2026 NORTH CAROLINA POSTDOC RESEARCH SYMPOSIUM

JUNE 12TH, 2026

NORTH CAROLINA BIOTECHNOLOGY CENTER

ABSTRACT BOOK

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Agenda

2026 Postdoc Research Symposium		
Start	**End**	**Session**
9:00	09:30	Registration & Poster Setup
09:30	09:45	Welcome/Opening Remarks
09:45	11:00	Postdoctoral Scholar Flash Presentations
11:00	11:15	Break
11:15	12:00	Poster Session A
12:00	1:00	Lunch & Networking
1:00	1:45	Poster Session B
1:45	2:45	Concurrent Panel Session
2:45	3:00	Break
3:00	3:45	Keynote Address
3:45	4:00	Final Remarks and Prize Winners

PANELS

Academic Panel | Exploring Opportunities in Faculty Life Across Institution Types

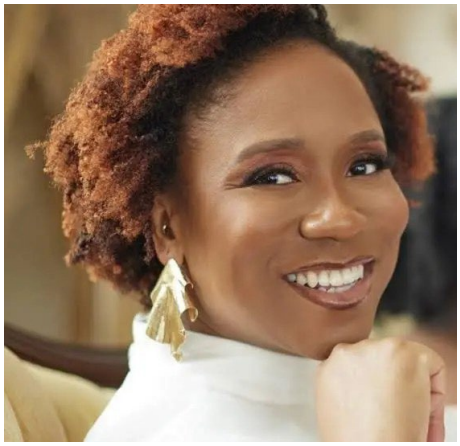
Many postdocs dream of becoming a professor or PI, but most have limited exposure to the different types of opportunities that exist outside of research-intensive universities. This panel will address the distinctions between R1s, R2s, and community colleges, with special attention paid to the expectations around research, teaching, and service at each type of institution. Showcasing faculty members from Eastern Carolina University, UNC Chapel Hill, Wake Forest, and Wake Technical Community College, this panel will equip attendees with a fuller understanding of the diverse, day-to-day experiences of faculty members to help them navigate their own pathways to the professoriate.

MODERATOR:

Dr Kylie R.J. Seltzer, PhD is a Postdoc in Residence in the Office of Postdoctoral Affairs at UNC-Chapel Hill, where she develops and facilitates professional development programs that support postdoctoral scholars in career growth, leadership, and community building. She is also Chair of the Advocacy Committee for the National Postdoctoral Association, contributing to national conversations around postdoctoral training and support. As a postdoctoral fellow with Carolina Public Humanities, Kylie has designed and led community-engaged initiatives that connect research with broader public audiences. She earned her PhD in History of Art and Architecture from the University of Pittsburgh, where her research explored the intersection of scholarship, culture, and public engagement. Kylie's work reflects her passion for building partnerships across higher education and community organizations to create impactful programs that support emerging leaders.

PANELISTS:

Dr. Kristin Z. Black, Department of Maternal and Child Health, UNC Chapel Hill

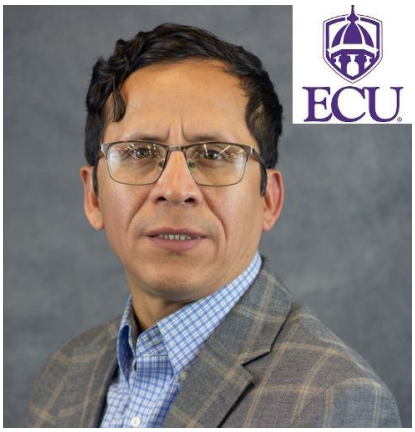


Kristin Z. Black, PhD, MPH, is an Assistant Professor in Maternal and Child Health at the UNC Gillings School of Global Public Health and a former NIH-funded Cancer Health Disparities Postdoctoral Fellow. Her research uses community-based participatory methods, mixed methods, and racial equity frameworks to address reproductive health and chronic disease inequities. She studies the links between maternal health and chronic disease, factors affecting access to and experiences within maternal healthcare, and community-driven strategies to reduce structural racism and health disparities. Dr. Black also serves in leadership roles focused on advancing maternal, child, and health equity outcomes.

Dr. Jackie Swanik, Mathematics and Science Division, Wake Forest Community College

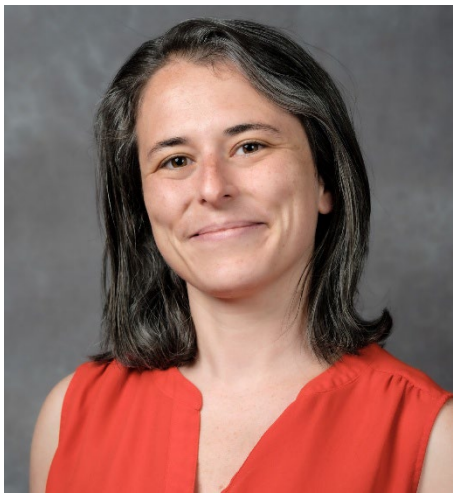
Dr. Jackie Swanik is Dean of Mathematics and Sciences at Wake Technical Community College and principal investigator of a National Science Foundation–funded study examining how undergraduate research participation influences graduation rates and belonging in STEM among community college students. Raised in rural North Carolina, Jackie earned a biology degree from Campbell University and a PhD in Biology from the University of Texas Southwestern Medical Center. After completing the SPIRE Postdoctoral Program at UNC–Chapel Hill, Jackie developed a strong commitment to student success. Since joining Wake Tech in 2009, Jackie has advanced through multiple academic leadership roles while championing excellence in science education and student achievement.

Professor Juan Beltran-Huarac, Department of Physics
Eastern Carolina University



Dr. Beltran Huarac is an Assistant Professor in the Biomedical Physics Program within the Department of Physics at East Carolina University. His research focuses on designing magnetic field-responsive nanomaterials with tailored properties for biomedical imaging and therapeutic applications. A key area of his work involves developing advanced magnetic nanoplatforms as MRI contrast agents to improve disease detection, diagnosis, and treatment monitoring. He also investigates magneto-mechanical actuation as a minimally invasive approach to cancer therapy. His interdisciplinary research integrates nanotechnology, biomedical physics, biology, and materials science to advance precision medicine. Dr. Beltran Huarac has published extensively and is dedicated to mentoring researchers at all academic levels.

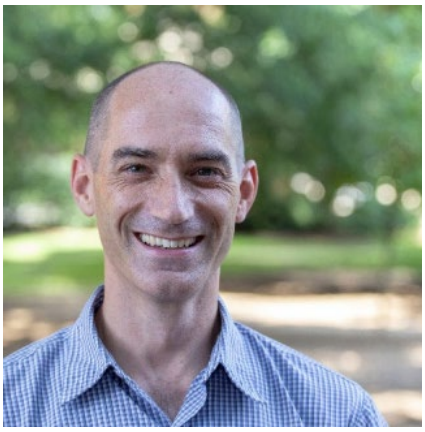
Professor Veronica Cole, Department of Psychology, Wake Forest University



Dr. Veronica Cole is an Assistant Professor of Psychology at Wake Forest University. She earned her psychology degree from UNC Chapel Hill in 2017 and completed an NICHD-funded postdoctoral fellowship at the Center for Developmental Science at UNC. Her research bridges quantitative and developmental psychology, focusing on adolescent psychopathology through advanced statistical and latent variable modeling approaches. She studies methodological issues in mixture models, integrative data analysis, and the measurement of psychological constructs such as substance use, mental health symptoms, and social connectedness. Supported by NIH, NSF, and the William T. Grant Foundation, she also teaches research methods, developmental psychology, and statistics while mentoring students.

Industry Panel | Navigating Careers Outside Academia

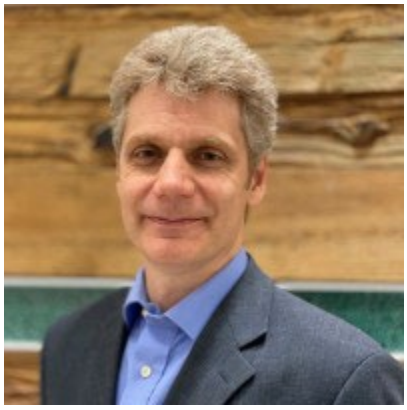
MODERATOR: Patrick Brandt, PhD Senior Director of Career Development and Science Outreach, School of Medicine, UNC-Chapel Hill



Dr. Patrick Brandt is Senior Director of Career Development and Science Outreach at UNC-Chapel Hill and Director of the TIBBS Program (Training Initiatives in Biomedical and Biological Sciences). He leads efforts to support graduate students and postdocs as they prepare for diverse scientific careers, with a strong focus on transitions beyond academia. Patrick directs the ImPACT internship program and the Certificate Program in Translational Medicine, both of which provide hands-on experience and professional development opportunities. He is passionate about helping trainees identify career goals and gain the skills and confidence to pursue them. Patrick earned his PhD in Biochemistry from the University of Rochester and completed postdoctoral training at the National Institute of Environmental Health Sciences. https://www.linkedin.com/in/patrickdbrandt/

PANELISTS:

Joerg Bauer, PhD, Head of Global R&D Seed Treatment at BASF

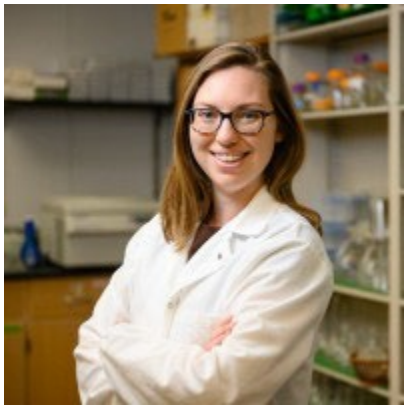


Joerg Bauer, PhD is Head of Global R&D Seed Treatment at BASF, where he leads research and innovation efforts focused on developing agricultural solutions that improve crop productivity and sustainability. During his more than two decades at BASF, Joerg has held a variety of scientific and leadership roles spanning research, technology scouting, and global collaboration management. His work has focused on translating scientific discoveries into innovative products through multidisciplinary partnerships across chemistry, biology, and biotechnology. Joerg earned his PhD in Plant Biochemistry from ETH Zürich, where his research focused on chloroplast protein biology, and began his career as a research scientist before moving into industry leadership. His career demonstrates how deep scientific expertise can evolve into strategic innovation and global R&D leadership.

Brooke Bissinger, PhD, Technical Marketing Manager at BASF

Brooke Bissinger, PhD is Technical Marketing Manager at BASF, where she supports product strategy and commercialization efforts within agricultural biotechnology. She brings extensive experience spanning research, product development, marketing, and business strategy across crop, human, and animal health industries. Prior to joining BASF, Brooke held multiple leadership roles at AgBiome, where she contributed to biological product development, commercialization, and cross-functional team leadership. Earlier in her career, she worked in research and development roles focused on molecular biology, insect biology, and product innovation. Brooke completed her PhD in Entomology at North Carolina State University and later conducted postdoctoral research at NC State, where she applied genomics and bioinformatics approaches to study tick biology. Her career reflects the wide range of opportunities available for scientists who combine technical expertise with business and product-focused skills.

Jessica Deaver PhD, Principal Scientist, Hazen and Sawyer

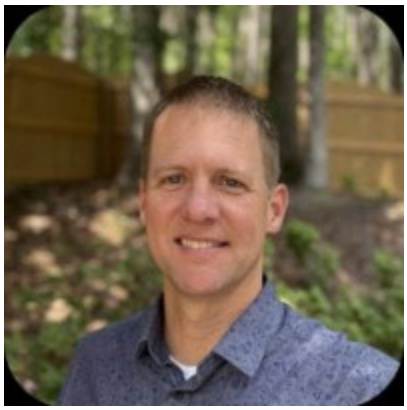


Jessica Deaver, PhD is Principal Scientist at Hazen and Sawyer, where she applies expertise in environmental engineering, microbiology, and analytical chemistry to address challenges in water and wastewater treatment. Her work focuses on developing science-based solutions through interdisciplinary collaboration, integrating molecular approaches, bioinformatics, and engineering principles. Prior to joining Hazen and Sawyer, Jessica completed postdoctoral research at North Carolina State University, where she investigated biological phosphorus removal processes through microbial community analysis and advanced sequencing approaches. She earned her PhD in Environmental Engineering and Science from Clemson University, where her research focused on environmental biotechnology and biological treatment systems. Jessica's career highlights the opportunities for scientists to apply academic research expertise to complex real-world challenges in consulting and environmental innovation.

Melyssa Minto, PhD, Research Scientist, Statistical Programmer at Flatiron Health

Melyssa Minto, PhD is a computational biologist and healthcare data scientist at Flatiron Health, where she applies statistical modeling, machine learning, and data science approaches to advance real-world evidence research. Her work focuses on integrating large-scale genomic, clinical, and multi-omic datasets to uncover biological insights and improve understanding of disease outcomes. Prior to joining Flatiron Health, Melyssa was a Bioinformatic Scientist at RTI International, where she developed scalable computational pipelines and applied machine learning approaches to genomic and clinical data. She earned her PhD from Duke University, where her research focused on integrating transcriptomic and epigenomic datasets to investigate mechanisms underlying neuronal development and disease. Her experience bridging computational biology, data science, and healthcare applications highlights the diverse career opportunities available at the intersection of biology and technology.

Will Thompson, PhD, Founding Partner and Operations Lead at Move Analytical



Will Thompson, PhD is Founding Partner and Operations Lead at Move Analytical, a company focused on developing and advancing analytical solutions for metabolomics applications. Throughout his career, Will has worked at the intersection of analytical chemistry, technology development, and commercialization, helping translate emerging scientific platforms into impactful tools for researchers and industry partners. Prior to founding Move Analytical, he held leadership roles at 908 Devices, where he supported product development, customer applications, and commercialization strategies for mass spectrometry-based technologies. He also serves as Adjunct Assistant Professor at Duke University, maintaining strong connections with academic research and training. Will earned his PhD in Chemistry and has built a career focused on bringing innovative analytical technologies from the laboratory into real-world applications.

KEYNOTE

Dara Wilson-Grant, LCMHC, *Director of Career and Professional Development, Office of Postdoctoral Affairs, UNC-Chapel Hill*

Dara Wilson-Grant has spent more than two decades doing one thing exceptionally well: turning career uncertainty into confident, clear direction. As a Career Coach and Licensed Clinical Mental Health Counselor, she brings a rare blend of clinical insight and practical career strategy to every room she enters.

Specializing in the distinct challenges facing postdocs and graduate students, Dara has delivered career programming for institutions across the country, including Duke University, NIEHS, Moffitt Cancer Center, and St. Jude Children's Research Hospital. Her workshops don't just inspire—they equip participants with concrete tools, step-by-step frameworks, and ready-to-use scripts they can apply immediately.

As Director of Career and Professional Development in the Office of Postdoctoral Affairs at UNC-Chapel Hill, Dara brings that same practical philosophy to scholars at every stage of their journey—from postdoc to their next big leap.

FLASH TALKS

1. **Rapid POC Electrochemical Lateral Flow sensor to support asthma phenotyping** | ***Ayemeh Bagheri Hashkavayi***

Asthma is a complex chronic respiratory condition marked by persistent airway inflammation and reversible airflow limitation. Effective management relies on distinguishing between allergic and non-allergic phenotypes, as treatment responses differ significantly between these subtypes. According to WHO estimates, asthma affected approximately 262 million people worldwide in 2019 and caused nearly 455,000 deaths that year, with mortality decreasing to about 436,190 deaths in 2021 [1]. However, current diagnostic approaches such as spirometry, skin testing, and IgE-based assays are often centralized, resource-intensive, and largely qualitative, making them less suitable for rapid, point-of-care use [2].

Quantitative assessment of biomarkers can play a critical role in improving clinical decisions. Interleukin-5 (IL-5) is typically present at very low concentrations in serum (0-5 pg/mL), whereas immunoglobulin E (IgE) spans a wide physiological range (5-1500 ng/mL) and varies significantly with age. Because of this variability, relying on qualitative or semi-quantitative methods may lead to incomplete or misleading interpretation. Access to precise concentration data in a short time frame can help clinicians better stratify patients and tailor treatment strategies.

In this work, we developed a rapid, portable, housing-free electrochemical lateral flow biosensor for asthma phenotyping through multiplex detection of IgE and IL-5 [3]. The platform combines the simplicity of lateral flow assays with electrochemical signal readout, enabling sensitive and quantitative detection directly from human serum. Antibody pairs were carefully selected through lateral flow screening to ensure optimal performance.

The sensor detects IL-5 in the range of 5–50 pg/mL and IgE in the range of 10-1000 ng/mL, with a total assay time of approximately 2 minutes using differential pulse voltammetry redox signal of gold nanoparticle labels. By supporting both colorimetric and electrochemical readouts, this platform enables multiplexed, quantitative analysis in a compact format, offering a practical route toward decentralized asthma phenotyping and faster clinical decision-making.

2. **From Ice-Cold to Red-Hot: Designing Materials for Extreme Environments** | ***Jorge Galeano-Cabral***

Modern technologies increasingly rely on materials that can operate far beyond everyday conditions; from near absolute zero in quantum technologies and deep space exploration to the intense heat and reactive environments of energy and aerospace systems. Under these extremes, materials often behave in unexpected ways, limiting performance and reliability. My research focuses on understanding and designing materials that not only survive but perform reliably under such conditions. At cryogenic temperatures, I have worked with quantum materials where subtle changes in structure and composition can dramatically alter electronic behavior, enabling next-generation sensing and energy technologies. At the opposite extreme, I develop oxidation-resistant alloys that withstand high temperatures and chemically aggressive environments for applications in energy production and advanced manufacturing. Despite the differences in temperature and application, both challenges share a common goal: controlling how materials respond to extreme environments at the atomic level. By bridging insights across these seemingly opposite regimes, this work contributes to the development of more resilient materials that can expand the limits of current technologies. Ultimately, designing materials for extremes is not just

about durability, it is about enabling the future of energy, infrastructure, and emerging technologies that society increasingly depends on.

3. **Real-World Gait Cadence and Sit-to-Stand Power as Complementary Predictors of Functional Performance in Older Adults** | ***Guido Mascia***

The assessment of functional performance in older adults has become increasingly critical as life expectancy continues to rise. Constructs of typical gait speed (GS), and the ability of performing sit-to-stands (SI-ST) are known predictors of one's functional status, and they are widely assessed in laboratory visits via the short physical performance battery of tests (SPPB). However, this framework requires participants to be physically present at a clinical facility, bringing them burden and constraining the clinical evaluation to specific time-points. A possible solution is offered by wearable-based remote monitoring, capable of unveiling insights that uniquely belong to movements performed in real-world settings. Thus, we analyzed real-world, accelerometer-based features of GS and SI-ST to assess whether their association with laboratory-derived SPPB outcomes of the homologues constructs. Older adults (N=212) attended a clinical visit where they were asked to perform several cognitive and physical tests. We focused on the SPPB total score, the 5-times SI-ST (CSTx5) time and the 4m walking test (4mWT) GS. After the visit, participants worn an accelerometer on their thigh for a 7-day period, which measures were processed to compute metrics of real-world cadence and SI-ST rotational power. Subsequently, the association with their homologues SPPB-derived constructs was assessed. The strongest associations with CSTx5 time and 4mWT GS were found with SI-ST peak capacity (RP95c, $r=-0.35$, $p<0.05$) and typical walking performance (Cad50c, $r=0.31$, $p<0.05$), respectively. An ordinary least squares regression fitted to predict SPPB scores revealed a significant negative interaction between RP95c and Cad50c, highlighting that in individuals with low SI-ST rotational power, typical daily cadence is a stronger differentiator of SPPB performance. These findings advocate for consistent implementation of wearable-based remote monitoring as a part of the diagnostic tools, possibly offering clinicians valuable insights to guide decision-making and tailor interventions to an individual's current functional status.

