals. Racial-ethnic categorization shapes how individuals are perceived by institutions and society, thereby impacting their access to resources, opportunities, and lived experiences. With this study, our hope is to improve how identities are articulated on demographic forms while also providing insights into the complexity of the Latino identity more broadly.

ABSTRACT NO. 62A

CATALOGING ORAL HISTORIES OF INDEPENDENT COMIC CREATORS IN DURHAM

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Our project explores the independent comics scene in Durham while highlighting their contributions to the local community and the broader arts scene. These comics are alternatives to mainstream superhero comics and remain relatively unexplored locally. To understand what makes creating independent comics in Durham different, we are cataloging oral histories of independent creators and community members. Using ethnographic methods such as oral interviews, both in person and on Zoom, we document people's stories to gain an understanding about the local independent comics community. Our interviews have generated a host of considerations surrounding gender identity, the intersection between the personal and the political, and the ableness and affordability of the city which point to larger themes of space, place, and identity. As the comics community acts as a microcosm for the larger arts community, a common theme has been visibility. Many of our conversations center around two main ideas: One, the sheer number of artists in Durham, given its population size is surprising and inspiring; and two, despite a smaller community, their work often remains unknown outside their circle which creates a feeling of being unacknowledged. Despite these challenges, many are optimistic about the future

of comics creation in Durham. Going forward, we will document additional oral histories to develop a more robust set of data surrounding the Durham independent comics community. We will also house the interview transcripts at the Durham public library and create a zine highlighting shared themes from our interviews to give back to the public.

ABSTRACT NO. 62B

FEMALE IMMIGRANT ENTREPRENEURSHIP THROUGH AN ECONOMIC LENS

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Immigration is rising around the world, making it essential to understand what immigrants do after arriving in a new country. Immigrants often select entrepreneurship, for reasons such as integration and job scarcity, contributing to economic growth in countries. My research aims to examine female immigrant entrepreneurship because it is an understudied area of immigrant entrepreneurship. Previous research has shown that immigrant entrepreneurship is a male-dominated field where a gender gap exists, which can lead to layered disadvantages for female immigrant entrepreneurs. I conduct a literature review of empirical economic articles to further identify patterns, debates, and gaps. One key theme in this review is female immigrant entrepreneurs' access to specific resources—such as financial capital, human capital, and social capital—compared to male or native entrepreneurs. Among other gaps, there is an evident lack of research on the performance of female immigrant entrepreneurs. My next steps involve utilizing these findings on gaps and patterns to guide data analysis of national and international datasets. To begin, I compose descriptive statistics of 10 key variables of the Global Entrepreneurship Monitor Adult Population Survey. Through future data work, I expect to find relationships between female immigrant entrepreneurs and various factors that can help inform policy to effectively support female immigrant entrepreneurs.

ABSTRACT NO. 63A

CLUSTERED VASCULAR ENDOTHELIAL GROWTH FACTOR NANOPARTICLES BIOMATERIAL FOR THE TREATMENT OF MOYAMOYA DISEASE

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Cerebrovascular ischemia caused by moyamoya disease, poses a significant threat to neurological function. This condition often arises from the narrowing or blockage of cerebral arteries. Addressing the complex nature of cerebrovascular ischemia requires innovative therapeutic strategies, and one promising avenue involves the utilization of hydrogel biomaterials infused with Vascular Endothelial Growth Factor (VEGF). Hydrogels, due to their water-absorbing properties and ability to mimic the extracellular matrix, offer an ideal platform for controlled delivery of VEGF. By incorporating VEGF within hydrogel matrices, we aim to enhance the local concentration and controlled release of this growth factor, promoting angiogenesis, fostering tissue repair, and ultimately improving neurological outcomes. This approach holds the potential to revolutionize the treatment landscape for this debilitating condition by providing a targeted and effective means of restoring cerebral blood flow using minimally invasive procedures. Using therapeutic angiogenic biomaterials, such as hyaluronic acid (HA) gels, either with or without

Vascular Endothelial Growth Factor (VEGF), leads to substantial enhancements in cellular populations, including endothelial cells, and improved blood flow in mice with forebrain ischemia. We hypothesize that the use of such treatments will lead to an improvement in behavioral outcomes in spatial learning following a dual procedure involving unilateral internal carotid artery (ICA) occlusion and contralateral ICA stenosis, a surgical model mimicking the ischemia caused by moyamoya disease.