4. **A Robust Rat Optic Nerve Crush Model for Testing Neuroregenerative Therapy** | ***Qingqi Li***

Introduction: Eye injuries in the United States result in over 50,000 cases of permanent vision loss annually, with incidence varying by etiology. Because the optic nerve lacks intrinsic regenerative capacity, therapeutic options remain limited. Placental-derived stem cells (PSCs), initially identified by Wake Forest Institute for Regenerative Medicine (WFIRM) faculty, exhibit multipotency, including neuronal differentiation, positioning them as promising candidates for optic nerve repair. This study aims to establish reproducible protocols to evaluate PSC efficacy in promoting optic nerve regeneration.

Methods: Optic nerve crush injury was induced using Dumont crossover forceps. During surgery, electrodes were implanted over the visual cortex and interfaced with a BlackRock electrophysiology system for visual evoked potential (VEP) acquisition and MATLAB based analysis. Retinal morphology was assessed via Optical Coherence Tomography (OCT), and visual function evaluated using Optokinetic Nystagmus (OKN). Immunohistochemistry (IHC) employed βIII-tubulin and neurofilament (NF) for neuronal and axonal labeling, while VE-cadherin assessed vascular junction integrity. Luxol Fast Blue staining quantified myelin integrity within the optic nerve.

Results: A reproducible rat optic nerve injury model was successfully established and validated using visual evoked potentials (VEP), which consistently demonstrated N1 latency prolongation and amplitude reduction. Optimization of OCT and OKN protocols is currently underway. Histological analysis revealed significant reductions in neuronal density, vascularity, and myelination within injured optic nerves and retinas. **Conclusion:** We successfully developed a reproducible optic nerve injury model with integrated functional and structural assessments using VEP, OCT, and histology.

These findings provide a robust platform for investigating PSC based therapies aimed at restoring vision following optic nerve damage.

5. **Quantum Explorer Packs: Bringing quantum education to K-12 classrooms across the US** | ***Brean Prefontaine***

The demand for a quantum information science and engineering (QISE) workforce has led to an increase in QISE educational opportunities across the U.S. At the K-12 level, QISE content is not yet explicitly part of national or most state standards, and there are only a handful of opportunities for teachers to learn more about how to incorporate QISE into their instruction. However, incorporating QISE content into K-12 instruction is vital for a strong QISE workforce. Thus, this project expands the initial work of the National Q-12 Education Partnership's QuanTime program to bring well-designed QISE activities to K-12 teachers nationwide. This expansion will include designing Quantum Explorer Packs, grade-level and content-specific kits that will be distributed to teachers in all 50 states, Puerto Rico, and Washington, D.C. Each pack will include reusable materials for a full class of students, teacher guides for several QISE activities, and information for both students and educators about QISE career opportunities. This talk will describe the design process for the Quantum Explorer Packs and the accompanying research study examining the impact of this model. We will also discuss lessons learned, next steps, and how you can get involved!

6. **When Treatment Fails: The Biology of Breast Tumors That Don't Respond** | ***Patrick Raedler***

Triple negative breast cancer, or TNBC, is the most aggressive type of breast cancer. While chemotherapy given before surgery has improved the survival of patients, a major challenge remains: many patients still have cancer left after treatment, called residual disease. This remaining disease is of significance because it is strongly linked to worse survival outcome.

In our study, we wanted to better understand why some tumors do not fully respond to chemotherapy. To accomplish this, we looked at tumor samples from patients before treatment and after treatment to see how tumor biology impacts response to chemotherapy and how these tumors change after treatment.

What we found is that a specific group of tumors that remained largely biologically unchanged after treatment resulted in worse survival for those patients. Based on their biological features, we call these tumors "Basal-like" tumors, and we were able to show that even before treatment these tumors showed signs that they may resist treatment.

One Key finding was related to the immune system. Tumors that did not respond well tended to have fewer immune cells (i.e., B-cells and T-cells) present. After treatment, the number of immune cells declined even further, creating what we call an "immune-cold" environment. This means the body's natural defense system is less able to recognize and attack the cancer, which can significantly dampen chemotherapy response.

To test alternatives to standard chemotherapy, we evaluated newer targeted therapies in models that mimic treatment-resistant tumors. These therapies showed promising results, even when standard chemotherapy did not work.

Overall, this study shows that understanding tumor biology before and after treatment, and the tumors' interaction with the immune system, can be helpful to identify high-risk patients and guide the development and use of better treatments to improve patient lives.

7. **Mobility Edges in Modified Three-Dimensional Lattices with Enhanced Connectivity** | ***Mohammed Zahid Malik***

Building upon the foundational framework of Bloch theory and the disorder-induced breakdown of electronic delocalization, the phenomenon of Anderson localization continues to be a cornerstone in understanding transport suppression in disordered systems [1–4]. While classical studies primarily

focused on simple cubic or regular lattice geometries, recent investigations have shown that the underlying lattice topology and coordination number play pivotal roles in shaping the localization behavior and critical disorder threshold. In our work, we focus on Anderson localization in modified three-dimensional (3D) lattices, where structural modifications are introduced through an increase in coordination number and lattice connectivity.

Specifically, we explore 3D checkerboard lattices, 2D stacked checkerboard lattices, and 3D Lieb lattices, each offering distinct connectivity patterns and local geometrical variations compared to the conventional cubic framework. These structural alterations are expected to influence the degree of quantum interference and modify the mobility edge: the critical energy separating localized and extended states. By systematically tuning disorder strength and lattice topology, we aim to uncover how enhanced coordination and lattice complexity govern the transition between metallic and insulating regimes.

Using numerical simulations of tight-binding Hamiltonians, we analyze the scaling of the average level spacing ratio [5], Inverse participation ratio [6], and density of states to characterize localization properties across different lattice types. Our numerical study provides new insights into how lattice modifications in higher dimensions can reshape the fundamental nature of Anderson localization.

8. **The essential moral self: A cross-cultural regularity in eight cultures** | ***Julia Smith***

Although infinite personal traits and features can be said to make up a person's self, not all traits are seen as equally essential. Compared to non-moral features such as memories, personality traits, and sensory experiences, a person's moral beliefs and behaviors are seen as more important to their "true" or "essential" self. Given cross-cultural diversity in moral beliefs and norms, as well as in the self-concept, we examined the prevalence of moral essential self beliefs in eight countries (N = 1,676). We found that although the moral valence of specific behaviors varies between societies, participants considered more morally relevant traits to be more essential with striking regularity across cultures, religions, and beliefs about the self. This suggests that assigning particular importance to moral traits may be a universal human tendency that aids in cooperation within and across diverse groups.

9. **Primary Cilia Rewire Lung Fibroblast Metabolism to Promote Lung Fibrosis** | ***Serife Gulberk Ozcebe***

Idiopathic pulmonary fibrosis (IPF) is a fatal lung disease marked by progressive scarring, with most patients dying within five years of diagnosis. Current therapies slow progression but cannot stop or reverse fibrosis, partly because the mechanisms driving persistent scarring remain poorly understood.

We identified primary cilia as an unexpected regulator of this process. Primary cilia are small, antenna-like structures that allow cells to sense and respond to their environment. In IPF, the lungs progressively stiffen as scar tissue accumulates. We observed that fibroblasts driving scar formation exhibit structurally abnormal primary cilia, a previously unreported finding. Whether this contributes to the fibrotic response was unknown.

Primary cilia regulate fibroblast metabolism to sustain collagen production. Producing scar tissue is energetically expensive, demanding sustained energy output from fibroblasts. In mice, cilia deletion reduced lung collagen and fibrosis, with single-cell RNA sequencing identifying mitochondrial metabolism as the most altered pathway. In human IPF fibroblasts, cilia knockdown impaired mitochondrial function and reduced energy output, limiting collagen synthesis. In live human IPF lung slices, pharmacologic cilia inhibition decreased collagen levels and secretion. Across all models, loss of cilia consistently reduced fibrosis.

Mechanistically, profibrotic signaling pathways (i.e., Hedgehog, ROCK) did not account for the effect of primary cilia on fibrosis. Instead, ciliary signaling is linked to AMPK, a master energy-sensing

kinase. AMPK activation tracked with collagen output and was reduced upon cilia loss on both soft and stiff matrices mimicking healthy and fibrotic lung. Untargeted metabolomics of human lung tissue further confirmed broad metabolic rewiring after cilia inhibition, suggesting fibrotic lung fibroblasts shift how they generate and use energy when ciliary signaling is lost.
These findings identify primary cilia as a metabolic checkpoint in IPF fibroblasts and point toward AMPK signaling and mitochondrial pathways as downstream therapeutic targets for a disease that urgently needs effective treatments.

10. **Light-Assisted Drying - The End of Cold Chain Distribution for Temperature Sensitive Biologics** | ***Alex Suptela***

Vaccination against infectious diseases is one of the greatest achievements in modern medicine. However, many vaccines must be kept at refrigerated or freezing temperatures after manufacturing, during distribution, and prior to administration. Consequently, any temperature excursions outside the recommended range in the cold chain can affect vaccine efficacy. This reliance on the cold chain is particularly challenging in low-resource areas and remains a major contributor to under-vaccination globally. Furthermore, the WHO estimates that approximately 50% of vaccines produced annually are wasted annually due to limitations of the cold chain. Thus, there is a major need for a system that allows for the storage of vaccines at ambient temperatures.
This study uses a novel technology called light-assisted drying (LAD) to create a protective amorphous trehalose matrix that allows room-temperature storage of the meningococcal serogroup B vaccine, 4CMenB (BEXSERO). During LAD processing, the vaccine was mixed with a trehalose solution and then irradiated with a 1064 nm laser, forming an amorphous trehalose matrix. Samples of 0.5 mL were processed in glass vials for 2 hours and 50 minutes at a laser power of 5 W. After LAD processing, polarized light imaging was used to verify that the matrix was amorphous and stable against crystallization.
In vitro direct ELISAs were used to assess the 4CMenB component factor H binding protein (fHbp) antigenicity to confirm that processed vaccine integrity was maintained. Additionally, BALBc/J mice were vaccinated with buffer alone, LAD processed 4CMenB, or unprocessed 4CMenB three times over a nine-week period. Specific capture ELISAs were performed for four antibody isotypes in mouse sera to assess the generation of adaptive immune responses following vaccination. Our results indicate that fHbp antigenicity was maintained following LAD processing, and that mice vaccinated with LAD processed 4CMenB generated statistically similar antibody concentrations to those vaccinated with unprocessed 4CMenB.

11. **Combination Therapies for Improved Treatment of Pancreatic Cancer** | ***Ryan Mouery***

Pancreatic cancer is the third-leading cause of U.S. cancer-related deaths and has the highest mortality rate with a five-year survival rate of 13%. Despite advances in treatment options for other cancer types, the standard-of-care for pancreatic cancer remains chemotherapy and is largely ineffective. However, a new class of therapeutics has progressed through clinical development showing increased efficacy in patients and has led to the FDA-approval of two novel drugs (RAS inhibitors). Newer RAS inhibitors have doubled the overall survival rate in phase III clinical trials. While this offers new hope for a difficult-to-treat disease, most patients will not benefit from these therapies and those that do will ultimately relapse on therapy. Therefore, a major challenge in the field is to understand the reasons patients do not respond so that these therapies may be improved upon. One strategy to enhance the efficacy and durability of these therapies is to combine them with other therapeutic agents and understanding the reasons for patient relapse helps the selection of rational combination strategies. Recently, it was found that a genetic deletion (in MTAP) that occurs in ~25% of pancreatic cancer diagnoses lead tumors to be susceptible to a second, distinct therapeutic (PRMT5 inhibitors). Our lab has demonstrated that combining RAS and PRMT5

inhibitors is an effective combination in pancreatic cancer and clinical trials evaluating this combination are ongoing. My studies build on our previous observations to understand the reasoning why this combination is effective in patients. Importantly, we found that resistance to either therapy alone does not affect the efficacy of the other therapy. Therefore, our studies support the notion that these may be administered concurrently or sequentially after relapse from the primary therapeutic. This will add to the available treatment options for the subset of patients with pancreatic cancer harboring this genetic alteration.

12. Cannabis Electronic Cigarettes: Defining the Risks to Pregnancy | ***Samuel Cripps***

With recent legalization of cannabis across North America, 20% of pregnant women use cannabis as a supposed safe means to treat nausea. Unfortunately, cannabis is known to impair fetal development. Yet, there exists a lack of communication regarding these risks. Thus, additional research is needed and communication to public health is warranted. Given that miscarriage occurs in 15% of pregnancies, it is urgent to further define the risks of cannabis use in causing pregnancy complications.

Popular new methods for using cannabis have further complicated risk assessment. These include electronic(e) cigarettes, which heat a liquid cannabis extract to release an inhaled vapor. Many pregnant women use e-cigarettes with the belief that they are 'safe' compared to smoking cannabis. Certainly, burning cannabis emits multiple chemicals that are harmful to pregnancy. However, e-cigarettes also produce a variety of similar toxic chemicals from superheating the cannabis extract. Furthermore, the psychoactive drug in cannabis, THC, is far more concentrated in e-cigarettes (up to 95%) compared to traditional smoking methods. THC not only affects the brain to produce the cannabis 'high', but it also interferes with uterine function. The uterus houses and maintains the early embryo and developing fetus and is thus critical for pregnancy. Surprisingly, no research has explored whether cannabis e-cigarettes harm the uterus.

To address this shortfall, we expose pregnant mice to cannabis e-cigarette vapor (all methods follow ethical regulations for animal research). We aim to test how these vapors impact uterine function and the development of the early embryo. Our results will determine whether cannabis e-cigarettes harm key processes of pregnancy. In turn, physicians and public health policy can offer more evidence-backed advice to pregnant women and lower overall substance use during pregnancy. As a result, we anticipate observing reduced rates of miscarriage and other pregnancy complications.

13. What can germanium detectors demonstrate regarding the origins of matter? | ***Aparajita Mazumdar***

Why didn't the universe *annihilate* after the big bang, and why is the universe filled with matter? Neutrinos may reveal hints to the answer. This is the 70th anniversary of the discovery of the neutrino, but we are still learning new properties of this fascinating particle, and one such experiment could be tied to this existential question. Neutrinoless Double Beta Decay ($0\nu\beta\beta$) experiments attempt to search for a yet undiscovered rare decay, which is thought to occur in certain nuclei. If observed, it would conclusively establish that neutrinos are their own anti-particles, provide a crucial ingredient of the matter-antimatter asymmetry, and could also constrain the absolute mass of the neutrinos.

^{76}Ge is a candidate nucleus for observing $0\nu\beta\beta$, and can be adapted to existing germanium detector technology. The LEGEND experimental program aims to have an ultimate discovery sensitivity to a $0\nu\beta\beta$ half-life beyond 10^{28} years for ^{76}Ge, which improves upon the current limits by approximately 2 orders of magnitude. Currently, the first phase of the experiment, LEGEND-200 has acquired a year

of stable data with 142 kg of enriched germanium detectors. In this flash talk, we'll discuss what LEGEND-200 is, why 0νββ is important, and our first results.
This work is supported by the U.S. DOE, and the NSF, the LANL, ORNL and LBNL LDRD programs; the European ERC and Horizon programs; the German DFG, BMBF, and MPG; the Italian INFN; the Polish NCN and MNiSW; the Czech MEYS; the Slovak RDA; the Swiss SNF; the UK STFC; the Canadian NSERC and CFI; the LNGS and SURF facilities.

14. **Region- and cell-type-specific chromatin accessibility can reveal epigenetic memory in cystic fibrosis airways** | ***Augustin De Ganzo***

Background: Cystic fibrosis (CF) is a genetic disease caused by mutations in the CFTR gene. In the airways, CF manifests as thick mucus builds up leading to chronic inflammation and impaired clearance of pathogens. Although highly effective modulator therapies (HEMT) improve CFTR function, many patients continue to experience defective mucociliary clearance (MCC). We hypothesize that this is partly due to "epigenetic memory": stable changes in how DNA is packaged and regulated in airway progenitor cells and influence their behaviour even after treatment.
Methods: We used primary human airway epithelial cells grown in culture to model both large and small airways. Using cell sorting, we isolated distinct cell populations, including basal (progenitor) cells and specialised secretory cells. We then applied ATAC-seq, a genome-wide technique that identifies regions of accessible DNA, to map regulatory differences across cell types and airway regions. We focused on genes involved in mucus production, lung identity, ion transport, and inflammation.
Results: We found that cells from small and large airways have distinct patterns of chromatin accessibility, reflecting region-specific regulatory programs. Basal cells and differentiated cells also showed unique accessibility profiles, particularly at genes controlling mucus production. Markers of distal airway identity were enriched in small airway secretory cells, confirming functional specialization. Importantly, regions linked to inflammatory signalling pathways showed differences across cell states.
Conclusion: We found that airway cell identity and function are encoded at the level of chromatin organization and differ across regions and cell types. Targeting epigenetic mechanisms could represent a new strategy to restore MCC and improve outcomes in CF and other chronic lung diseases.

POSTER PRESENTATIONS

1. **Sex-Specific Effects of Estrogen on Cardiac Circadian Clock Protein Period 2 via Adora2b Signaling and IL-6–Driven Ferroptosis| *Syed Anees Ahmed***

Background: Estrogen (E2) confers cardioprotection in menopausal women while a similar E2 regimen increases CVD risks in men. Emerging evidence implicates the: (1) circadian clock protein period 2 (Per2) in E2-dependent inhibition of ferroptosis, (regulated cell death) and preservation of cardiac function in females, and (2) adenosine A2b receptor (Adora2b) in Per2 stabilization and interleukin-6 (IL-6) inhibition. However, it remains unknown if differences in these signaling pathways contribute to the divergent sex-specific cardiac effects of E2.
Aim: To investigate the unknown role of Adora2b-Per2 modulation of Per2 and IL-6-driven ferroptosis in the divergent cardiac effects of E2 in surgical menopause and male rats.
Methods: Age-matched E2-deficient male and ovariectomized (OVX) female Sprague-Dawley rats (surgical menopause model) received daily E2 (20 μg/kg) or vehicle for eight weeks. Blood pressure and cardiac function were measured by radiotelemetry and echocardiography. Cardiac tissues were analyzed for Adora2b, Per2, ferroptosis mediators, and cardioprotective miRNAs.
Results: Contrary to the cardioprotective effects in OVX females, E2 treatment impaired cardiac function in males. E2 significantly reduced blood pressure in OVX females, but had no effect in males. Echocardiographic analyses demonstrated improved cardiac function in E2-treated OVX females, but worsened cardiac function in male rats (reduced ejection fraction and fractional shortening). At the molecular level, E2 upregulated Adora2b and Per2 expressions in OVX females, accompanied by increased expression of cardioprotective microRNAs (miR-1, miR-133a, miR-208a, and miR-499). In contrast, males showed significant reductions in these molecular studies. Furthermore, E2 suppressed IL-6 levels and ferroptosis level in OVX females, but increasing them in males.
Conclusion: These findings showed that Adora2b-related Per2 upregulation contributes, at least partly, via E2-dependent inhibition of IL-6-driven ferroptosis, leading to improved cardiac function in OVX females. This premise is supported by novel demonstration of the opposing molecular and cardiac effects of E2 in males. This study identifies new targets for the sex-specific cardiac effects of E2 in females.
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2. **Serum Artemin Rises in Dogs Undergoing Radiotherapy for Head and Neck Cancer | *Faihaa Ahmed***

The biological basis of acute orofacial radiation-associated pain (RAP) in head and neck cancer remains unclear. Cold-sensing TRPM8 pathways (Transient Receptor Potential Melastatin 8) may contribute to RAP and are activated by the neurotrophic factor artemin (ARTN) via its receptor, GFRα3. To investigate whether radiation induces ARTN release, modulate TRPM8 signaling pathway and RAP, a prospective clinical trial enrolled 24 pet dogs undergoing RT (32 or 36 Gy total, given in four-weekly fractions) for oral melanoma or intranasal carcinoma. Radiotoxicity was scored at each

visit, per Veterinary Radiation Therapy Oncology Group criteria. Pain was assessed using a validated composite oral and maxillofacial scale. Blood and oral mucosal biopsies were collected from the RT field for ARTN and GFRα3 gene and protein expression. Data were analyzed using twoway ANOVA. At end-RT, 79% of dogs had grade 1-2 oral mucositis; decreasing to 58% at the two-week recheck. Pain scores were variable. Transcriptomics showed increased ARTN expression (1.11-fold at 32 G; 1.35-fold at36 Gy; $P < 0.01$). GFRα3 expression decreased (1.02-fold at 36 Gy at end-RT, 1.23-fold after RT; $P < 0.05$). TRPM8 gene expression didn't change. ARTN and GFRα3 protein expression was unchanged in oral mucosa and neither mucositis nor pain severity correlated with their levels. Local gene expression did not correlate with pain severity. However, dogs with worsening pain after RT, had increase serum ARTN ($P = 0.01$). These findings suggest that irradiation induces systematic ARTN release, potentially reflecting nerve regeneration and tissue
repair rather than direct local receptor activation.
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3. **The ENL–USP7 Complex Regulates HIV Latency Through BRD4 Stabilization| *Waqas Ahmed***

HIV-1 persists in $CD4^+$ T cells and brain microglia through host factors that enforce viral latency, yet the mechanisms that stabilize key transcriptional regulators remain incompletely understood. Here, we identify the YEATS domain-containing protein ENL and its associated deubiquitinase USP7 as a host complex that maintains HIV-1 latency. USP7 stabilizes BRD4 by deubiquitination, suppressing HIV transcription and sustaining viral quiescence. Disruption of the ENL–USP7 complex using selective PROTACs reactivates latent HIV in cell line models, as well as in resting $CD4^+$ T cells and microglia isolated from people with HIV on antiretroviral therapy. These findings uncover a critical ENL–USP7–BRD4 axis that enforces HIV-1 latency and highlight USP7 as a potential target for latency-reversing strategies.
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4. **Circadian Controlled Transcription in Brain and Peripheral Organs of Juvenile and Adult Mice| *Yasemin Akyel***

Background: Circadian clocks generate daily rhythms of gene expression that influence physiology, disease, and responses to therapeutics, yet how circadian transcription differs between juvenile and adult organisms remains unresolved. Such age-dependent differences in rhythmicity may lead to significantly different treatment outcomes, particularly for drugs whose efficacy or toxicity is affected by the circadian clock. In this study, we aimed to characterize how tissue and developmental stage influence circadian transcription using genome-wide eXcision Repair sequencing (XR-seq). **Methods:** Juvenile (3-week-old) and adult (20-24-week-old) male mice were injected with cisplatin at 4-h intervals across a 24-h cycle (2 biological replicates; 2 pooled mice per sample). Mice were sacrificed 2-h after injection at ZT00-ZT20, and the whole brain, liver, kidney, and testis were harvested for XR-seq to quantify genome-wide transcription through transcription-coupled excision repair of cisplatin-induced DNA lesions. Rhythmic XR-Seq TS signal was identified via rhythmicity analysis incorporating non-parametric methods (RAIN, adjusted p value < 0.05, FDR < 0.20). **Results**: In all organs of juvenile and adult mice except the testis, rhythmic transcription phases clustered near dawn and dusk for most genes. While core clock gene rhythms are largely preserved between juveniles and adults, with only modest tissue-specific changes in phase and amplitude, rhythms of many clock-controlled genes differ markedly by age. Rhythmic genes are strongly organ-specific, yet overlap between ages is limited, indicating substantial developmental changes in circadian control. We report age- and tissue-specific circadian regulation of pathways including signaling, transport, apoptosis, and metabolism. **Conclusions:** Our findings provide a multi-organ map of circadian transcription in juvenile and adult mice, revealing substantial age- and

tissue-specific differences. These results suggest that treatment schedules optimized in adults may not directly translate to younger individuals, as differences in circadian rhythms may shift optimal therapeutic times for efficacy and tolerability.
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5. **Impact of Fungal Diversity on Wheat Growth Under Drought Stress** | ***Brianna Almeida***

Increasingly frequent and severe droughts pose a threat to our food systems, with cereal crop yield projected to decrease by 10-20% by 2050. Although plant breeding will improve drought tolerance traits, the foliar microbiome has been shown to improve plant drought resistance. However, synthetic microbial communities (syncoms) applications often fail, and understanding mechanisms of effective assembly is key to unlocking this resource. Here, we grew wheat with fungal syncoms to investigate how fungal assembly mechanisms (priority, diversity) impacted the plants response to drought. The syncoms contained a single pioneer fungus applied first, followed by low diversity (3 fungi) or high diversity (9 fungi) community inoculations. We imposed drought and measured plant growth and physiological performance. Final fungal community composition was assessed with amplicon sequencing.
We found that only two of the five pioneers persisted in the syncoms—one universally (*Stagonosporopsis* sp.) and the other in 33% (*Daldinia* sp.). Composition of the final syncoms were best predicted by cooccurrence of taxa in the field at the time of collection. When investigating the relationship between field data and community persistence we found that persistent members have a greater number of connections in a network compared to all other community members. Drought did not influence final fungal community composition, likely because treatments were paired inside a microcosm. Final syncom composition influenced plant height, root mass, leaf dieback, and leaf lesions, but not in a systematic way. This study demonstrates the importance of looking to field assembled communities before creating fungal syncoms.
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6. **Mapping the Active Site Schiff Base Nucleophile in the dRP Lyase Activity and the Role of the K-tract Domain in the Human Pol Î³**

DNA polymerase γ (Pol γ) is the only DNA polymerase responsible for mitochondrial DNA replication but also plays a key role in base excision DNA repair (BER). During single-nucleotide BER (SN-BER) Pol γ performs two essential functions: gap-filling DNA synthesis and 5′-deoxyribose 5-phosphate (dRP) lyase. During SN-BER, removal of a damaged base leaves behind a 5′-dRP moiety that needs to be removed prior to ligation. Pol γ removes this dRP group through its dRP lyase activity so that DNA ligase then seals the nick. Excision of the dRP moiety proceeds via a Schiff base intermediate as evidenced by the reduction and trapping of the Pol γ amino-substrate with sodium borohydride ($NaBH_4$). Mapping of Pol γ by $NaBH_4$ cross-linking, limited proteolysis and mass spectrometry revealed that the active site residue which acts as the Schiff base nucleophile in trapping the dRP group of the substrate is Lys^{512}.
Lys^{512} variants were constructed and expressed to investigate the mechanism of the dRP lyase activity of Pol γ. Results from binding studies showed comparable binding affinities of WT Pol γ and the variants for dsDNA but varying affinities for ssDNA substrates. Interestingly, the Lys^{512} variants showed trapped products by $NABH_4$ cross-linking with dsDNA/ssDNA substrates and measurable dRP lyase activity comparable to WT Pol γ. We hypothesized that a lysine patch (K-tract domain) in the structure of Pol γ in proximity to Lys^{512} may be augmenting the dRP lyase activity. This phenomenon has been observed in other DNA polymerases with dRP lyase activity like DNA Pol β and Pol ι. Variants of the K-tract domain were constructed based on their proximity to Lys^{512} and

dsDNA. Future studies will investigate the dRP lyase activity and covalent cross-linking of the variants to identify the lysine residues that acts as the Schiff base nucleophile augmenting Lys^{512}.

7. **Bridging Access and Impact: Primary Care Parenting Intervention Reduces Early Behavior Problems in Both Virtual and In-Person Delivery Modes** | ***Fithi Andom***

Background: Early childhood behavior problems are common and associated with adverse outcomes, including risk for maltreatment. Child-Adult Relationship Enhancement in primary care (PriCARE) is an evidence-based group parenting intervention delivered in pediatric primary care to reduce disruptive behaviors and strengthen caregiver-child relationships. Although in-person randomized controlled trials (RCTs) demonstrate efficacy, structural barriers such as workforce shortages, transportation challenges, and limited behavioral health infrastructure restrict access. Virtual delivery may improve reach, but its effectiveness relative to in-person delivery is not well established.
Objective: To evaluate the effectiveness of virtual PriCARE in improving child behavior outcomes and compare outcomes with prior in-person trials.
Methods: A multi-site RCT of virtual PriCARE is underway with caregivers of children aged 18 months to 6 years. Child behavior was assessed using the Eyberg Child Behavior Inventory (ECBI) at baseline and 6-8 month follow-up. This interim analysis includes 698 virtual participants and 417 participants from three prior in-person trials. Attendance was compared using the Cochran-Armitage trend test. Intervention effects were estimated using linear regression with ANCOVA adjustment for baseline ECBI scores and caregiver/child covariates.
Results: Attendance was higher in the virtual condition, with 23.8% completing all sessions versus 18.9% in-person ($p < .001$). Virtual participants demonstrated significant reductions in ECBI Intensity (-7.81 vs. 1.45, $p < .001$) and Problem scores (-3.80 vs. -1.91, $p < .001$). The delivery mode × intervention interaction was not significant for ECBI Intensity ($p = .833$) or Problem scores ($p = .744$), indicating no evidence of differential effects by delivery modality.
Conclusions: Virtual PriCARE was associated with improved child behavior outcomes and higher completion rates, with no evidence of differential effects compared to in-person delivery. These findings support virtual behavioral parenting intervention in pediatric primary care as a scalable approach to expanding access and preventing early childhood behavior problems and maltreatment risk.
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8. **Reprogramming Microglia to Rescue Negative Affect Due to Binge Ethanol** | ***Paige Anton***

Purpose: Negative effect resulting from alcohol misuse contributes to Alcohol Use Disorder (AUD) symptomatology. We recently reported that persistent dysregulation of microglia following binge ethanol promotes long-lasting negative affect. Here, we explore if microglial regeneration can reverse persistent AUD-related behavioral dysfunction. Further, we aim to determine the underlying mechanisms by which microglial regeneration may improve ethanol-related outcomes.
Methods: C57BL/6J mice were given daily gavages of ethanol (5g/kg, i.g.) or water for 10 consecutive days. Twenty-four hours after the final gavage, mice were subjected to microglia depletion using the colony-stimulating factor receptor 1 antagonist PLX5622 in chow for 3 weeks. Mice were then returned to normal chow for 3 weeks for microglial regeneration. Following regeneration, negative affect was characterized using the open field task and fear conditioning with extinction. qRT-PCR was performed for metabolic makers. immunohistochemistry for neuronal activation marker, c-Fos, was performed the infralimbic cortex (IL), a brain region that promotes fear memory extinction. Neurogenesis was examined in brain regions necessary for memory formation (i.e., dentate gyrus) via doublecortin (DCX) immunohistochemistry.

Results: Binge ethanol increased novelty induced freezing 8 weeks into withdrawal as well as reduced extinction of conditioned fear memory, which were rescued by microglia regeneration. Ethanol reduced c-Fos in the IL and reduced DCX expression the dentate gyrus, with improvement by microglia regeneration. Ethanol-exposed mice exhibited increased expression of metabolic enzymes which was normalized by regeneration.
Conclusions: Microglia regeneration improves neuronal dysfunction and reduces negative effect after binge ethanol. Our data suggest this improvement may occur through a metabolic mechanism. Further investigation into the unique metabolic features of regenerative microglia may lead to promising therapeutic targets to improve negative effect related to AUD.

9. **Mechanically Degradable Hydrogel Microparticles Towards Advanced Tissue Engineering** | ***Meagan Arguien***

Hydrogels are a class of polymeric materials that have been widely exposed for biomedical applications. The swellability and tunable mechanical properties of hydrogel networks readily facilitates their incorporation into applications including drug delivery mechanisms, cell scaffolding, biosensors, or wound therapies. As wound therapies, hydrogels have proven to be instrumental in supporting the retention of water to facilitate cellular activities while also providing mechanical properties ideal for the mitigation of contraction, scarring, and exacerbation of inflammation. Additionally, the ability to incorporate various chemical functionalities into these materials has enabled the tunable and triggerable material degradation over time as well as the release of therapeutic molecules to the impacted region. This work leverages hydrogel microparticles (HMPs) crosslinked through stereocomplexation with built in mechanically labile junctions to provide a dual degradable system. The stereocomplexation via poly(lactic acid) provides a robust means of physically crosslinking the hydrophilic PEG-based HMPs together with a means of hydrolytic degradation at long time scales, permitting the extended use of these materials in wound therapies, while the mechanically labile linking elements provide a means of controllably triggering the degradation of the crosslinked HMP network at a desired timepoint. Through the addition of the triggerable degradation, the use of these HMPs is made more patient specific as a wound therapy while maintaining the benefits of injectability and enhanced oxygen permeability afforded by the HMPs.
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10. **Cross-Ancestry Meta-analysis of Primary Open-Angle Glaucoma Identifies Novel Loci** | ***Osahon Asowata***

Primary open-angle glaucoma (POAG), a highly heritable complex disease, remains the leading global cause of irreversible blindness. Despite extensive genomic investigations involving tens of thousands of cases and controls, a substantial proportion of its heritability remains unexplained. In this study, we conducted one of the largest multi-ancestry genome-wide association study (GWAS) meta-analyses to date, examining genetic susceptibility to POAG across European (EUR), African (AFR), and Hispanic (HIS) populations.
Using data from the Million Veteran Program, POAG cases and controls were defined using two complementary approaches: (a) incorporating age restrictions alongside ICD-9/10 diagnosis, procedure, and medication codes, while excluding conflicting diagnoses; and (b) requiring ≥2 POAG-specific phecodes (365.11, H40.11, or related child codes) for cases and none for controls, without age restriction. To evaluate cross-ancestry heterogeneity, we performed trans-ethnic meta-analysis using MR-MEGA, incorporating multidimensional scaling axes to account for population structure and allelic heterogeneity. Genome-wide significant (GWS; $p < 5\times10^{-8}$) variants were further assessed in independent African cohorts (GIGA, GERA, TwinsUK, UK Biobank) and the FinnGen+UK Biobank resource.

Across both phenotyping strategies, case/control counts were as follows: (a) EUR (10,738/223,415), AFR (6,889/31,042), HIS (1,270/14,442); and (b) EUR (24,268/429,244), AFR (16,083/102,972), HIS (3,096/47,898). We replicated multiple established POAG loci and identified genome-wide significant associations at 6 loci under approach (a) and 22 loci under approach (b), with three loci (*CHSY1, ITGA11*, and *SBSPON*) consistently observed across both definitions. Of the 25 GWS loci identified, 8 demonstrated nominal replication ($p < 0.05$) in independent African cohorts, while 11 replicated in the FinnGen+UK Biobank dataset. Notably, *SBSPON* has been shown to be associated with different tissues, including the sigmoid colon, tibial artery, muscularis esophagus, coronary artery, skin, brain, and other tissues. RNLS, previously implicated in oxidoreductase activity and vitamin metabolism, has also been associated with corneal traits and cataract.
In summary, this large-scale multi-ancestry GWAS meta-analysis identified novel loci associated with POAG that are consistent across populations, providing deeper insight into its genetic architecture and supporting the advancement of ancestry-informed precision medicine.
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11. **In Situ Detection of Naegleria Fowleri in Recreational Waters: Opportunities and Challenges | *Andrei Badilla-Aguilar***

The "brain-eating" amoeba *Naegleria fowleri* occurs worldwide in soils and freshwater environments, particularly in regions with warm climates (> 15 °C). People can contract *N. fowleri* when contaminated water enters the body through the nasal passages, commonly during swimming, diving, or nasal irrigation. The amoeba causes Primary Meningoencephalitis (PAM), a rapidly progressing disease with a fatality rate exceeding 95%. Current methodologies to detect the amoeba in clinical specimens and environmental waters rely exclusively on microscopy and molecular techniques (e.g., PCR) that require specialized personnel. These analyses often take more than 24 hours and are typically initiated only after epidemiological evidence of exposure, rather than as a proactive surveillance tool. In recreational waters, there is a need for rapid, sensitive, and easy-to-interpret tests that can proactively inform public health decisions and recreational use across the world. The development of such tools is limited by gaps in our understanding of *Naegleria* ecology, including its abundance, persistence, and behavior in environmental waters. Our work aims to develop an actionable, field-deployable workflow capable of detecting *N. fowleri* and producing qualitative results in under two hours following sample collection. To do this safely, we use the non-pathogenic surrogate *N. gruberi* to study key characteristics of *Naegleria* in water, including persistence, particle association, filtration strategies, and amplification methods. Our results show that *N. gruberi* exhibits minimal particle attachment, indicating that pre-filtration could improve detection efficiency. Furthermore, initial evidence has demonstrated that PCR-free technologies, such as Loop Mediated Isothermal Amplification and Aptamer-based Detection systems, can be promising approaches for *N. fowleri* rapid detection given their sensitive and field deployment potential. Ultimately, our research will aid the development of an early-alert system to better inform recreational water use in temperate regions and reduce exposure to waters that may pose a risk of contracting PAM.
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12. **Design and Validation of an AI-Assisted Sequential Screening Framework for Psychological Distress in Glaucoma | *Youngsoo Baek***

Psychological distress is highly prevalent in glaucoma and is associated with worse follow-up adherence, lower quality-of-life, and faster disease progression. Despite its clinical relevance, distress is rarely assessed in ophthalmology due to time, workflow, and staffing constraints. Artificial intelligence (AI) and machine learning hold great promise for reducing screening budget, but due to a lack of large data with accurate measurements, they can offer poor diagnostic characteristics in

real-world deployment. We propose a two-stage sequential screening design, which borrows the strengths of both AI and clinical input. In the first stage, an AI model is trained to predict a "silver standard" distress measurement readily available in a large electronic health records data. In the second stage, AI predictions are used to flag patients high at risk, to whom questionnaires are administered. Only the patients with positives in the second-stage questionnaires are referred to further treatment. Our evaluation study on a prospective cohort of Duke glaucoma patients demonstrates that the sequential screening approach can achieve higher specificity, precision, and overall accuracy than either questionnaires or AI alone, and that it does so at a significantly lower screening cost when compared with manual questionnaire administration. Our sequential design is broadly applicable to budget-strapped clinical settings beyond ophthalmology, and its performance can be further improved by using more data and/or other generic AI prediction methods. This framework thus opens a new path to early recognition and referrals of distressed patients, and also an efficient redirection of clinical resources in limited resource settings.