ABSTRACT NO. 63B

MOLECULAR EVIDENCE FOR THE ROLE OF OLFACTION IN ANTBIRD FORAGING

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Olfaction is a sense critical to the survival and reproduction of organisms. In vertebrate species, olfaction is predominantly mediated by a large family of odorant receptors (ORs), a class of transmembrane G-protein coupled receptors expressed in olfactory sensory neurons. Most studies on vertebrate olfaction have focused on mammals, with little attention given to birds, who were thought to rely more on senses like vision. However, behavioral studies suggest that several birds use olfaction in behaviors like foraging and kin recognition. One example is the antbirds (Aves: *Thamnophilidae*), a family of more than 230 species found in tropical Central and South America. Several species of antbirds follow army ant Eciton burchellii raids to prey on small fleeing invertebrates at the front of the raid. E. burchellii colonies move daily and are found on the forest floor, making them difficult to detect by sight. Preliminary behavioral studies suggest antbirds can locate ant raids via detection of ant-related odors, but there are no molecular-level studies investigating antbird ORs. To efficiently screen odorants that may activate antbird ORs, we created antbird consensus ORs, engineered ORs based on consensus amino acid residues of the native ORs, to avoid testing each of the hundreds of native ORs. We performed a literature search to identify compounds found in ant secretions and exposed the antbird consensus ORs to these odors. We found some consensus ORs responded to *E. burchellii* secretions such as geranylacetone and S-2-heptanol, which is consistent with the hypothesis that antbirds can smell *E. burchellii*. Our research provides insight into the ecology of antbirds alongside *E. burchellii*, an important keystone species. To conclude, our results advance bird olfaction research, a historically neglected field, and open up new possibilities for behavioral studies with antbirds and similar experiments on other birds who forage for sparsely located resources.

ABSTRACT NO. 64A

INVESTIGATING UBE2A MUTATIONS IN NASCIMENTO SYNDROME THROUGH UBIQUITINATION PATHWAY ANALYSIS

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Nascimento Syndrome is a rare and poorly understood intellectual disability that is linked to the x chromosome, and as a result, mostly affects males. Common symptoms include severe speech impairment, dysmorphic facial features, depressed nasal bridges, skin abnormalities, and more. Mutations on one specific gene – called UBE2A – has been identified as an underlying cause of the disease. UBE2A is a ubiquitin-conjugating enzyme or E2, that catalyzes the transfer of ubiquitin to protein

substrates, in a process known as ubiquitination. Ubiquitination provides a pathway for the degradation of proteins, which is important for protein regulation within the cell, along with other processes. Previous research has demonstrated that a mutation in position 128 of the UBE2A gene causes an amino acid substitution from glutamic acid to a premature stop codon, leading to the elimination of important terminal sequences. Hence, indicating a potential causation for the disease. This project aims to establish a greater understanding of the cause of the disease by experimenting with different mutations of UBE2A. Specifically, we aim to test whether the mutated versions of the gene retain their function as E2 enzymes during the ubiquitination process. To further investigate, we are using several techniques, including DNA cloning to construct the mutants, chromatography to isolate the proteins, and western blotting to visualize our results. We hypothesize that a difference in the functionality of the UBE2A gene will be observed, which aligns with previous publications and further supports these specific mutations as the cause of Nascimento syndrome. The implications of this process can lead to a better understanding of ubiquitin, the role it plays in the body, and possible treatments for Nascimento, and other diseases with similar, underlying causes. Our results can also provide further understanding of E2 enzymes and their functionalities during different body processes.

ABSTRACT NO. 64B

IMMIGRANT ENTREPRENEURSHIP: THE NATIVE-IMMIGRANT DIVIDE

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As migration rates rise, immigrants are continually increasing their participation in economies around the world. Our research seeks to hone in on one dimension of their activity: entrepreneurship. Through a wide-ranging literature review and future data analysis, we compare the behavior of immigrant and native entrepreneurs and identify differing characteristics between their businesses. A review of empirical studies revealed some common trends: immigrant-owned firms tend to be smaller than their native counterparts and more productive, innovative, and transnationally oriented. The available research likewise emphasized the importance of social capital among both types of entrepreneurs. Individual articles included in the review also introduced strong evidence for the relative advantages of more diverse entrepreneurial teams, behavioral differences between groups impacting their entrepreneurial intentions, and the strong influence of economic, sociocultural, and institutional factors in influencing differences in entrepreneurial activity among immigrants and natives. Our next steps involve engaging in further literature review to verify and expand upon these findings. We are also engaging in data analysis to target identified gaps in the literature, beginning with a dissection of the 2020 Global Entrepreneurship Monitor (GEM) Adult survey. Some understudied areas of interest thus far include analyzing specific policy impacts, fundraising performance, success and failure rates of new ventures, and a better understanding of specific factors that spur entrepreneurship. Our research seeks to

enhance the conversation surrounding this critical dimension of the immigrant experience that has an outsized impact on economic growth and job creation. By better understanding native-immigrant differences in this field, we hope to inform policy that seeks to support entrepreneurial activity across all groups.