13. **Nutrigenomic Influence of a Curcumin-Supplemented High Glycemic Diet on Hippocampal Microvasculature in Male C57BL/6J Mice** | ***Emilio Balbuena***

Introduction: Curcumin, a dietary polyphenol primarily derived from turmeric, has potent antioxidant and anti-inflammatory capabilities against diet-related chronic diseases. A high glycemic diet (HGD) has been shown to contribute to cognitive decline and dysfunction of murine brain microvasculature. The goal of our study was to elucidate the multi-genomic effects of curcumin on hippocampal microvessels in mice during consumption of a high glycemic diet.
Methods: Male C57BL/6J mice were fed a low glycemic diet (LGD, 12% sucrose/weight), a high glycemic diet (HGD, 34% sucrose), or a HGD with 0.2% curcumin (HGD + Curc) for 12 weeks. Global transcriptomic profiles, including protein coding and non-coding genes, of lasercaptured endothelial microvessels of the hippocampus were analyzed via microarrays. Bioinformatic tools were utilized to uncover networks and functional pathways of differentially expressed genes modulated by curcumin as well as interactivity between transcription factors and major curcumin metabolites via in silico docking analysis.
Results: The HGD + Curc treatment influenced the differential expression of 1887 genes compared to HGD alone, which included messenger RNAs, microRNAs, long noncoding RNAs, and small nucleolar RNAs. Of these modulated genes, 307 overlapped and were negatively correlated with the fold change expression of the HGD versus LGD comparison. These protein coding and non-coding gene targets regulated by HGD+Curc were involved in pathways related to neurodegeneration, oxidative phosphorylation, blood-brain barrier permeability, cell signaling, and cellular metabolism.
Discussion/conclusion: The results from this study show that curcumin induces complex nutrigenomic modifications that could elucidate its neuroprotective effect against hippocampal microvascular dysfunction induced by a high glycemic diet.
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14. **How Cells Control and Solve Stalls in Protein Production** | ***Gessica Barros***

Cells tightly regulate how proteins are made by controlling translation, the process in which ribosomes read the instructions encoded in the messenger RNA (mRNA) into an amino acid sequence to build new proteins. The sequence of an mRNA strongly influences how smoothly ribosomes move along it. Certain sequences act as "roadblocks", stalling ribosomes. When a ribosome stall happens, cellular quality control systems are recruited to solve the problem, often by clearing the stalled ribosomes, degrading incomplete proteins, and removing faulty mRNAs. These safeguards are essential for preventing the accumulation of defective proteins that can harm cells. My research investigates how different types of mRNA-encoded challenges influence the behavior of stalled ribosomes and the engagement of quality control pathways. Specifically, my

project compares two types of stalls: those that arise when the ribosome struggles to read the mRNA message, and those caused by the properties of the amino acids in the growing protein itself. Although both types of stalls recruit the same quality control machinery, my findings show that they differ in key ways, including how well the ribosome maintains the correct reading frame and how the stalled protein is processed by the clearance system. In addition, my work identifies key regions within the ribosome that strongly influence the persistence of the amino-acid driven stalls and consequently the engagement of quality control systems. By uncovering how cells distinguish between different types of translational stalls, this research advances our understanding of how protein production is finely tuned and protected, with implications for molecular biology, disease research, and biotechnology.
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15. **Catalytic Pyrolysis of Polyethylene for the Synthesis of Jet Fuel Using Fe and Ru on H-Mordenite Catalyst** | ***Sujoy Bepari***

Polyethylene (PE) is one of the most commonly used plastics because it is strong and resistant to chemicals. However, these same properties make it difficult to break down, leading to large amounts of persistent plastic waste. This study focuses on converting PE into useful products through a process called catalytic pyrolysis, which uses heat and catalysts to break the plastic into smaller, valuable molecules such as light hydrocarbons, jet fuel-range liquids (C8–C16), and hydrogen.
To improve this process, catalysts based on H-mordenite (HM) zeolite were modified with iron (Fe) and ruthenium (Ru). These catalysts were carefully analyzed to understand their surface area, acidity, structure, and chemical composition using standard techniques. The breakdown of PE was also studied by heating it under controlled conditions and analyzing the gases and products formed. The performance of three catalysts—HM, Fe-HM, and FeRu-HM—was tested at different temperatures and catalyst-to-plastic ratios. Among them, the FeRu-HM catalyst showed the best results, achieving more than 90% conversion of PE and about 45% selectivity toward jet fuel-range products at 500 °C. Temperature was found to strongly affect the types of products formed.
To further improve the process, a statistical method called design of experiments (DOE) was used to study how key factors—such as temperature, catalyst amount, and nitrogen flow rate—work together. This helped identify the most effective conditions for maximizing fuel production.
Overall, this study presents a promising approach for turning plastic waste into valuable fuels in a more efficient and sustainable way.
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16. **Physicochemical Interventions for Shaping Microbial Communities in Built Environments** | ***Shilpi Bhatia***

Silver-based nanomaterials are potent antimicrobial agents effective against a broad range of microorganisms, including Gram-negative and Gram-positive bacteria. Their use in healthcare settings, particularly on high-touch hospital surfaces, is promising; however, repeated exposure to conventional silver nanoparticles can drive resistance in *Escherichia coli* (*E. coli*), raising concerns about long-term efficacy and the potential enrichment of antibiotic resistance genes (ARGs).
As part of the PreMiEr initiative to engineer the microbiome of the built environment (MoBE), this work advances physico-chemical strategies that move beyond conventional chemical disinfection. Rather than relying on repeated eradication, which may select for resistance. We focus on designing evolution-informed antimicrobial materials that combine physical and chemical modes of action.
Here, we evaluated whether *E. coli* can evolve resistance to silver nanowires, a shape-controlled nanomaterial whose high-aspect-ratio structure may enhance membrane penetration and antimicrobial activity. We hypothesized that this dual mode of action would limit adaptation by creating an evolutionary constraint. Using *E. coli* K-12 MG1655, we determined the minimum

inhibitory concentration (MIC) of silver nanowires (10 mg/mL) and conducted a 21-day experimental evolution study at a sub-MIC concentration (8 mg/mL) with daily serial passaging. Post-evolution MIC assays showed that *E. coli* developed increased resistance, indicating that nanowire-induced stress does not fully prevent adaptation. Ongoing whole-genome sequencing is expected to identify mutations in *cusS*, a regulator of the copper-silver efflux system.

This work informs the design of antimicrobial surfaces based on electrostatically assembled, shape-controlled silver nanoparticles (e.g., spheres, cubes, wires, platelets). By integrating nanoparticle synthesis, resistance evolution assays, and surface stability testing, we further aim to identify geometries that reduce the likelihood of resistance under repeated exposure. A complementary aerosol-based evolution assay will further assess resistance trajectories under more realistic exposure conditions.

Overall, these results highlight that nanoparticle shape alone may not prevent resistance evolution and underscore the need to pair material design with evolutionary testing to identify configurations that maintain antimicrobial efficacy over time.

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17. **Role of Fork Remodeling Translocases SMARCAL1 and ZRANB3 in Stalled Replication Fork Repair | *Chayan Bhattacharya***

Replication stress is a major driver of genome instability and tumorigenesis, particularly at DNA–protein barriers such as DNA–protein crosslinks (DPCs). Site-specific fork stalling using the Tus–Ter DNA–protein barrier system has shown that stalled replication forks are repaired through recombination mechanisms distinct from canonical two-ended double-strand break (DSB) repair. Fork remodeling enzymes, including SMARCAL1 and ZRANB3, are recruited in response to replication stress and promote fork reversal and restart. However, the molecular mechanisms by which these translocases regulate repair at DPC-induced stalled replication forks remain unclear. We hypothesize that these remodelers selectively regulate repair outcomes during replication stress and function upstream in the stalled fork repair cascade.

To test this, we generated SMARCAL1 knockout clones and ZRANB3 ATPase-dead mutants (Δexons 4–7) in mouse embryonic stem (mES) cells using CRISPR–Cas9. We employed a Rosa26-integrated homologous recombination (HR) reporter containing both a Ter replication fork barrier and an I-SceI endonuclease site, enabling direct comparison between stalled fork repair and classical DSB repair at the same genomic locus. HR outcomes, including short-tract gene conversion (STGC) and long-tract gene conversion (LTGC), were quantified by flow cytometry.

Loss of SMARCAL1 resulted in a consistent reduction in STGC frequency at Tus–Ter–induced stalled forks without a significant change in LTGC, suggesting a selective role in facilitating repair of a subset of stalled forks. Additionally, SMARCAL1 deficiency reduced I-SceI–induced DSB repair, consistent with previous reports. Colony formation assays following exposure to DPC-inducing agents showed no significant difference between wild-type and SMARCAL1-deficient cells, indicating that SMARCAL1 promotes efficient short-tract recombination without being essential for overall cell viability.

Functional characterization of ZRANB3 mutants and planned double knockout studies will further define the interplay between fork remodeling and FA pathway–mediated fork protection in regulating genome stability during replication stress.

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18. **Dishevelled 2 Promotes Tumor Progression by Suppressing Anti-Tumor Immunity in Triple-Negative Breast Cancer | *Geetha Priya Boligala***

Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer with limited targeted treatment options. Although immune checkpoint inhibitors have improved outcomes for a subset of

patients, many TNBC tumors remain poorly responsive to immunotherapy due to mechanisms of immune evasion. Aberrant activation of Wnt signaling has been linked to tumor progression and immune evasion in multiple cancers, including TNBC. Dishevelled 2 (DVL2) is a central scaffold protein in the Wnt signaling pathway that integrates signals from upstream Wnt ligands to downstream effectors. While DVL2 has been studied for its role in tumor cell signaling, its contribution to regulating tumor-immune interactions in TNBC remains poorly understood.To investigate the role of DVL2 in tumor immune regulation, we generated CRISPR-mediated knockout of DVL2 in two mouse mammary carcinoma cell lines, 4T1 and EO771, and orthotopically implanted them into syngeneic BALB/c and C57BL/6 mice, respectively. Loss of DVL2 (sgDVL2) resulted in significant tumor regression and improved overall survival in both models. In BALB/c mice bearing 4T1 tumors, DVL2 loss was associated with significantly reduced tumor burden and spleen weights compared to controls. Analysis of the tumor microenvironment revealed that sgDVL2 tumors harbor increased frequencies of cytotoxic and anti-tumor immune populations relative to control (NTC) tumors, as assessed by RT-qPCR and flow cytometry. Importantly, implantation of 4T1 NTC and sgDVL2 cells into immunodeficient nude mice lacking functional cytotoxic T cells diminished the survival advantage observed in immunocompetent mice, supporting a critical role for immune mediated mechanisms in DVL2-dependent tumor suppression.
Collectively, these findings identify DVL2 as a key regulator for tumor progression and anti-tumor immunity in TNBC. These results suggest that targeting DVL2 may enhance immunemediated tumor control and improve responses to immunotherapy in aggressive breast
cancers.
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19. **Platelet-Like Particles Modulate the Intercellular Signaling of Mesenchymal Stem Cells** | ***Jacob Brown***

Platelet-like particles (PLPs) are a polymeric microparticle-based wound healing technology developed to enhance hemostatic responses to injury. They are comprised of an ultra-low crosslinked 90:10 pNIPAM:AAc microgel (ULC) functionalized with fibrin-binding motifs. At the site of a wound, the fibrin-binding antibodies interact with the blood clot while it is forming, applying mechanical contractile forces which mimic the mechanical function of platelets. This causes the wound to stabilize faster and show improved healing characteristics. As part of their function, native platelets also release cytokines into the wound site which recruit fibroblasts and contribute to the coordination of the wound healing process more broadly. Fibroblasts are crucial to the wound healing and regeneration process, responsible for depositing and remodeling ECM. Augmenting the delivery of PLPs with mesenchymal stem cells (MSCs), which also produce signaling factors in the form of small extracellular vesicles (sEVs) that enhance fibroblasts recruitment and proliferation, would further mimic native platelet functionality. This study aims to determine how the PLP-enhanced clot environment influences MSC sEV production and fibroblast function.
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20. **Respiratory Neuroplasticity in a Pre-clinical Model of Duchenne Muscular Dystrophy** | ***Kayla Burrowes***

Duchenne muscular dystrophy (DMD) is a fatal X-linked neuromuscular disorder marked by dystrophin deficiency and progressive muscle degeneration. Respiratory muscles are critically affected, and ventilatory insufficiency remains the primary cause of death. Although current therapies and corticosteroids attenuate symptoms, they do not reverse the underlying pathophysiology, underscoring the need for strategies that preserve and strengthen ventilation long-term.

Acute intermittent hypoxia (AIH) is a neuromodulatory strategy that enhances respiratory function by inducing long-term facilitation (LTF) of respiratory motor output. AIH-induced LTF has benefited individuals with spinal cord injury and ALS, but its therapeutic potential in DMD is unknown. Because AIH-induced plasticity relies on serotonin signaling and is easily undermined by inflammation, the chronic inflammation associated with DMD poses a challenge. Consistent with this, our proteomics reveal a 3.8-fold reduction in 5-HT2A receptor expression in *mdx* mice, a key receptor mediating AIH-induced LTF. Given this serotonergic deficit and inflammatory load, we hypothesized that respiratory neuroplasticity would be diminished in *mdx* mice.
C57BL/10ScSn-*Dmd*^{mdx}/J (*mdx*) and C57Bl/10ScSnJ (WT) mice (3-4 months) received prednisolone (2mg/kg) or vehicle for 3 days prior to terminal neurophysiology. Mice were exposed to 3, 1-minute hypoxic episodes (10% O_2), interspersed by 3-minute normoxic intervals (60% O_2). Integrated hypoglossal nerve activity was measured at baseline, during hypoxia and 60 minutes post-AIH. Hypoglossal LTF, assessed as percent change in nerve burst amplitude from baseline to 60 mins post-AIH, was markedly reduced in *mdx versus* WT mice (33.5 ± 11% vs. 144 ± 42%; p=0.015). Acute prednisolone treatment restored LTF in mdx mice (155 ± 36%) and significantly reduced CD68+ microglial activation (p=0.0097). These findings identify a previously unrecognized deficit in respiratory neuroplasticity in DMD and show that it is pharmacologically reversible. AIH-based therapies, paired with targeted anti-inflammatory strategies, could be a viable therapeutic avenue to enhance respiratory function in individuals with DMD.
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21. **Redox Preservation of Clinical Specimens for Biomarker Discovery and Mechanistic Studies of Disease** | ***Maria Luiza Carneiro Buchele***

Blood is the most used biospecimen for diagnostics and the discovery of biomarkers for early disease detection and treatment. It is rapidly accessible, easily handled, and versatile for various applications. However, its utility in assessing redox biomarkers of disease is often compromised due to artifactual oxidation during processing and storage, leading to the loss of specimen integrity. To enhance our understanding of disease pathophysiology, reduce pre-analytical variability, improve patient staging, and aid in the development of new therapies, we have developed and tested a new formulation (RMX) as an alternative to the most used EDTA or Heparin blood collection methods.
RMX's ability to preserve the endogenous redox state of proteins while maintaining sample stability and its performance under variable volume conditions were evaluated, by assessing redox sensors such as peroxiredoxins and glutathione. Furthermore, blood from patients with sepsis was used to determine RMX's applicability in quenching the endogenous redox state of critically ill patients. Vascular endothelial growth factor (VEGF) degradation over time was also evaluated, as was RMX's compatibility with blood through the hemolysis assay.
The results demonstrate that RMX is compatible with Clinical Laboratory operations and provides a rapid and effective quenching of the redox state. The peroxiredoxins analysis and GSH/GSSG ratio of samples collected with RMX tubes indicate preservation of the intrinsic redox state of blood specimens. Notably, samples remained stable during storage up to a year. This innovative approach to mitigating artifactual oxidation allows for accurate redox state measurements and enhances the quantitative analytical precision of biomarker measurements in clinical specimens. The RMX formulation holds significant potential for identifying patient redox and molecular heterogeneity and tracking disease progression, thereby improving clinical staging and precision, and supporting the development of new therapeutic targets across diseases.
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22. **A High-Throughput Assay Platform to Discover Small Molecule Activators of the Phospholipase PLC-gamma2 to Treat Alzheimer's Disease | *Adam Carr***

The lipid metabolizing phospholipase C isozyme PLC-g2 is expressed in hematopoietic cells, including microglia. Recently, genome-wide association studies identified a single substitution variant (P522R) that protects against several neurodegenerative diseases, including Alzheimer's disease. PLC-g2 (P522R) is slightly hypermorphic versus the wildtype isozyme, and this elevated activity likely augments beneficial functions in microglia in the brain. Thus, pharmacological tools that recapitulate the elevated activity of PLC-g2 (P522R) in the wild-type isozyme are essential for studying the protective role of PLC-g2 in neurodegenerative disease and could serve as highly valuable lead compounds for drug discovery. In this work, we develop a biochemical screening platform to identify small molecule activators of PLC-g2. We establish a series of assays for characterizing biochemical potency, direct binding, and in-cell activity. Through this process, we identify several PLC-g2 activators that enhance phagocytosis in microglial BV2 cells. While only performed at a pilot scale of 6000 screening compounds, this work demonstrates the potential of our platform to rapidly identify and validate PLC-g2 activators that could be developed into novel chemical probes and lead compounds for drug discovery.

23. **"That May Be What You Are, but That's Not What I Am": Aging, Ageism, and Well Being Among Older Black Women | *Jacquelyn Coats***

Background and Purpose: Ageism is a recognized social determinant of health associated with poorer well-being, yet older Black women's perspectives and lived experiences remain underrepresented in age discrimination research. This qualitative study sought to fill this gap by exploring older Black women's lived experiences of ageism and its impact on well-being.

Methods: Semi-structured interviews were conducted with 16 Black women aged 65–79 years recruited through ResearchMatch.org, a national health research registry. Participants were asked about common assumptions and misconceptions they believed were held about older people generally and older Black women specifically. Data were analyzed using a thematic analysis approach; reflexivity and peer debriefings increased rigor.

Results: Four salient themes emerged: Theme 1—participants described older adulthood as an externally imposed identity, actively resisting labels such as "senior" when those labels implied decline or diminished capacity; Theme 2—women emphasized continuity of self across the life course, rejecting narratives that equate aging with loss of identity or agency; Theme 3—participants framed later life as a period of expansion and discovery, describing aging as a "second coming" characterized by renewed autonomy, future orientation, and personal rediscovery; and Theme 4—participants highlighted the devaluation of historical and lived knowledge, noting that despite long histories of community contribution, older Black women are often "moved to the corner" and rendered socially irrelevant.

Conclusions and Implications: These findings illustrate how age discrimination intersects with other forms of marginalization to shape well-being, social inclusion, and access to meaningful roles in later life. Addressing ageism among older Black women requires interventions beyond individual behavior change, including workforce training to reduce age-based bias, intergenerational programming, and broader efforts to reframe societal narratives of aging. Centering older Black women's lived expertise and community contributions may mitigate the impacts of ageism and promote dignity and sustained engagement.

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24. **A Spatiotemporal Investigation of Exodus Phase of S. Aureus Developmental Stages and Nanopattern Spacing on Bactericidal Properties of Nanopatterned Surfaces | *Parth Desai***

The paradigm in bioimplants suggests that nanostructured surfaces act as universal, static mechanical stressors. However, this model fails to account for the dynamic developmental stages of bacterial biofilms. In this study, we present a novel space and time-based framework integrating PDMS-bonded multi-well interfaces with TiO2 nanopatterns to map the mechanobiological fate of two clinically significant pathogens: S. aureus and E. coli.Our framework reveals a profound divergence in species-specific behavior on identical pitch topographies. While S. aureus shows community collapse with killing efficiency >80% synchronized with the biofilm cycle called exodus phase, while E. coli maintains high-density colonization through a strategy of geometric bridging and natural biological growth. These results provide a direct rejection of the one-size-fits-all antibacterial surface topography model. We demonstrate that mechanical lysis is not only engineered surface's property, but timebased biological event triggered by the synchronization of surface geometry with the bacterial life cycle. By correlating coverage area and killing efficiency on engineered surfaces with ultrastructural membrane deformations via fiducial based correlative light and electron microscopy(CLEM), we provide a blueprint for the next generation of smart orthopedic, dental, and urological implants. These implants can be strategically engineered to exploit the time-based susceptibility of specific pathogens that provide deterministic outcomes based on the life cycle of a pathogen in synchronization with structural geometry. Which help us target the most susceptible window of the bacterial colonization cycle on any engineered surfaces.
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25. **PPARα Restricts Pathological Monocyte Activation Through Mitochondrial Metabolic Regulation and cGAS–STING Signaling in Diabetes**

26. **Evolution and Functional Characterization of Olfactory Receptors in Birds** | ***Robert Driver***

Vertebrates detect odor molecules with olfactory receptors (ORs), a gene family expressed in the olfactory epithelium. Among species, OR diversity is associated with reliance on smell, with some mammals exceeding 2,000 OR genes. Birds are the most speciose class of terrestrial vertebrates, inhabiting nearly all land environments and with diverse social structures and foraging strategies, yet were long thought to make limited use of olfactory signals. Recent behavioral work in birds has shown important roles for olfaction in foraging and species recognition, among other behaviors. Contributing to this surge of interest in avian olfaction, our recent work has shown that birds have hundreds more OR genes in their genomes than previously realized. We have examined the genomic OR repertoire of over 150 bird species spanning the avian phylogeny, revealing between 7 and 3,800 intact ORs in all species surveyed. To discern the functional roles of ORs, we found that the ORs are expressed in the bird olfactory epithelium of four species and that bird ORs specifically localize to the olfactory sensory neurons of the posterior turbinate within the chicken maxilla. To confirm the ability of bird ORs to detect odors, we expressed chicken ORs in mammalian cell culture, exposed ORs to multiple odors, and measured OR activation in response to each odor. We found that chicken ORs respond to several types of pyrazines, a group of chemicals that are found in the scent of green peppers. Together, these results show that bird OR genomic counts are diverse, evolve dynamically, are expressed in olfactory sensory neurons, and are capable of functionally detecting odors. This work provides the foundation for future functional characterization of bird ORs across a variety of bird species.

27. **The Moments That Matter: Paraspinal Muscle Force and Moment Potentials in Adolescent Idiopathic Scoliosis** | ***Phoebe Duncombe***

Introduction: Adolescent idiopathic scoliosis (AIS) describes an asymmetrical spinal curvature that develops rapidly during adolescence. The magnitude and direction of skeletal forces during development are key moderators of bone growth. We aimed to quantify multifidus and longissimus

force and moment potential during flexion-extension, lateral bending, and axial rotation, and compare adolescents with AIS with matched controls with symmetrical spines.
Methods: T1-weighted, mDixon, and diffusion-tensor MRI (DTI) scans were acquired from females with primary right thoracic AIS (n=29, 13.6±1.6 years) and typically developing controls (n=16, 12.9±1.7 years). Using anatomically constrained DTI tractography, multifidus and longissimus fascicles were reconstructed and physiological cross-sectional area calculated. Muscle moment arms, maximal isometric force, and moment-generating potential were estimated. Linear mixed-effects models were used, with between-group effects evaluated using Wald t-tests (α=0.05).
Results: Adolescents with AIS showed significant asymmetries in paraspinal muscle moment potential compared with controls. For multifidus, asymmetry in lateral bending was observed, with greater left-directed moments at T5-T9 and right-directed moments at L1-L2. In axial rotation, multifidus showed a right-directed moment at T6 and left-directed moments from T8-T12 (Fig.1). For longissimus, asymmetry in lateral-bending was present, with greater right-directed moments at T12 only. In axial-rotation, longissimus exhibited a greater right-directed moment at T10 and a left-directed moment at T12. All $p<0.05$.
Counterfactual modelling indicated that lateral-bending asymmetry was mainly driven by moment-arm differences due to spine curvature, while axial-rotation differences stemmed from altered force-generating capacity. Multifidus moment asymmetries in lateral-bending and axial-rotation were moderately associated with Cobb angle (curve severity) ($r>0.40$; $p<0.05$).
Conclusion: This study provides evidence of asymmetries in paraspinal muscle moments in AIS associated with altered muscle force generation and moment arm along the spine. We contend that paraspinal muscles do not simply mirror spinal deformity but may actively contribute to progression by producing imbalanced forces capable of modulating vertebral growth.
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28. **Graded ERK Activation Promotes Distinct Functional Properties of Engineered Cardiac Tissues** | ***James Emerson***

29. **Uncovering the Functional Role of UBE2A in Neurodevelopmental Disorder UBE2A Deficiency Syndrome** | ***Tonie Farris***

How can gene mutations in a small 17.6kDa ubiquitin protein, UBE2A, cause a devastating neurodevelopmental disease? UBE2A deficiency syndrome is caused by mutations or complete deletion to the UBE2A gene. UBE2A Deficiency syndrome is an X-linked neurodevelopmental disorder that exclusively affects male individuals, while females are asymptomatic carriers. Patients' disease severity is dependent on the type of mutation to the gene. The most common symptoms observed across patients include cognitive disabilities, developmental delays, brain abnormalities, and heart defects, which require patients to have caregiver support throughout their lives. Currently, there is no cure or therapeutic interventions available for patients. Previous studies report that under conditions of stress, UBE2A-deficient cells exhibit mitochondrial dysfunctions including loss of membrane potential and altered mitochondrial morphology. Research further suggests that UBE2A deficiency is associated with deficits in neuronal synaptic plasticity. However, the precise molecular mechanisms by which UBE2A regulates these processes, and how their disruption contributes to disease pathology remain largely unknown. To address this critical knowledge gap, I propose to test the hypothesis that under conditions of cellular stress, loss-of-function mutations in UBE2A impair ubiquitin-dependent regulation of mitochondrial quality control pathways, leading to accumulation of dysfunctional mitochondria and ultimately disrupting neuronal synaptic networks. I will elucidate the role of UBE2A in regulating mitochondrial physiology and determine how these functions impact intracellular signaling in the CNS with the following aims: Aim 1, I will investigate the mechanisms by

which UBE2A regulates mitochondrial membrane potential. Aim 2, I will determine how UBE2A modulates the integrated stress response following mitochondrial stress. Aim 3, I will elucidate the mechanism by which UBE2A regulates hippocampal-dependent learning and memory. Collectively, this work has the potential to catalyze new discoveries and contribute to the broader conceptual framework defining how disruptions in ubiquitin signaling intersect with mitochondrial function to drive neurodevelopment.
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30. **Oxidation of KRASG12C Effects Covalent Inhibitor Engagement and Therapeutic Response in Non-Small Cell Lung Cancer | *Yismeilin Feliz Mosquea***

Mutations in the KRAS gene are common drivers of non-small cell lung cancer (NSCLC). One specific mutation, KRASG12C, can be targeted by new drugs such as Sotorasib (AMG510) and MRTX849. While these therapies have improved outcomes for some patients, many eventually develop resistance, limiting their long-term effectiveness. In this study, we investigated whether changes in the chemical state of KRASG12C, specifically oxidation that affect how well these drugs work. Oxidation is a natural process in cells that can modify proteins and alter their function. Because KRASG12C contains a reactive cysteine residue, we hypothesized that oxidative changes at this site could interfere with drug binding. Using purified protein and mass spectrometry, we found that exposure to oxidative conditions modifies KRASG12C at its key cysteine residue. These changes reduce the ability of covalent inhibitors to effectively bind the protein. We confirmed these findings in lung cancer cells, where oxidative stress induced by factors such as hydrogen peroxide or growth signals, altered how cancer cells responded to KRAS-targeted therapies. Importantly, our results suggest that the tumor's oxidative environment can directly influence treatment response. This may help explain why some patients do not respond well or develop resistance over time. Overall, this work highlights a previously underappreciated mechanism of drug resistance and suggests that targeting redox processes could improve the effectiveness of KRAS-directed therapies. Understanding these interactions may lead to better treatment strategies for patients with lung cancer.

31. **The Impact of New Awareness of a Sexually Transmitted Infection on Internalized HIV Stigma and Depressive Symptoms among Women Living with HIV in the United States | *Tess Filipowics***

Women living with HIV (WLWH) experience internalized HIV stigma (hereafter *stigma*) and increased depressive symptoms compared to women without HIV and men with HIV in the United States (US). Stigma and depression's impact on WLWH's mental health remains underexplored, particularly in the US where structural racism and sexism intersect to worsen WLWH's quality of life.

To test the hypothesis that new, non-HIV sexually transmitted infections (STIs) increase stigma and depressive symptoms via retraumatization, I modeled mean differences in stigma and depressive symptom scores at visits with an STI versus visits without using data from the Women's Interagency HIV Study (WIHS). I used generalized linear models with generalized estimating equations, weighted for confounding and censoring. Results were stratified by race/ethnicity categories, and 95% confidence intervals (CIs) were bootstrapped.

Mean differences in stigma scores between visits with and without an STI varied by race/ethnicity and ranged from -0.43 (95% CI: -1.18, 0.32) to 0.42 (-0.10, 0.93). All Hispanic ethnicity groups (White, Hispanic; Black, Hispanic; and Other, Hispanic) experienced increased scores at visits with STIs; Black, non-Hispanic and Asian/Pacific Islander participants had no change; and White, non-Hispanic and Native American/Alaskan Native participants had decreased stigma scores. Mean differences in depression scores also varied by race/ethnicity. Black, non-Hispanic participants had

a 1.46 (0.57, 2.34) point increase in depression scores, and Native American/Alaskan Native participants had a similar increase. Four race/ethnicity groups experienced decreased depression scores at visits with a reported STI, and Other, Hispanic participants' estimate was nearly null.
Analyses suggest that increased mental health support following a new STI may reduce stigma and depressive symptom burden in some WLWH but must be tailored to different race/ethnicity groups. Interventions focusing on stigma reduction are one potential way to improve WLWH's mental health and are desperately needed so WLWH can thrive, not just survive.
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32. **Decoding ATPase-Driven Ribosome Remodeling in Live Cells Using FLIM-FRET and Phasor Analysis** | ***Rajen Goutam***

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33. **Exploring CRF+ Lateral Hypothalamus to Ventral Tegmental Area Neural Pathway in the Modulation of Binge-like Ethanol Drinking** | ***Sara Guarino***

CRF is a peptide widely expressed in the brain and known to regulate stress responses. Our research showed that silencing central amygdala CRF+ neurons innervating the lateral hypothalamus (LH) blunted binge-like ethanol intake in male, but not female, mice. Our initial study targeting LH CRF+ neurons revealed that silencing these neurons blunted binge-like ethanol intake in CRH-Cre(+) mice. To further investigate the role of CRF neurocircuitry in modulating binge-like ethanol drinking, we identified CRF+ neural pathways arising from the LH and innervating regions, including the ventral tegmental area (VTA), known to modulate responses to ethanol. Our research combined CRH-Cre(+) mice and chemogenetics to manipulate this pathway. Mice received bilateral infusions of Flp-dependent Gi-DREADD (or control virus) in the LH and retrograde Cre-dependent-Flp virus into the VTA to inhibit the LH-VTA pathway on specific test days of the "drinking-in-the-dark" (DID) procedure, known to induce binge-like ethanol drinking. During the first two weeks of the DID procedure, mice were given two-hour access to 20% ethanol daily on each of four consecutive days followed by three days of access to water. On the fourth day of testing, mice received clozapine-N-Oxide (CNO) or vehicle injections in a Latin-square design. Based on the amount of ethanol intake following vehicle injections, mice were identified as High or Low drinkers, and data for these groups were analyzed separately. Control studies were also included to assess the effects of silencing this pathway on sucrose consumption and locomotor activity, and to test specificity of manipulations to ethanol intake. LH-VTA chemogenetic silencing blunted ethanol intake in Gi-DREADD High drinkers relative to Low drinkers. Specifically, these effects seem to be female driven. This research supports a role for this pathway in the modulation of binge-like ethanol consumption and suggests differential functioning in CRF signaling between High and Low ethanol drinker mice.

34. **Adeno-associated Virus (AAV) Synthetic Inverted Terminal Repeats Enhance Transduction and Decrease Vector Induced persistent Gamma-H2AX in a Tissue-Specific Manner** | ***Tomoko Hasegawa***

Adeno-associated virus (AAV) vectors are widely used for gene therapy and have shown therapeutic benefit in clinical applications. However, noted challenges include low transduction efficiencies, poor cellular targeting, and vector related adverse events, including AAV vector-induced apoptosis in human embryonic stem cells. Recently, we demonstrated that a rationally designed synthetic inverted terminal repeat (SynITR) altered the AAV vector-induced DNA damage response and abrogated apoptosis in human embryonic stem cells. In the current study, in order to explore the utility of AAV-SynITR for diverse gene therapy applications, vector production, transduction, and the cellular response were evaluated. Regardingproduction, SynITR vector preparations exhibited com

parable titers to wtITR, largely in a serotype/transgene-independent manner. As to transduction in vitro, SynITR vector showed diminished transduction compared wtITR in various cell lines. However, when administered intravenously to wt mice, in-life imaging demonstrated SynITR AAV8 vectors enhanced transduction through day 7 to the end of the experiment (day 21). Moreover, postmortem analysis showed transduction enhancement by SynITR in a tissue-specific manner in liver (>7-fold), kidney (>2-fold) and pancreas (>2-fold) at equivalent vector copy numbers; however, no differences were observed in muscle/heart/spleen tissues. Interestingly, persistent gH2AX, a marker of aging/chronic inflammation, was abundant in the liver and spleen following wtITR (but not SynITR) transduction. Towards the development of future clinical translational applications, the transduction was tested in a viable human tissue; corneas. As a result, SynITR enhanced transduction up to 16-fold over wtITRs in human corneas.
These data demonstrate that SynITRs elicit tissue-specific transduction enhancement and alter the cellular stress response. Importantly, the SynITRs offer an alternative context to elucidate wtITR biology for targeted, enhanced, and potentially safer human gene therapy.

35. **Effects of Weight Loss and Exercise on Muscle Mass Using D3-Creatine Dilution in Older Adults | *Nina Heilmann***

Several indicators of reduced muscle health, including lower muscle mass and strength, are associated with higher mortality risk in older adults, but they do not fully capture the ability to generate force rapidly, or muscle power (i.e., force × velocity). We examined associations of leg power and its components (force and velocity) with all-cause mortality in older men from the Osteoporotic Fractures in Men (MrOS) Study (n=1242; mean age 84±4 years at Visit 4). Leg power was assessed with 3–5 countermovement jumps on an AMTI force plate; the trial with the highest peak power (W) was analyzed, along with force (N) and velocity (m/s) at peak power. Deaths were ascertained every four months and centrally adjudicated from death certificates. Cox proportional hazards models estimated associations (per standard deviation [SD]) of power, force, and velocity with mortality, adjusting for weight, height, race, clinic site, age, smoking, alcohol use, self-reported physical activity, cognitive function, self-rated health, medication count, and comorbidity count. During 6.8±2.5 years of follow-up, 562 (45%) men died. Each SD increment in jump power was associated with a 33% lower risk of death (HR: 0.67, 95% CI 0.60-0.76). Each SD increment in force (HR: 0.74, 95% CI 0.64-0.86) and velocity (HR: 0.74, 95% CI 0.67-0.83) were also associated with a lower risk of death. Force and velocity were weakly correlated *(r*=0.04*),* and when entered in the same model, effect sizes for force (HR 0.77, 95% CI 0.67-0.89) and velocity (HR 0.75, 95% CI 0.68-0.84) were similar. In conclusion, higher jump power, force, and velocity were each associated with a lower risk of mortality in older men. These findings suggest that both the ability to generate force and the speed of movement are associated with mortality risk. Future work should examine these associations in women and diverse populations.
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36. **Roots to Neurons: Evaluating Developmental Neurotoxicity (DNT) Potential of Botanicals Using an In Vitro Testing Battery | *Zakiyah Henry***

The usage of botanicals is widespread and growing in the United States. Most botanicals have not been evaluated for developmental neurotoxic (DNT) potential, and some have been shown to adversely affect the central nervous system. International efforts have proposed new approach methodologies (NAMs) for DNT testing resulting in the DNT *In Vitro* battery (DNT IVB) which consists of multiple assays designed to detect changes in key neurodevelopmental processes (e.g. proliferation, apoptosis). The objective of this project was to screen botanicals in the DNT IVB to assess potential DNT hazard. Eight botanicals selected based on signals of neurotoxicity in the literature (Aconite, Bupleurum, Cassava, Guarana, Kratom, Oleander, Wormwood, and

Yohimbe) were assessed for DNT potential using a DNT Battery comprised of 2D and 3D *in vitro* assays to assess the impact on neurodevelopmental processes and a zebrafish assay to measure neurobehavior. In our findings, Oleander exhibited the greatest potential for DNT effects as it displayed the highest selectivity and potency in multiple DNT assays. Fu Zi (Zhi), a popular Chinese herbal medicine and a processed root of Aconite, was the only botanical sample that showed no activity in any of the assays. Our findings also show that potency and activity of the botanicals can differ not only by ingredient but also by preparation of the same ingredient and by lot number (e.g., Kratom samples differed across preparations and lot numbers). In summary, exposure to botanical extracts affects neurodevelopmental activity, although consistent results across samples of the same ingredient were not observed. These inconsistencies are likely due to the variations in botanical processing and preparation which affects their chemical composition and potency. The diverse activity phenotypes of botanicals and botanical-derived compounds further highlight the complexity of hazard characterization, including DNT evaluation.
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37. Heterogeneous Myocardial Mechanics in Human Heart Failure Associate with Vascular Dysfunction and Fibrosis | ***Yaqing Huang***

Cardiovascular disease remains a leading cause of morbidity and mortality, particularly in aging populations. Fibrosis, characterized by progressive extracellular matrix (ECM) remodeling, is a hallmark of heart failure and contributes to altered tissue mechanics and impaired cardiac function. However, fibrosis rarely develops uniformly, creating localized microenvironments whose mechanical and biochemical interplay with vascular phenotypes remains poorly understood.
To address this gap, we performed high-resolution mapping of tissue stiffness alongside fibrosis and vascular markers in human failing hearts (ischemic cardiomyopathy, ICM, n=3) and non-failing controls (NF, n=3) using atomic force microscopy and immunofluorescence. While mean stiffness did not differ significantly between groups, ICM tissues exhibited markedly increased heterogeneity, with a broader distribution and higher variance in stiffness. Spatial alignment of stiffness maps with ECM remodeling (COL1/3, LOX) and vascular markers (CD31, ACKR1) revealed that regions of increased fibrosis were stiffer, whereas areas with greater vascular density and larger vessels were more compliant. These relationships were supported by correlation analyses (e.g., LOX: $r \approx 0.5$; CD31: $r \approx -0.7$ to -0.8). Integration with publicly available single-cell RNA sequencing data further indicated that vascular cell populations associated with mechanically stiffer regions exhibited elevated injury activation and senescence signatures, implicating a potential mechanistic link between the microenvironment and cellular activity.
Collectively, these findings demonstrate that failing human hearts exhibit pronounced and previously underappreciated heterogeneity in mechanical, structural, and cellular states. Understanding this hidden heterogeneity could improve the diagnosis of disease progression and inform the development of more targeted therapies. Ongoing work aims to further uncover how these local environments drive disease and how they can be therapeutically targeted.
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38. Role of Astrocytic CLPB in Alzheimer's Disease | ***Natasha Jaiswal***

Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline, synaptic dysfunction, and chronic neuroinflammation. While neuronal vulnerability has been extensively studied, astrocytes are increasingly recognized as central regulators of synapse formation, metabolic homeostasis, and neuroinflammatory signaling. Given their high bioenergetic demand, astrocytes are particularly susceptible to mitochondrial dysfunction, which may propagate neuronal injury. CLPB, a mitochondrial disaggregase involved in protein quality control and metabolic regulation, has not been investigated in AD. Our preliminary data reveal elevated CLPB

expression in postmortem AD patient brain tissue, AD mouse models, and cellular systems. Furthermore, genome-wide association studies identify a CLPB gene variant (rs74766959) associated with AD risk, suggesting clinical relevance. Methods: To define the role of astrocytic CLPB in AD, we employed both in-vitro and in-vivo approaches. Human SVGp12 astrocytes were used to examine CLPB-dependent mitochondrial and metabolic alterations. In-vivo, we generated an inducible astrocyte-specific *Clpb* knockout model (Aldh1l1-CreERT2 X *Clpb*$^{fl/fl}$) crossed with the *App*^{SAA}-KI AD mouse line. Conditional deletion was induced with tamoxifen, and cohorts were analyzed at 3, 6, and 9 months of age. Behavioral assessments included open field tests to evaluate anxiety-like behavior and Y-Maze tests to evaluate working spatial memory. Results: Initial data indicate that astrocyte-specific conditional loss of *Clpb* in an AD mouse model is associated with reduced anxiety-like behavior, improved spatial working memory, and decreased body weight. In-vitro, CLPB overexpression was associated with increased ATP production and elevated mitochondrial superoxide levels, suggesting altered mitochondrial bioenergetics. Conclusion: These initial findings suggest that astrocytic CLPB may influence mitochondrial function and behavior in AD. Ongoing age-dependent behavioral, transcriptomic, and biochemical studies will assess the effects of astrocytic *Clpb* deletion on Aβ accumulation, tau pathology, synaptic integrity, and bioenergetic remodeling, aiming to clarify a mechanistic link between mitochondrial protein quality control, astrocyte metabolism, and neurodegeneration in AD.