ABSTRACT NO. 65A

THE REACH OF THE CARCERAL STATE: EXAMINING THE ROLE OF COMMUNITY SUPERVISION ON RACIAL DISPARITIES IN INFANT MORTALITY

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Black White disparities in infant mortality (the death of children under one year of age) are a critical public health concern that cannot be explained by racial differences in the health and health behaviors of mothers. In 2020, the black infant mortality rate was estimated at 10.4 infant deaths per 1,000 live births, as compared to a rate of 4.4 for white infants. An increasing body of research has examined the role of social factors in driving these disparities. Researchers have begun to examine the criminal legal system, particularly mass incarceration, as a social determinant of racial disparities in health, including infant health. Research has shown that communities with higher rates of incarceration are accompanied by higher rates of adverse infant health outcomes. However, this work has mainly focused on jail and prison incarceration and has not captured critical parts of the carceral state – such as community supervision. Community supervision includes probation and parole. Probation is an alternative to incarceration issued at the initial sentencing. Parole is a period of community supervision following conditional release from incarceration. In 2022, more than two-thirds of those under correctional supervision were under probation or parole with probation being the leading type of correctional control. Research has found that individuals on probation and parole have a mortality rate that is estimated to be two to three times greater than that of the general population. These individuals tend to experience higher rates of substance abuse, physical and cognitive disabilities, economic disadvantage, and limited healthcare access, all contributing to their greater mortality risk. The aim of this project is to better understand community supervision as a social determinant of infant health disparities.

ABSTRACT NO. 65B

IDENTIFYING NEW TARGETS OF SALMONELLA INDUCED GSK3 TYROSINE PHOSPHORYLATION

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Non-typhoidal *Salmonella enterica* causes approximately 1 million cases of gastroenteritis annually in the United States, resulting in the highest morbidity rate among all foodborne illnesses. *S. enterica* depends on secreted protein effectors to hijack host cellular functions and enable further bacterial infection. We previously discovered that the protein effector SarA (Salmonella anti-inflammatory response activator) is required for phosphorylation of the transcription factor STAT3 and leads to increased production of the anti-inflammatory cytokine IL-10 (interleukin-10). SarA facilitates phosphorylation of STAT3 through binding of GSK3 (glycogen synthase kinase-3). This interaction alters the amino acid specificity of the serine-threonine kinase GSK3 to phosphorylate a tyrosine in both SarA and STAT3,

inducing an anti-inflammatory effect in host cells. We hypothesize that the conversion of GSK3 to a tyrosine-directed kinase will result in the phosphorylation of additional proteins that GSK3 does not typically target. We will use mass spectrometry to analyze what proteins are phosphorylated during overexpression of wild type and mutant SarA. Based on these results, we plan on conducting further analyses through GSK3 knockdown, inhibition, or purification, to determine the direct cause of protein phosphorylation. The conversion of GSK3 to a tyrosine-directed kinase by SarA allows a bacterial protein to reprogram host cell signaling and create a beneficial environment for bacterial infection. Understanding novel GSK3 phosphorylation of other tyrosines will help to uncover SarA's role in *S. enterica* pathogenicity and its effects on the host cell. Furthermore, studying SarA's manipulation of GSK3 may reveal new pathways and biological processes where GSK3 could play a role, such as cell signaling and bacterial replication, and advance knowledge of how kinase-substrate interactions are modified.

ABSTRACT NO. 66A

THE PSYCHOLOGY OF COMPASSION FOR SUFFERING: A CROSS-RELIGIOUS STUDY OF BUDDHIST AND CHRISTIAN PERSPECTIVES

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Compassion, the capacity to comprehend and care for another's emotions, including suffering, is a prevalent motif in religious traditions. While humans often face the choice to extend compassion in response to suffering, previous studies have shown how this choice involves cognitive and emotional costs. This cross-religious study of Buddhists and Christians examines how different religious identities and beliefs influence compassion for suffering. We hypothesized that Buddhists may find compassion less cognitively costly and show greater compassion towards animals compared to Christians. An online survey was administered to 200 Christians and 200 Buddhists who have self-identified with their faith for at least 5 years. Participants completed an 18-trial behavioral task to measure whether they wanted to "care" (engage in compassion) or "describe" images of suffering war victims. They then reported their level of concern for the person in the picture. Analyses will assess the influence of different religious teachings, practices, and traditions on 1) the cost of compassionate behavior and frequency of choosing to "care," and 2) compassion towards animals. Understanding these influences sheds light on how religious contexts affect responses to suffering, applicable to daily distress, war, and other tragedies, offering insights into why people choose to act compassionately—or avoid doing so.

ABSTRACT NO. 66B

SYNAPSE STARGAZING: HIGH RESOLUTION MICROSCOPY TO INVESTIGATE ASTROCYTE-DENDRITIC INTERACTIONS

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Astrocytes and microglia, two primary glial cell types of the central nervous system, play many essential roles in maintaining neuronal health, namely regulating synaptic function and providing neuronal support. Although astrocytes and microglia are functionally distinct, both are important in mediating neuroinflammation, and

interglial communication is a growing field of interest in relation to neurodevelopment and synaptogenesis. Understanding how glial cells and neurons interact with one another at the synapse is of particular interest due to the vast implications of these interactions in learning, memory, and neurological disease.