39. Illuminating the Endolysosomal System in Neurodegenerative Disease | ***Kajal Kamble***

Dysregulated endolysosomal pathway is a hallmark of many neurodegenerative disorders. Visualizing and understanding the dynamics of the endolysosomal pathway remains a major bottleneck in the development of potential therapies. Here, we introduce a high-resolution multispectral live-cell imaging approach and computational 3D morphometric analysis pipeline to comprehensively evaluate the effects of perturbations and mutations on the morpho-dynamics of multiple endosomal compartments simultaneously in live cells. This approach captures coordinated structural remodeling across endosomal, lysosomal and Golgi compartments, enabling quantitative detection of organelle morphology, distribution, intensity, co-localization, dynamics and pathway balance under perturbation and mutation conditions. As a proof-of-principle, we leveraged Brefeldin A (BFA), an inhibitor of ARF1-dependent ER–Golgi trafficking, to induce acute and defined disruption of membrane flux. Our approach sensitively captured coordinated remodeling across the pathway. BFA treatment induced pronounced Golgi fragmentation, with increased object count, total volume, surface area, and volume fraction. Recycling endosomes displayed increased Rab11-positive structural variability and elevated surface area-to-volume ratios, consistent with altered recycling dynamics. Lysosomes exhibited increased LAMP1-associated signal, enhanced volume heterogeneity, and higher surface area-to-volume ratios, alongside reduced mean surface area, indicating stress-induced remodeling. In contrast, early endosomes showed reduced variability in surface area, suggesting constrained morphological states. Strikingly, principal component analysis (PCA) robustly separated BFA-treated cells from controls, demonstrating that our pipeline captures high-dimensional phenotypic signatures of trafficking disruption. We applied multispectral imaging to human iPSC-derived neurons (iNeurons) to investigate endolysosomal remodeling in the context of neurodegenerative disease and extended the approach to additional neural cell types, including iPSC-derived astrocytes (iAstrocytes). Together, this work establishes a scalable imaging and analysis framework to define how endolysosomal morpho-dynamics are altered across diseaserelevant cell types, providing a foundation for mechanistic investigation of lysosome and endosome dysfunction in neurodegenerative disease.

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40. **High-Resolution U.S. Indoor Radon Gas Concentration Estimates via Bayesian Spatial Modeling with Preferential Sampling Adjustment** | ***Ayesha Kumari Ekanayaka Katugoda Gedara***

Radon—a naturally occurring radioactive gas that often accumulates indoors—is a known cause of lung cancer and an emerging risk factor for cardiovascular disease. However, radon testing is more likely among U.S. homes in communities with higher suspected radon concentrations. Such dependence can distort inference about the true spatial distribution of radon-related risk to the extent that observed radon concentrations reflect where testing is concentrated, not the underlying true pattern of exposure. To address the distortion, we developed a Bayesian, hierarchical, spatial model for estimating home radon concentrations while accounting for selection bias arising from the non-random distribution of radon testing. Using residential radon survey data from across the U.S., we estimated high-resolution, 10x10 km^2 radon concentrations in picoCuries per liter of indoor air and corresponding measures of uncertainty. We found that correcting for uneven testing increases accuracy of estimated radon concentrations. Mapping the concentrations and their uncertainties also revealed local spatial variation masked in existing coarser maps and provided additional guidance regarding precision across locations. These features have important implications for public health practice because they more precisely identify communities at elevated risk, help target radon testing / mitigation, and provide a more reliable exposure surface for health-effects modeling. More broadly, this work demonstrates the combined value of spatial refinement, selection bias correction, and uncertainty quantification in environmental risk assessment.
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41. **Burrow Depth Mitigates Energetic and Hydric Depletion of Desert Tortoises During Summer Droughts** | ***Ellen Keaveny***

Environment, physiology, and behavior influence the energy balance of organisms, particularly amid warming climates, with cascading effects on fitness. Organisms that burrow underground are often assumed to be buffered from challenging temperatures, minimizing their energetic and hydric costs. Yet, the degree to which burrow-use mitigates these costs may be context-dependent, for instance, across age classes, which may vary in their sensitivity to rising temperatures. We measured the temperature-dependence of metabolic and evaporative water loss rates of hatchling, juvenile, and adult desert tortoises (*Gopherus agassizii*) using flow-through respirometry. We developed mechanistic models that combined the thermal sensitivity of metabolic and water loss rates with burrow temperatures across three depths to determine age class-specific differences in energetic and hydric costs of desert tortoises throughout a summer dry season. Our findings suggest that energy is more limiting than water during summer droughts, and that hatchlings are most vulnerable across physiological metrics, incurring the greatest energetic and hydric costs, especially at shallower burrow depths. Such predictions are informative for conservation in prioritizing current suitable habitats and identifying future areas of conservation for translocations that minimize physiological costs as the climate continues to change. Our results also suggest that seemingly minor differences in physiological metrics across age classes can have compounding effects on energetic costs that shape vulnerability to environmental change.

42. **SIRT1 Organizes Nuclear RNA Condensates to Safeguard Male Meiosis**

43. **Development of a Stable Mammalian Expression Platform for Recombinant Human Fibrinogen Production** | ***Abigael Kosgei***

Fibrinogen is a multidomain glycoprotein essential for blood clot formation whose recombinant production remains challenging due to its large size and complex heterohexameric assembly.

Consequently, most fibrinogen used in research is plasma-derived, limiting scalability, molecular customization, and experimental control. Here, we are establishing a stable mammalian expression platform to generate recombinant human fibrinogen as a renewable and tunable alternative.
Transient transfection strategies were evaluated in HEK293 cells using polyethylenimine (PEI) at a 3:1 PEI:DNA ratio. Two expression approaches were compared: a three-plasmid (3P) system encoding the α, β, and γ chains with distinct fluorescent reporters, and a combined single-plasmid construct (CSP) containing all three chains with a single fluorescent marker. The 3P system demonstrated higher transfection efficiency and increased fibrinogen production, serving as an effective benchmark for expression.
Fluorescence-activated cell sorting enabled isolation of cells exhibiting all three reporters; however, expanded populations showed minimal fluorescence, suggesting transient expression without stable genomic integration. While the 3P approach improves short-term expression, reliance on multiple plasmids complicates selection and may hinder the development of a stable production line.
Despite lower initial transfection efficiency, the CSP construct remains the preferred strategy for stable cell line generation due to simplified selection through a single fluorescent reporter. Current efforts focus on improving CSP performance through optimization of transfection conditions, evaluation of alternative reagents such as ExpiFectamine, and testing constructs containing varying numbers of autonomously replicating sequence elements to enhance construct retention and expression stability.
Establishing a robust mammalian cell line for recombinant fibrinogen production will generate a scalable and reproducible protein source while providing full genetic control over fibrinogen composition. Unlike plasma-derived material, this platform enables engineered variants to directly interrogate structure–function relationships and supports controlled biochemical and binding assays to characterize molecular interactions. Together, these capabilities create a versatile experimental system that advances mechanistic understanding of fibrinogen biology and facilitates the exploration of fibrinogen-targeting molecules with potential therapeutic significance.

44. Does the Dose Make the Poison? Time Will Tell | Paul Kruse

The GeoTox framework and R package provide source-to-outcome modeling of exposures to chemicals and their downstream effects on different biological mechanisms. Users supply geo-spatially resolved steady-state exposure data and study how this affects a given population through *in vitro* endpoints.
Currently, GeoTox implements purely spatial exposures and steady-state toxicokinetics. Here, we develop the GeoTox framework to model time varying exposures and non-steady state kinetic scenarios. Using new GeoTox functions, user-supplied time-series exposure data can be analyzed to determine the impact of varying exposure scenarios on biological response using traditional dose-response curves given by the Hill equation. We also derived a novel Hill equation model with a dose- and time-dependent decay factor to model pre-equilibrium dose-response.
We completed numeric simulations of three exposure scenarios (acute, periodic, and constant) on populations in six ten-year age ranges and in two weight classifications for 39 chemicals. Blood plasma concentration data showed greater differentiation between exposure scenarios for chemicals with fast convergence time to steady-state plasma concentration than with slow convergence. We observed a tradeoff between acute to periodic peak plasma concentration ratios and the blood plasma area under the curve (AUC) ratios, where chemicals with higher peak plasma ratios have lower AUC ratios.
In pre-equilibrium dose-response modeling we observed behavior of time-varying dose-response falling between two limiting behaviors, with a tradeoff between peak response values and total

response AUC above set response thresholds. Comparing the decay rate associated to the average dose and a period of five minutes with a threshold of 1E-3 and 1 - 1E-3 roughly determines the dose-response behavior.
Expanding the functionality of GeoTox to handle dynamic exposure data provides users with tools to explore dynamic exposure scenarios. Our simulations demonstrate a need for more time-resolved dose-response experimental data as well as time-dependent dose-response models to study more complex exposure scenarios.
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45. Growth of Large-Area Diamond Films for Protective Coatings and High-Power Electronics | *Kishan Kumawat*

We have obtained the growth of continuous diamond films over large sapphire wafers. First, a specialized form of carbon known as Q-carbon was deposited onto sapphire using a plasma-based technique. During deposition, low-energy argon ions bombard the surface, creating nanoscale defects that transform amorphous carbon into Q-carbon. This material, characterized by a random tetrahedral structure, serves as an effective seeding layer for subsequent diamond growth.
The Q-carbon layer was then converted into a continuous diamond film using a high-temperature filament chemical vapor deposition process. The resulting films were systematically characterized to evaluate their structural, optical, electrical, and mechanical properties.
Our results demonstrate that uniform diamond films can be grown over relatively large areas, reaching wafer sizes of up to 2 inches. Additionally, the introduction of buffer layers between the sapphire substrate and the diamond film improves crystal alignment during growth. Overall, this work provides valuable insight into scalable fabrication of large-area diamond films for applications in protective coatings and high-power electronic devices.
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46. The Functional Strength Landscape of the Human Foot-Ankle Complex | *Yujin Kwon*

Introduction: The human foot-ankle system is governed by interactions among active muscle force, passive series elastic structures, and joint articulation, creating a strength landscape of force-generating potential for the plantar flexors (PF) and plantar intrinsic muscles (PIM). However, this landscape has not been characterized across ankle and metatarsal phalangeal (MTP) joint postures in context of walking. We hypothesized that MTP extension would offset declines in the force-generating potential with ankle plantarflexion, coinciding with late stance kinematics and peak muscle excitations.
Methods: 22 younger adults completed maximum voluntary isometric contractions on an isokinetic dynamometer (PF) and a foot dynamometer (PIM) across combinations of 3 ankle joint (20˚ dorsiflexion, 0˚ neutral, and 20˚ plantarflexion) and 3 MTP joint angles (0˚, 30˚ and 60˚ extension). Participants walked at 1.4 m/s while we recorded joint kinematics and PF and PIM excitations.
Results: An interaction revealed that ankle angle ($p=0.018$) more than MTP angle ($p=0.062$) affected PF strength. Specifically, PF strength decreased with increasing MTP extension during ankle dorsiflexion and increased with increasing MTP extension during ankle plantarflexion (Fig. 1A). No significant interaction was observed for PIM strength while MTP ($p<0.001$) but not ankle angle ($p=0.558$) affected PIM strength (Fig. 1B). Both peak PF and PIM excitation occurred during late stance kinematics. Peak PF excitation coincided with the maximum force-generating potential of the landscape, while PIM excitation did not.
Discussion: These findings demonstrate that the interaction between ankle and toe postures plays a critical role in preserving force-generating potential of the foot-ankle complex during walking. MTP

extension may enhance PF force generation by optimizing force–length conditions and reducing series elastic slack in biarticular extrinsic foot muscles contributing to push-off. PF excitation may align to exploit the maximal capacity, whereas PIM excitation does not, instead contributing to stabilization and stiffening of the foot during push-off.
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47. Wearable Ultrasound for Muscle Intent Prediction | *Krysten Lambeth*

Robot-assisted gait therapy can improve mobility and leg muscle strength in people with disabilities. It is critical that the robot adapt to the user during rehabilitation exercises, providing the minimum assistance necessary to complete the task in order to maximize functional improvement. Traditionally, electromyography (EMG) has been used to predict human muscle intent, but EMG cannot noninvasively measure the activities of deeply located muscles, and it is subject to muscle crosstalk. Ultrasound can measure muscle intent from deeply located muscles, but traditional probes are bulky and impractical for gait therapy. In this work, we use wearable ultrasound sensors (WUS), EMG, and WUS-EMG fusion to inform neural networks and predict volitional leg muscle torque during isometric muscle contractions. The ultrasound sensors are specifically designed to be form fitting for gait therapy. Despite having fewer sensing elements than a traditional probe, WUS is able to provide enough information to capture muscle deformation during contractions and reliably estimate volitional joint torque. WUS-informed neural networks outperform EMG-informed networks, with WUS-EMG fusion having the highest prediction accuracy.
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48. Transient Dynamics of Open Quantum Systems using the Multiparticle Holstein Hamiltonian | *Sreeja Loho Choudhury*

How can we design materials that efficiently move energy and charge at the quantum level? This question lies at the heart of technologies such as organic solar cells, flexible electronics, and nextgeneration quantum devices. In these systems, energy is carried by quasiparticles like excitons and polarons, whose motion is strongly affected by interactions with their environment [1]. These interactions can rapidly destroy quantum coherence (known as phenomenon of decoherence) [2]—a key ingredient for efficient transport—limiting device performance. In this work, we investigate how environmental effects drive the loss of quantum coherence in molecular materials. We simulate a chain of molecules interacting with surrounding vibrations that mimic real-world conditions. By tracking the system's evolution in time, we directly observe how quantum coherence decays via subsystem purity [3] and identify the factors that control this process.
Our results reveal clear and systematic trends: as environmental complexity increases, coherence is lost more rapidly, fundamentally constraining energy and charge transport [4]. At the same time, we identify regimes where coherence can persist longer, offering potential pathways to improve material performance [5].These findings provide new insight into how quantum behavior survives—or fails—in realistic environments. By bridging fundamental physics with practical material design, this work contributes to the development of more efficient energy technologies and robust quantum devices.
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49. Assessing TROPICS SmallSat Precipitation for IMERG

50. Butyrate Synergizes With Glucose to Promote Anaerobic Growth of Staphylococcus Aureus Via Anaplerotic Metabolism and Stress Response Pathways | *Areej Malik*

Short-chain fatty acids (SCFAs) like butyrate and propionate are abundant microbiota-derived metabolites that influence bacterial physiology in host-associated niches such as the gastrointestinal tract. However, their effects on *Staphylococcus aureus* under varying nutritional

conditions remain incompletely understood. Here we investigated how SCFAs interact with glucose or galactose to regulate anaerobic growth, biofilm formation, and global transcription in *S. aureus*. Both SCFAs inhibit growth in a dose-dependent manner. Biofilm formation was differentially affected, with butyrate promoting and propionate suppressing biofilm formation. Glucose and galactose alleviated SCFA-mediated growth inhibition, with glucose exerting the strongest effect. Notably, glucose enhanced butyrate-associated growth and biofilm formation beyond glucose alone, whereas galactose produced more modest effects. Enzymatic and genetic analyses indicated that SCFA-sugar biofilms contain proteins and extracellular DNA, and involve VraSR-dependent regulation. Transcriptomic profiling revealed broad metabolic reprogramming, including induction of urease genes, amino acid biosynthesis pathways, and anaplerotic metabolism. Synergistic effects between butyrate and glucose were partially dependent on pyruvate carboxylase, linking carbon metabolism to SCFA adaptation. Together these findings demonstrate that the nutritional environment dictates whether SCFAs inhibit or reprogram *S. aureus* physiology, promoting metabolic adaptation and biofilm formation under sugar-replete conditions.

51. Fear as a Missing Link: The Relationship Between Knee Pain/Function and Physical Activity in Physically Active Adults with Patellofemoral Pain | *Hana Marmura*

Background: Patellofemoral pain (PFP), anterior knee pain intensified by knee-joint loading activities, affects ~25% of the population and can cause chronic pain and psychological distress. The fear avoidance model posits that pain may lead to pain-related fear which then contributes to a vicious cycle of avoidance behaviors (i.e., reduced physical activity) and worse outcomes. Therefore, the purpose of this study was to test the relationships between knee pain, pain-related fear, and physical activity in adults with PFP.

Methods: Adults who self-reported sport/physical activity participation and PFP symptoms were included. Eligible participants completed online questionnaires including a demographics survey, the Anterior Knee Pain Scale (AKPS), Tampa Scale of Kinesiophobia-11 (TSK-11), and International Physical Activity Short Form (IPAQ-SF). Descriptive statistics were calculated for all variables, and a structural equation model was built to test whether pain-related fear (TSK-11 scores) mediated the relationship between knee pain (AKPS scores) and weekly physical activity in metabolic equivalent minutes.

Results: 104 participants were included in the study (32.8 ± 15.1 years old, 64% female, 61% white). Less knee pain was associated with lower-injury related fear ($b = -0.2$ [-0.3 to -0.1], $p < 0.01$) and higher injury-related fear was associated with less weekly physical activity ($b = -43.5$ [-77.3 to -9.7], $p < 0.01$). Importantly, the indirect effect of knee pain on physical activity, acting through injury-related fear, was significant ($b = 8.2$ [1.0 to 15.5], $p = 0.03$). The direct relationship between knee pain and physical activity was also significant ($b = -15.0$ [-29.6 to -0.5], $p = 0.04$), suggesting a partial mediation model.

Conclusion: Pain-related fear was identified as a key psychological mediator linking knee function and pain to physical activity levels. These data support the fear avoidance model and justify targeted interventions addressing injury-related fear to enhance physical activity engagement in individuals with PFP.

52. What Can Germanium Detectors Demonstrate Regarding the Origins of Matter? | *Aparajita Mazumdar*

Why didn't the universe *annihilate* after the big bang, and why is the universe filled with matter? Neutrinos may reveal hints to the answer. This is the 70th anniversary of the discovery of the neutrino, but we are still learning new properties of this fascinating particle, and one such experiment could be tied to this existential question. Neutrinoless Double Beta Decay ($0\nu\beta\beta$)

experiments attempt to search for a yet undiscovered rare decay, which is thought to occur in certain nuclei. If observed, it would conclusively establish that neutrinos are their own anti-particles, provide a crucial ingredient of the matter-antimatter asymmetry, and could also constrain the absolute mass of the neutrinos.
^{76}Ge is a candidate nucleus for observing 0νββ, and can be adapted to existing germanium detector technology. The LEGEND experimental program aims to have an ultimate discovery sensitivity to a 0νββ half-life beyond 10^{28} years for ^{76}Ge, which improves upon the current limits by approximately 2 orders of magnitude. Currently, the first phase of the experiment, LEGEND-200 has acquired a year of stable data with 142 kg of enriched germanium detectors. In this flash talk, we'll discuss what LEGEND-200 is, why 0νββ is important, and our first results.
This work is supported by the U.S. DOE, and the NSF, the LANL, ORNL and LBNL LDRD programs; the European ERC and Horizon programs; the German DFG, BMBF, and MPG; the Italian INFN; the Polish NCN and MNiSW; the Czech MEYS; the Slovak RDA; the Swiss SNF; the UK STFC; the Canadian NSERC and CFI; the LNGS and SURF facilities.
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53. Alterations in Prelimbic Cortex Activity and Motivated Behavior in a Rat Model of Simultaneous Alcohol and Nicotine Exposure | *Julia Mitchell*

Simultaneous co-use of alcohol and nicotine is rising, as is the use of electronic nicotine delivery systems (ENDs). During early stages of alcohol and nicotine use, users express feelings of decreased anxiety and increased feelings of pleasure. The prelimbic (PL) region of the medial prefrontal cortex (mPFC) is critical in emotionally regulated behavior and is a target of alcohol- and nicotine-related plasticity. Using slice electrophysiology and the Novelty Suppressed feeding assay, this research investigates the consequences of acute, simultaneous alcohol and nicotine exposure on PL activity and anxiety-like and motivated behavior in female and male rats. In our first experiment, we found that alcohol led to a significant decrease in neuronal firing in females but not in males, while nicotine or co-exposure produced no effects. In our second experiment, animals underwent a single 3-hour vapor exposure in one of three groups: ethanol/nic vapor, ethanol/PGVG vapor, or an air/air control group. Immediately following vapor exposure, animals went through the novelty suppressed feeding assay to examine anxiety-like and motivated behaviors. Sixty minutes after the termination of vapor exposure, animals were perfused and tissue was stained for cFos, a proxy for neural activity, throughout the mPFC. Females and males showed both decreased anxiety and neuronal activation following simultaneous nicotine and alcohol exposure, compared to air control groups. In a third experiment, we investigated simultaneous nicotine and alcohol effects in the CRF1 neuron population in the PL. Results from this experiment indicate that, regardless of sex, alcohol reduces spontaneous firing while simultaneous alcohol and nicotine exposure leads to an increase in firing in females only. Together, these data suggest that simultaneous alcohol and nicotine use differentially effects PL activity in a sex-dependent and cell specific manner, thereby potentially contributing to sex differences in addiction pathology.