Here, we describe a novel approach using a triple-viral technique to map dendritic spines of ventral hippocampal neurons and astrocytes in contact with those dendrites in fixed tissue. We inject a Retrograde-CRE virus into the medial prefrontal cortex (mPFC) and a viral cocktail of floxed Flying Spaghetti Monster and GFAP-Lck-GFP into the ventral hippocampus (vHPC). This results in specific transfection of vHPC neurons projecting into the mPFC, which then express cytosolic FLAG protein, allowing for precise visualization of dendritic morphology. Immunofluorescent staining of Lck, FLAG, and Iba1 proteins facilitates high-resolution confocal microscopy imaging of entire astrocytes, microglia, and dendritic structures. Confocal data is then analyzed using Imaris analysis software. A surface-building tool enables three-dimensional reconstruction of astrocytes and microglia, and a filament tool traces the morphology of dendritic shafts and spines, allowing for precise measurements. This may aid in understanding functional interactions between glia and neurons across neurological circuits, such as the mPFC-vHPC axis.

Ultimately, this methodological approach may, not only enhance our understanding of glial interactions, but also provide insights into how they influence synaptic function and plasticity. This approach has the potential to introduce numerous new areas of study in neurological disorders where glial dysfunction is implicated.

ABSTRACT NO. 67A

SYNTHESIS OF REV-1 INHIBITORS TO OVERCOME CHEMORESISTANCE TOWARD CISPLATIN TREATMENT

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Cancer has a longstanding prevalence as it is the second leading cause of death globally with 1 in 5 people developing this disease during their lifetime. Great research efforts have been paid toward developing chemotherapeutics that induce DNA damage in cancer cells, inhibiting tumor progression. While chemotherapeutics such as cisplatin and carboplatinum have shown initial success in the treatment of bladder, testicular, and ovarian cancers, chemoresistance is an emerging problem. Evolutionarily, cells have developed tolerance mechanisms to combat DNA damage. Translesion DNA synthesis (TLS) is a tolerance mechanism that allows DNA polymerase to bypass DNA lesions, promoting chemoresistance. The Rev1 protein plays a critical role in the TLS pathway. Previous work developed the JH-RE-06 compound, the first TLS inhibitor to slow cancer development in mouse models when coupled with chemotherapeutic treatment (cisplatin). While effective, the JH-RE-06 compound is unsuitable for human therapy as it contains a nitro group, a structural alert in medicinal chemistry. Nitro moieties are metabolically unstable as they undergo rapid reduction to form a nitroso moiety which can oxidatively damage DNA and is thus toxic to humans. There are well-studied bioisosteres for the nitro group such as the pyridine, carboxylate, and nitrile groups. The nitrile moiety is a well-established isostere of the nitro moiety as they are both small, moderately polar, and hydrogen-bonding acceptors. At present, a bioisostere of Rev1 inhibitors is synthesized in which the toxic

nitro moiety is replaced with a nitrile moiety. The general synthetic route from previous reports was followed with slight modification. After the bioisostere was synthesized, an ELISA assay tested the newly synthesized inhibitor coupled with cisplatin (chemotherapeutic) to determine the efficacy of the Rev1 inhibition. Ultimately, this study investigates a bioisostere of the current JH-RE-06 Rev1 inhibitors to combat chemoresistance in humans.

ABSTRACT NO. 67B

ONLINE DICTIONARY OF ART HISTORIANS OF WESTERN ART

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Art historians employ various methodologies to approach art objects and disseminate knowledge, leading to differing degrees of recognition within the field. Art historiography is the study of the history and methodology of art history as a discipline. There are existing books on art historiography that examine the course of art history and name major art historians. However, these books often have limitations: 1) a short time span; 2) biased sources; 3) a lack of connections between included historians. To address these issues, we propose creating an inclusive, scholarly online database accessible to both researchers and the general public. We began by indexing historians cited in major art historiographies and expanded by including those mentioned by them. By collecting and synthesizing primary and secondary sources, we categorized historians, wrote biographical entries, and created a web of relations between art historians using hyperlinks. Part of my project includes James D. Breckenridge, an art history professor at Northwestern University. Though he was an authority on antique portraiture and numismatic motifs, his information can only be found in an physical archive at Northwestern. The value of our project lies in finding and cataloging people like Breckenridge, offering scholars a vital resource in the historiography of art history. Furthermore, we aim to include marginalized art historians, such as female and Black scholars, to create a more diverse and equitable representation within this traditionally white-male-dominated discipline.