54. Arc Gene Expression is Upregulated in the Nucleus Accumbens of EtOH-exposed Mice After Cue-induced Reinstatement of EtOH-seeking Behavior | *Cassandra Modrak*

Alcohol use disorder (AUD) is a chronically relapsing disorder wherein exposure to alcohol-associated cues can trigger relapse during abstinence. Elevated AMPAR signaling throughout limbic regions are implicated in alcohol-seeking behavior, alcohol cue salience and plasticity. Such effects appear to be mediated by transmembrane AMPAR regulatory proteins (TARPs) and Arc, an immediate early gene that regulates excitatory plasticity. Despite this, whether Arc is implicated in reinstatement to alcohol-paired cues by interacting with AMPAR signaling mechanisms remains to be fully elucidated. Here, we investigated changes in genes encoding for GluA1 plasticity and

transport throughout reward regions such as the amygdala, prefrontal cortex, and nucleus accumbens in mice following operant self-administration and reinstatement. Twenty female C57BL/6J mice were trained to self-administer sweetened alcohol (9% ethanol/2% sucrose) or sucrose (2%) in operant chambers for 40 days. After baseline self-administration, all mice underwent extinction procedures in which cues previously paired with the infusion of the reinforcer and the reinforcer itself were no longer present. Following successful completion of extinction training, mice were subjected to a reinstatement test one day later, in which the alcohol-paired cues were again present upon pressing, but no alcohol was delivered. Immediately after completion of reinstatement testing, all mice were sacrificed and tissue was extracted for RT-PCR. We found that while there were no group differences in lever responding during reinstatement, mice that self-administered ethanol significantly reinstated compared to the last day of extinction, while sucrose-exposed mice did not. Further, Arc and TARP mRNA expression was increased after reinstatement, with regional specificity to the nucleus accumbens. This suggests that Arc and TARP may interact to regulate AMPAR synapses during heightened alcohol cue salience and seeking, and in a regionally-specific manner. Future work will test the necessity of Arc in reinstatement and identify if unique Arc ensembles encode for alcohol-seeking.
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55. **de novo Donor-Specific Antibody Patterns in Rhesus Macaque Kidney Transplantation After Donor Apoptotic B Cell Infusionâ€“Mediated Tolerance Induction** | ***Fatemeh Mohammadi***

Infusion of donor apoptotic cells treated with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (ECDI) can modulate allorecognition pathways and facilitate transplant tolerance in mice and nonhuman primates. We evaluated the timing of *de novo* DSA formation in rhesus macaque kidney allograft recipients infused with donor-ECDI-B cells with or without coverage by temporary immunosuppression.
MHC-mismatched macaques underwent kidney transplantation. *Ex vivo* expanded donor-B cells were incubated with ECDI to induce apoptosis and infused at 0.25×10^9 cells/kg per dose. All recipients received rapamycin and anti-CD154 from day −8 to +28 (day 0=transplant). Recipients were assigned to control (no cell infusion), 2-dose (days −7,+1), 4-dose (days −7,+1,+7,+21), or 6-dose (days −7,+1,+7,+21,+62,+91) donor-ECDI-B infusion groups. The first four doses were administered during active immunosuppression therapy, while the fifth and sixth doses in the 6-dose group were given after immunosuppression cessation. DSAs were measured by flow crossmatch.
Both 2-dose and 4-dose groups revealed significantly delayed *de novo* DSA development compared to controls (p=0.017 and p=0.008, respectively) (Figure1). *De novo* DSAs strongly trended toward appearing later in the 4-dose group compared to the 2-dose group (p=0.059). Interestingly, in the 6-dose group, *de novo* DSAs appeared shortly after the 6th dose of donor-ECDI-B infusion, administered 63 days after immunosuppression cessation. In contrast, the last dose of donor-ECDI-B cells in the 2-and 4-dose groups was given under active immunosuppression therapy. This indicates that donor-ECDI-B cell infusions provided without immunosuppression coverage may trigger *de novo* DSA appearance.
Although donor-ECDI-B cell infusions can foster prolonged allograft survival, in the absence of immunosuppression, they may also promote *de novo* DSA formation. Extended donor-ECDI-B cell infusions will likely benefit from concomitant immunosuppression therapy.
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56. **DNA Ligase Fidelity Safeguards Genome Stability Through Cooperation with Mismatch Repair** | ***Mahina Monsur***

Lagging strand DNA replication proceeds through discontinuous synthesis of short Okazaki fragments. It requires repeated priming by low-fidelity Pol α, flap processing, gap filling, and final nick ligation by DNA ligase 1 (Lig1; encoded by *CDC9*). This multi-step process occurs tens of thousands of times per genome replication, creating frequent nicks and single-stranded regions highly prone to polymerase slippage, especially in homopolymeric runs. This renders the lagging strand inherently more mutation-prone than the continuous leading strand. To define the genome-wide consequences of reduced ligation fidelity in a eukaryotic model system, we used *Saccharomyces cerevisiae* whole-genome mutation accumulation experiments to investigate the interplay of DNA ligation and DNA mismatch repair (MMR). Lig1 executes the terminal sealing step with high fidelity; defects here risk persistent nicks that embed mutagenic intermediates. Previous studies have explored Lig1 mutational patterns through *in vitro* methods and yeast reporter genes, revealing distinct patterns of mutations. We compared wild type yeast with strains either lacking *MSH2*, which encodes an essential MMR component, and/or a mutator variant of Lig1 (*cdc9 F722A*). The 93,398 collected mutations revealed distinct mutational patterns in each strain. Rates of base substitutions, insertions and deletions (indels), and complex mutations were strongly increased by *cdc9 F722A*. Loss of Msh2 leads to strong synergistic increases in mutation rates in *cdc9 F722A* cells. This suggests a critical interdependence between the Ligase 1 fidelity and MMR. The mutation patterns were independent of replication timing, nucleosome occupancy, or coding status, and thus largely recapitulated the patterns found in reporter genes. These results establish Lig1 fidelity as a critical post-synthetic safeguard during lagging-strand replication and reveal MMR as an essential backup mechanism against ligation-dependent mutagenesis. Disruption of accurate ligation may underlie indel-biased mutagenesis and shape the evolutionary trajectory of human cancers.
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57. Non-lytic Poliovirus Spread Through TAM Receptor Tyrosine Kinases | *Steven Moran*

Virus-host cell interactions are typically mediated through surface viral proteins binding to cell receptors. This induces a conformational change in the virus that allows infection to start upon entry through mechanisms such as receptor-mediated endocytosis or viral-cell membrane fusion. After infection is complete, the virus exits the host cell and spreads to neighboring naïve cells through lytic or non-lytic mechanisms. Lytic spread results in host cell lysis unlike non-lytic spread, which allows for virus spread without cell lysis. Both viruses with a lipid bilayer envelope (enveloped viruses) and without (non-enveloped viruses) can undergo either type of spread depending on the condition of the extracellular environment. Poliovirus, the non-enveloped virus known to cause poliomyelitis, primarily undergoes lytic spread *in vitro* and *in vivo* through its native entry receptor CD155. There is emerging evidence that poliovirus also undergoes non-lytic spread with the help of additional receptors such as TAM receptor tyrosine kinases. TAM receptors, consisting of Tyro3, Axl and Mer, are plasma membrane receptors that primarily mediate the phagocytic clearance of apoptotic cells and downregulation of innate inflammatory immune responses when bound by activating ligands Gas6 or Protein S. Preliminary data from bulk spread assays assessing poliovirus spread has shown delayed spread in Tyro3 knockout HAP1 cells and HeLa cells treated with TAM receptor-specific inhibitors targeting one or all TAM receptors. The delayed spread is indicative of non-lytic spread possibly being mediated by Tyro3. The goal is to continue investigating the role of TAM receptors in poliovirus non-lytic spread through assays assessing spread and viral genome replication during receptor knockout or drug inhibition. The results from this research will uncover a novel alternative function for TAM receptors and can lead to the development of antiviral therapies that target viruses similar to poliovirus.
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58. Simultaneously Inhibiting Both the Active and Inactive Forms of Mutant KRASG12D Leads to Superior Growth Suppression Compared to Inhibiting Only the Active Form in Preclinical Models of Pancreatic Cancer | *Brandon Mouery*

KRAS is one of the most frequently mutated oncogenes in cancer, making it an attractive therapeutic target. However, until recently KRAS was considered "undruggable". The FDA approval of two KRAS inhibitors selectively targeting the G12C mutation for use in lung cancer patients has changed this paradigm and has subsequently stimulated development of inhibitors towards additional KRAS mutations. In particular, approximately 20 inhibitors targeting the G12D mutation (the most prevalent mutation in pancreatic cancer) are currently in clinical evaluation. $KRAS^{G12D}$ inhibitors being evaluated have varying mechanisms of action, and understanding the differences between these distinct mechanisms will be critical to maximize therapeutic response. To do so, we compared the activity of VS-7375, a non-covalent $KRAS^{G12D}$ inhibitor that binds both the active (ON) and inactive (OFF) forms of KRAS, with the covalent ON-only inhibitor zoldonrasib (RMC-9805). Using proliferation assays, we found that VS-7375 more potently inhibited the growth of a panel of $KRAS^{G12D}$-mutant pancreatic cancer cell lines in comparison to RMC-9805. In contrast, VS-7375 was 40-fold less potent in a $KRAS^{G12C}$ cell line, indicating high selectivity for $KRAS^{G12D}$. We extended these studies to show that VS-7375 also promotes more durable tumor regression in mouse models of pancreatic cancer. Target inhibition studies demonstrated that VS-7375 more potently and more durably suppressed KRAS-mediated signaling. We surprisingly found that the non-covalent inhibitor VS-7375 more durably suppressed KRAS-mediated signaling than the covalent inhibitor RMC-9805 even following the removal of each inhibitor. Recent phase 3 clinical trial data showing doubling of overall survival in pancreatic cancer patients provides optimism that RAS inhibitors will transform the treatment landscape of this historically difficult to treat cancer. Our results suggest that simultaneously targeting both the active and inactive states of mutant KRAS with VS-7375 may provide greater clinical benefit than covalent inhibition of the active state only.

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59. Mitochondrial Therapeutics in NSCLC: The Role of TP53 Isogenic Status in Modulating Redox Metabolism | *Debalina Mukhopadhyay*

Non-small cell lung cancer (NSCLC) frequently harbours TP53 mutations and MCL-1 amplification, two molecular alterations that profoundly impact tumor metabolism and immune evasion. TP53 mutations are known to impair mitochondrial function and redox homeostasis, while MCL-1, an anti-apoptotic BCL-2 family protein, supports mitochondrial integrity and survival under metabolic stress. Together, these alterations disrupt redox and lipid metabolism, leading to increased mitochondrial reactive oxygen species (ROS) and lipid accumulation. When secreted into the tumor microenvironment, these metabolites contribute to immune suppression and resistance to immune checkpoint blockade (ICB). H1299 NSCLC isogenic cell lines expressing different TP53 mutants in xenograft models were generated to test this mechanism. TP53-mutant tumors exhibited accelerated growth, altered vascularization, and distinct lipid profiles compared to empty vector controls. Interestingly, while basal intracellular and mitochondrial ROS levels were not significantly different among isogenics, lipid peroxidation was markedly elevated in TP53-mutant cells. Pharmacological inhibition of MCL-1 using VU661013, alone or in combination with the mitochondrial metabolism inhibitor CPI-613 (Devimistat), significantly increased ROS production and stabilized MCL-1 protein levels, suggesting a feedback mechanism. These findings indicate that MCL-1 inhibition in TP53-mutant NSCLC triggers a burst of mitochondrial and intracellular ROS, potentially reprogramming lipid metabolism and promoting tumor cell death. Thus, this study highlights the therapeutic potential of co-targeting mitochondrial metabolism and

anti-apoptotic signalling to overcome resistance and improve ICB efficacy in NSCLC. This approach may offer a novel strategy to exploit metabolic vulnerabilities in tumors with TP53 and MCL-1 alterations.
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60. CF10/LV Overcomes Acquired Resistance to 5-FU/LV by Promoting Degradation of the Myc Topoisome Complex | *Charles Okechukwu*

Introduction: Acquired resistance to chemotherapy with 5-FU-based regimens (FOLFOX, FOLFIRI) is a central cause of the low rate of long-term survival (<14% 5-year survival) for metastatic colorectal cancer (mCRC) patients, as most are treated with one or more 5-FU-based regimens, and unfortunately, experience progressive disease following an initial response.
Aim: We aim to: (i) test the molecular mechanisms underlying acquired 5-FU/LV resistance via Myc and Thymidylate synthase (TS); and (ii) to determine if a polymeric fluoropyrimidine (FP) CF10/LV can overcome resistance in vitro and in vivo.
Methods: Developed CRC 5-FU/LV-resistant cells under folate-restricted conditions. Identified Myc-associated topoisome in acquired 5-FU/LV-resistant CRC cells determined by Western blot and Myc siRNA knockdown. TS activity was determined using an *in situ* ^{3}H-release assay. DNA topoisomerase 1 (Top1), DNA Top1 cleavage complexes and DNA double strand breaks (DSBs) were determined by immunofluorescence.
Results: We identified elevated Myc and treatment-induced elevated levels of TS in multiple CRC cell lines selected for acquired resistance to 5-FU/LV in folate-restricted conditions. In this study, we showed that siRNA knockdown of Myc was sufficient to restore drug sensitivity to 5-FU/LV-resistant cells and that these cells displayed limited cross-resistance to the polymeric FP CF10/LV which strongly decreased Myc levels through increased proteasomal degradation. Myc was associated with a Topoisome complex in 5-FU/LV-resistant cells that includes Max, Top2a, and Top1. CF10 dual targets TS/Top1 and Myc co-localized with CF10-induced Top1cc in 5-FU/LV-resistant cells. In vivo studies showed CF10/LV was significantly more effective than 5-FU/LV in a MC38:C57BL6 syngeneic, orthotopic liver metastatic model and CF10 was also effective in tumors comprised of 5-FU/LV-resistant MC38 cells for which 5-FU/LV displayed no survival advantage.
Conclusion: This study reveals Myc-dependence in CRC cells selected for acquired 5-FU/LV resistance with limited cross-resistance to CF10/LV which caused Myc to co-localize with Top1cc and undergo proteasomal degradation.
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61. Differences in Social Motivation and Rates of Risk Taking Among Adolescents with ADHD | *Hope Peterson-Sockwell*

While adolescent risk-taking is traditionally considered detrimental, there are also advantageous risky behaviors adolescents engage in, such as positive or prosocial risk-taking. This analysis explored whether adolescents with ADHD, who are often considered risk-prone, may be motivated to engage in risk-taking by positive or prosocial tendencies. This analysis further explored whether these motivations and behaviors are supported by adaptive brain network differences. Understanding what motivates adolescents to engage in risky behavior is crucial for decoding risk-taking because it reveals the why behind behaviors, for example differentiating between goal-oriented pursuit and impulse sensation seeking. In this study, a latent profile analysis was used to identify subgroups of individuals based on their scores on a social motivation questionnaire and a questionnaire probing rates of real-world risk taking. We identified four subgroups of adolescents with and without ADHD (n=153, 101 ADHD). One subgroup, the "positive motivation group" (n=32, 24 ADHD), reported the highest scores on social motivation subscales related to admiration, prosocial interaction, and sociability, along with the lowest scores on a

negative social potency subscale. A second subgroup, the "negative motivation group" (n= 28, 20 ADHD), reported the lowest scores on the admiration, prosocial interaction, and sociability motivation subscales, along with the highest negative social potency subscale. The negative motivation group reported the highest rates of real-world risk taking, while the positive motivation group reported risk-taking rates that were among the middle of those reported by the full sample. Both groups showed an overrepresentation of ADHD participants. After identifying the subgroups, we conducted a functional brain network analysis assessing the integration and segregation of networks comprised of brain regions relating to social interactions and motivation. fMRI data was used to construct two functional networks per participant, one with data collected while participants were at rest in the scanner, and the other while they completed a risk-taking task in the scanner. Surprisingly, no differences were found between subgroups on measures of network integration or segregation, during either resting state or task. Future analyses are needed to assess other brain regions and other network metrics to evaluate further potential differences between these subgroups of participants. Together, these findings suggest that adolescents with ADHD may differ in their underlying social motivation for engaging in risk-taking, and we do not yet know how these differences are reflected in large scale brain networks.

62. **Ultrasound-assisted Dewatering of Microalgae: Mechanism and Performance Evaluation** | ***Atulkumar Raut***

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63. **Is the Cardiac Stress Response Genetically Driven at the Cell or Nuclear Level?** | ***Sriram Ravindran***

The heart's response to injury involves extensive changes in gene expression, yet it remains unclear whether these responses are regulated primarily at the level of the whole cell or within the nucleus, and how genetic factors shape this process. To address this, we examined cardiomyocyte stress responses at single-cell and single-nucleus resolution using a chronic mouse model of cardiac injury. Myocardial infarction was induced by ligation of the left anterior descending coronary artery (LAD) in wild-type C57BL/6J mice and in mice lacking *Tnni3k*, a cardiomyocyte-specific kinase implicated in alleviating cardiac stress response.

Cardiomyocytes were isolated 28 days after injury using Langendorff perfusion and enzymatic digestion. From each preparation, intact cardiomyocytes were processed for single-cell RNA sequencing, while nuclei isolated from matched cells were used for single-nucleus RNA sequencing. This paired design enabled comparison of cellular and nuclear gene expression responses within the same genetic and physiological context. RNA libraries were generated using a split-pool barcoding strategy and analyzed with standard single-cell analysis workflows.

In wild-type mice, chronic cardiac injury was associated with detectable transcriptional changes at the whole-cell level but not at the nuclear level. Notably, cell-level gene expression showed enrichment of pathways related to histamine-triggered and GABAergic signaling. In contrast, *Tnni3k*-deficient cardiomyocytes exhibited no significant injury-associated transcriptional changes at either the cellular or nuclear level. Across genotypes, nuclear transcriptomes remained largely stable, indicating that ongoing transcriptional reprogramming is minimal during chronic remodeling.

These findings suggest that genetic control of chronic cardiac stress responses is reflected primarily in persistent whole-cell gene expression rather than active nuclear transcription. Our study demonstrates the value of integrating single-cell and single-nucleus transcriptomics in large, multinucleated cells and highlights how conclusions about genetic regulation depend on the cellular compartment being measured. These approaches can be extended to understand cell-type specific responses in future.

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64. **Discovery of Peptide Binders for Histone-Binding Proteins via Post-Translationally Diversified mRNA Display Libraries**

65. **Using a Light-Based Treatment Approach to Target Chemotherapy Resistance Arising from Environmental Exposures in Ovarian Cancer Cells** | ***Brittany Rickard***

Ovarian cancer is the most lethal gynecologic cancer, largely due to the development of chemotherapy resistance which affects ~85% of patients. Thus, understanding sources of chemoresistance and developing mechanism-based treatments are critical. Recently, our group was the first to publish that chronic (35-day), human-relevant perfluoroalkyl substance (PFAS) exposures induce duration-dependent chemoresistance in ovarian cancer. PFAS are bioaccumulative environmental contaminants that frequently pollute drinking water supplies worldwide and interfere with nearly all body systems, including the female reproductive tract. Importantly, we also found that PFAS drive chemoresistance by promoting functional and structural enhancements of mitochondria, which are key energy producers of the cell. Thus, we hypothesized that therapeutic targeting of mitochondria would overcome PFAS-induced chemoresistance and re-sensitize cells to treatment. Photodynamic therapy (PDT) is a light-based therapeutic approach that has been shown to synergize with chemotherapeutics and is particularly promising in cancers where chemoresistance prevents successful treatment. Importantly, several light activatable molecules, or photosensitizers, used for PDT inherently localize to, and therefore preferentially damage, mitochondria. Here, we evaluated the ability of PDT using two clinically-approved, mitochondria-localized photosensitizers (benzoporphyrin derivative (BPD) and aminolevulinic acid (ALA)), to overcome PFAS-induced chemoresistance and associated mitochondrial enhancements. In PFAS chronically-exposed cells, which displayed significant resistance to both carboplatin, a first-line platinum agent, and doxorubicin, a second-line agent for platinum-resistant disease, significantly heightened chemotherapy sensitivity was observed when cells were treated with sub-cytotoxic BPD-PDT or ALA-PDT in combination with low-dose carboplatin or doxorubicin. When evaluating mitochondrial parameters, significant decreases in mitochondrial membrane potential, suggestive of apoptosis, occurred following treatment with PDT-based combinations. Mitochondrial network area also significantly decreased within 1-hour of combination therapy, indicative of potent mitochondrial photodamage. These findings highlight the pivotal role of mitochondria in driving PFAS-induced chemoresistance in ovarian cancer and the efficacy of PDT-based combinations for chemoresistant disease.
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66. **Antibiotic-coated Nanoparticles and Their Impact on Antibacterial Activity**

67. **Understanding The Pathogenesis of Airway Disease Phenotype in "Early COPD"** | ***Prashamsa Sannareddy***

Background: Chronic obstructive pulmonary disease (COPD) is persistent, progressive and poorly responsive to treatment. To better understand the pathogenesis of COPD in 30-55 years adults, SPIROMICS study of Early COPD Progression (SOURCE) recruited individuals exposed to tobacco with normal lung function across various study sites. Tobacco exposed individuals with preserved spirometry (TEPS) are further classified as non-symptomatic (nTEPS) and symptomatic (sTEPS) based on COPD assessment score and symptoms. The disease phenotype in "early COPD" is assessed by airway mucins, mucin-interacting proteins, and regional airway markers in TEPS and COPD.

Methods: Induced sputum samples collected from the SOURCE cohort were used for label-free and airway mucins targeted quantitation in mass spectrometry. The total mucin concentration was measured by size exclusion chromatography with multi-angle light scattering coupled with refractometry.
Results: Sputum samples of 275 subjects were analyzed, of which 101 were nTEPS, 143 were sTEPS, and 31 had COPD. The absolute MUC5AC and total mucin concentrations, and MUC5AC/ MUC5B ratio were significantly elevated in sTEPS and COPD groups compared to nTEPS, while MUC5B concentrations did not differ significantly between all groups. Regional airway markers unique to large and small airways significantly increased in sTEPS and COPD compared to nTEPS. Mucin interacting proteins, such as FcGBP and LPLUNC1 were significantly increased in sTEPS and COPD compared to nTEPS.
Conclusion/Significance: The findings demonstrate that similar to COPD group, the sTEPS group exhibits increased levels of MUC5AC, total mucin concentration, mucin interacting proteins and show that both small and large airways are affected. The results suggest that abnormal mucus composition in sTEPS group resembles that of the COPD group, which can lead to failed mucociliary clearance, plug formation, and thereby contribute to chronic bronchitis and airway obstruction. The mucus compositional similarity between sTEPS and COPD supports the concept of a continuum of disease pathogenesis.

68. Heme-sensitive nascent RNA G-quadruplexes Regulate Mitochondrial Transcription Elongation | *Uma Shankar*

Pigment nephropathy is a clinical syndrome where renal proximal tubule cells (PTC) are injured due to excess free heme. PTCs rely heavily on ATP from oxidative phosphorylation and reduced mitochondrial function can lead to their dysfunction. Previously, we found that mitochondrial RNA polymerase (POLRMT) pauses downstream of guanine-rich motifs where the nascent RNA form guanine-quadruplexes (rG4s). Stabilizing these rG4 structures was sufficient to reduce mitochondrial transcription, decrease oxidative phosphorylation, and compromise PTC function. As heme is an endogenous G4 ligand, we considered that heme-stabilization of rG4s may contribute to mitochondrial dysfunction in pigment nephropathy through altered transcription by POLRMT. To test the extent of G4-dependant pausing, we established an in vitro transcription assay (IVT) using a rG4 sequence from the MT-CO1 gene (CO1-rG4), or a sequence with a single G to A mutation that does not form a stable G4 (CO1-rG4mut). This assay revealed 30% more pausing following the CO1-rG4 relative to CO1-rG4mut. This differential pausing was abrogated when rG4 folding was destabilized using guanine nucleotide analogs (7-deaza-G) or non-stabilizing ionic conditions (lithium ion), indicating that POLRMT pausing is due to rG4 structure rather than primary sequence. Next, we performed the IVT in the presence of heme and found 50% fewer RNA transcripts when using the CO1-rG4 sequence. We confirmed heme stabilizes the CO1-rG4 by thermal melting assays and infer that heme-mediated rG4 stabilization causes more POLRMT pausing and less transcriptional output. To localize the structural determinants of rG4-mediated pausing, we performed molecular dynamics simulations of the CO1-rG4 transiting the POLRMT RNA-exit channel. We found persistent contacts with the intercalating hairpin and specificity loop, two domains in POLRMT that are critical for DNA melting during transcription initiation. Their function during transcription elongation is unclear so we made targeted deletions of the intercalating hairpin (Δ612–616, Δ611–618) and the specificity loop (Δ1088–1105). When tested by IVT, each deletion eliminated rG4-dependent POLRMT pausing, establishing these two domains as necessary for rG4-dependent pausing. This study suggests that rG4 stability can be a heme-sensitive regulator of mitochondrial gene expression

and implicates rG4 stabilization by excess heme as a driver of mitochondrial dysfunction in pigment nephropathy.
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69. **Real-world Evaluation of CYP2C19 Inhibitor Phenoconversion on Clopidogrel Clinical Effectiveness After Percutaneous Coronary Intervention | *Danwei Shao***

Background: Both CYP2C19 and CYP3A4 contribute to clopidogrel bioactivation. CYP2C19 no function alleles reduce clopidogrel's antiplatelet effects and clinical effectiveness. Concomitant use of clopidogrel and CYP2C19 or CYP3A4 inhibitors can also reduce clopidogrel's antiplatelet effects and may convert patients without a CYP2C19 no function allele from normal, rapid and ultrarapid metabolizers (NM/RM/UMs) to intermediate or poor metabolizers (IM/PMs). However, it remains unclear whether CYP2C19 or CYP3A4 inhibitor use impacts clinical outcomes in clopidogrel-treated NM/RM/UMs after percutaneous coronary intervention (PCI).
Methods: A multi-center retrospective study included 2,046 clopidogrel-treated patients who underwent PCI and clinical CYP2C19 genotype testing. Data were abstracted from electronic health records. FDA defined moderate or strong inhibitors of CYP2C19 or CYP3A4 were considered. Rates of major atherothrombotic events (MAE: all-cause death, myocardial infarction, ischemic stroke, stent thrombosis, or unstable angina requiring revascularization) over 1-year post-PCI were compared by multivariable Cox regression in clopidogrel-treated patients: NM/RM/UMs with a CYP2C19 inhibitor vs. IM/PM patients vs. NM/RM/UMs with a CYP3A4 inhibitor vs. NM/RM/UMs with no inhibitor.
Results: In clopidogrel-treated NM/RM/UMs (n = 1,624), 48 (3.0%) received a CYP2C19 inhibitor and 70 (4.3%) received a CYP3A4 inhibitor. MAE rate was higher in NM/RM/UMs receiving a CYP2C19 inhibitor compared to those receiving no inhibitor (adjusted HR 2.34, 95% CI 1.07 – 5.14, p = 0.034). MAE rate was also higher in IM/PMs compared to NM/RM/UMs receiving no inhibitor (adjusted HR 1.43, 95% CI 1.01 – 2.05, p = 0.047). No difference was observed in NM/RM/UMs receiving a CYP3A4 inhibitor compared to those receiving no inhibitor (adjusted HR 1.25, 95% CI 0.58 – 2.73, p = 0.569).
Conclusion: Our findings suggest that use of a CYP2C19 inhibitor, but not a CYP3A4 inhibitor, was associated with reduced clopidogrel clinical effectiveness, and may lead to CYP2C19 phenoconversion, in clopidogrel-treated NM/RM/UMs after PCI. Validation in a larger study is necessary**.**
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70. **CryoEM Structure of a Unique Thermophilic Carbon Fixing Enzyme, 2-Oxoglutarate Carboxylase | *Anjani Sharma***

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71. **Insights Into RNA Polymerase II Dynamics Mediated by Stress-Responsive Factor, MEF2a, in Renal Cells | *Deepti Shrivastava***

Osmoregulation helps cells maintain water balance, and dehydration (osmotic stress) is linked to conditions such as hypertension, metabolic disease, and increased mortality. Human cells adapt to osmotic stress by increasing organic osmolytes and ion transporters, while at the organism level, the hypothalamus releases arginine vasopressin (AVP) to help the kidneys conserve water. At the molecular level, the key transcriptional regulators involved in the pathway that responds to hypertonic stress remains unclear. RNA polymerase II (Pol II) pausing is crucial for fine-tuning gene expression in response to environmental stress. Our previous work identified MEF2a as a transcription factor that regulates the expression of Pol II pause-dependent tonicity-responsive genes. In this study, we investigate how protein cofactors contribute to MEF2a-mediated Pol II pause

release under hypertonic conditions. Using biochemical and genomic approaches in kidney cells, we found that under high-salt conditions, MEF2a interacts with key "pause-release" factors, PTEF-b (CDK9) and TRIM28, and helps assemble them on chromatin. This promotes the activation of important osmo-protective genes such as SLC5A3 and AKR1B1, which help cells survive dehydration. Disrupting MEF2aor its partner proteins reduce expression of these genes, highlighting their functional importance. We are further testing how loss of MEF2a affects transcriptional pause release dynamics and recruitment of pause-release machinery in renal cells. So what? This research identifies MEF2a as a key regulator that links environmental stress to gene activation. Understanding the role of this novel osmotic stress-responsive factor in transcriptional regulation and RNA polymerase II pausing dynamics will provide insights into how renal cells defend against under-hydration and their role in human disease.
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72. **Chronic TMJ Arthralgia with Disc Degeneration is Associated With Increased Oral Parafunctions** | ***Jacob Soliman***

Aim of Investigation: To investigate self-reported oral parafunctional behavior in patients with chronic temporomandibular joint (TMJ) arthralgia with and without disc degeneration (DD).
Methods: Cross-sectional study included adults (≥18 years) diagnosed with TMJ arthralgia (DC/TMD 2014). Exclusion criteria included inability to provide consent and trigeminal neuropathic pain. DD was confirmed using MRI. Oral parafunctional behavior was assessed using the Oral Behavior Checklist (OBC). Statistical analysis used the Mann-Whitney U test and the Fisher Exact Test. Statistical significance was set at $p<0.05$.
Results: 56 participants (82% female; mean age 45.61 ± 17.31 years; mean pain duration 10.76 ± 9.74 years; mean pain intensity in 30 days on a 0-10 scale was 5.66 ± 2.04), 12 TMJs had unilateral DD, while the rest were bilateral. Patients with TMJ DD reported statistically significantly higher OBC total scores than those without DD (23.54±11.11 vs 16.89±5.79; $p<0.004$). Participants with TMJ DD were more likely to report sleep clenching (OR=5.3, $p<0.006$), daytime clenching (OR=4.6, $p=0.010$), object holding between teeth (OR=10.5, $p=0.047$), and side-only chewing (OR=3.3, $p=0.034$).
Conclusion: In Patients with chronic TMJ arthralgia, TMJ DD was associated with increased oral parafunctional behavior.

73. **Unraveling the Molecular Basis of Mitochondrial Diseases Caused by SSBP1 Mutations** | ***Shruti Somai-Hyatt***

Single-stranded DNA binding proteins (SSBs) are one of the most common class of proteins found in all domains of life. SSBs bind single-stranded DNA (ssDNA) nonspecifically and with high affinity and are important for protecting exposed ssDNA during replication. In the human mitochondria, several proteins including the mitochondrial single-stranded DNA binding protein (mtSSB) are responsible for replicating the mitochondrial DNA. Since 2019, mutations in the *SSBP1* gene, encoding the tetrameric mtSSB, have been reported to cause a broad range of mitochondrial disorders, affecting nearly all organs; however, the underlying mechanism of disease remains elusive. To systematically understand the molecular basis of *SSBP1* disease mutations, we focused on the biochemical and structural characterization of six SSBP1 disease variants. Some of these disease-associated amino acids reside at the monomer-monomer interface of mtSSB and have been proposed to impair ssDNA binding as well as tetramerization. To test this hypothesis, we performed fluorescence polarization experiments evaluating the binding affinity of six SSBP1 disease variants for both a short dT_{20} and a longer dT_{65} ssDNA substrate. While E27K and E111Q SSBP1 had comparable binding affinity as the wild type, R38Q, G40V, N62D and R107Q SSBP1 exhibited significant decrease in binding affinity for dT_{20} ssDNA. Conversely, all six disease variants displayed

similar binding affinities as wild type for dT_{65} ssDNA. Results from size exclusion chromatography coupled with multi-angle light scattering studies revealed that all six disease variants form stable tetramers in solution. To further obtain structural insights into the effects of *SSBP1* disease mutations, we determined a 1.7Å X-ray crystallography structure of apo R38Q SSBP1. Our structural analysis revealed significant movement of Arg107 and Glu27 at the monomer-monomer interface, thereby explaining the observed decrease in ssDNA binding affinity. We propose that these studies will provide new molecular insights into the disease mechanism pertaining *SSBP1* mutations.

74. **CYFIP2-Deficiency Causes Reduced Gabaergic Signaling in Larval Zebrafish Brain** | ***Sureni Sumathipala***

75. **Assessing the Contribution of Rare DNA States to Cancer Mutational Signatures Using Sequence-Specific Conformational Fingerprinting** | ***Or Szekely***

Rare and short-lived DNA conformations are proposed to be key drivers of mutagenesis, yet assessing their contribution to mutational signatures found in human cancers remains challenging. Here, we developed a ^{19}F NMR based approach that quantifies the sequence-dependent propensity to form a rare DNA conformation and compared the resulting fingerprint against cancer mutational signatures. A ^{5F}dU modification lowers the apparent pK_a of thymine N3, enabling detection of a rare anionic Watson-Crick-like (WC-like) G•T$^-$ conformation by one-dimensional ^{19}F NMR at experimentally obtainable pH conditions. We measured the propensity to form this WC-like conformation across all sixteen triplet sequence contexts and discovered a conformational fingerprint with striking 50-fold variation, driven by suboptimal interactions between anionic thymine and its 3' neighbor. To evaluate the contribution of this and other rare DNA states to mutagenesis, we calculate the Jensen-Shannon Divergence (JSD) between the conformational fingerprint and mutational signatures from the Catalogue of Somatic Mutations in Cancer (COSMIC) database. Resulting similarities with single-base substitutions (SBS) uncovered plausible links to mutational processes associated with exposure to damaging agents and therapies. Thus, integrating molecular biophysics with genomic epidemiology provides a powerful framework to explore how DNA's dynamic properties shape genome stability and influence human disease.
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76. **Mapping Excitation Energy Transfer Pathways in the Light-Harvesting Protein C-Phycocyanin** | ***Kiriko Terai***

Light-harvesting proteins serve as nature's front end for converting photons into usable chemical energy. Understanding how they shuttle excitation energy - rapidly, efficiently, and reliably, selecting productive pathways with near-unity yield on picosecond timescales - reveals how biology sustains life[1,2] and provides a blueprint for harnessing light to drive biological and chemical function. In this work, we focus on C-phycocyanin as a model light-harvesting system. C-phycocyanin is a pigment-protein complex that houses multiple chromophores, the open-chain tetrapyrrole phycocyanobilin (PCB), which together form an excitation energy transfer network.[3] By capturing sunlight and funnelling the resulting excitation energy through these PCBs, C-phycocyanin delivers photon energy to the photosynthetic reaction center.[4,5] However, the specific pathways through which excitation energy migrates across the complex PCB network remain unclear. Here, we aim to map the excitation energy pathways in C-phycocyanin through simulation. Assuming that Förster resonance energy transfer (FRET) is the dominant mechanism governing excitation energy transfer between chromophores in light-harvesting proteins,[6,7] we compute the electronic couplings and spectral overlaps for PCB pairs to determine the FRET rate constants. To do so, we leverage GPU-

accelerated hybrid Quantum Mechanics/Molecular Mechanics (QM/MM) frameworks together with nonadiabatic dynamics. This approach enables us to resolve, at atomistic detail, how the protein environment modulates the spectral properties of PCBs and how these environment-dependent shifts influence energy-transfer pathways and efficiencies.
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77. Stimulus-Responsive Perselenide, Thioselenide, and Selenosulfide Donors: A New Frontier in Reactive Selenium Species Chemical Biology | *Ravi Tripathi*

Reactive selenium species (RSeS), including perselenides (RSeSeH), thioselenides (RSSeH), and selenosulfides (RSeSH), have long been proposed as fleeting yet biologically important intermediates in hydrogen selenide (H_2Se) signaling and cellular redox regulation. However, their inherent instability and the absence of suitable small-molecule precursors have precluded direct experimental access under physiologically relevant conditions. Here, we report the first synthesis, isolation, and comprehensive characterization of a stimulus-responsive donor platform capable of controlled RSeS generation in biological environments. These donors employ a modular 1,6-elimination architecture that enables precisely triggered release of discrete RSeS, exemplified here by esterase activation, with tunable stability and release kinetics achieved through systematic electronic and steric modification of the dichalcogenide framework and supported by computational analysis. Importantly, studies under thiol-rich conditions reveal that thioselenide and perselenide donors converge to generate common reactive selenium species, providing mechanistic insight into their behavior in cellular settings. Consistent with this finding, biological evaluation demonstrates that thioselenide and perselenide donors exhibit exceptionally potent antioxidative activity—effective at concentrations up to 100-fold lower than sulfur analogs (RSSH)—and pronounced antiproliferative effects in cancer cells. Collectively, this work establishes an entirely new and tunable class of RSeS donors and introduces the first general platform for the controlled generation of RSeSeH, RSSeH, and RSeSH, enabling systematic investigation of their reactivity, redox signaling, and therapeutic potential in both simplified buffer systems and living cells.
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78. Reprogramming the Clot: Antimicrobial Platelet-Mimetic Platforms for Infection Mitigation | *Luke Tucker*

Background: Chronic wounds and traumatic injuries are frequently complicated by simultaneous hemorrhage and infection. To address this, we developed silver nanoparticle-incorporated platelet-like particles (AgPLPs). These synthetic, fibrin-specific particles combine the clot-reinforcing properties of PLPs with the antimicrobial efficacy of silver. Our **objective** is to evaluate AgPLP safety, biodistribution, and therapeutic impact in two animal models of traumatic injury. Our **hypothesis** is that the AgPLPs will have lower bacterial numbers, enhanced wound healing properties, less blood loss, and improved blood brain barrier functionality when compared to saline or non-targeting microgels.

Methods and Results: Physical characterization confirmed successful silver incorporation (~10 nm) and AgPLP diameters of 1−2 μm. In vivo safety was assessed via biodistribution studies in C57BL/6 mice. At 15 minutes post-injection, AgPLPs showed transient accumulation in the lungs, liver, spleen, and kidneys, with complete clearance into the urine within 6 hours. Histological analysis (H&E) and creatinine levels confirmed no tissue damage or nephrotoxicity.

The efficacy of AgPLPs was tested in a rat polytrauma model (traumatic brain injury and femoral artery hemorrhage). AgPLP treatment significantly reduced blood loss compared to saline controls and improved blood-brain barrier sealing. Notably, AgPLP-treated groups showed lower bacterial counts in spontaneous lung infections compared to saline. Evaluation is also ongoing in a murine

infected liver laceration model, which has successfully demonstrated stable infection and consistent bleeding.
Conclusions: AgPLPs are biocompatible, rapidly cleared, and do not cause systemic tissue damage. In complex injury scenarios, they provide a multi-functional therapeutic approach by reducing hemorrhage, preserving neural barrier integrity, and suppressing bacterial growth.
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79. **Insula Connectivity in Relation to Memory Performance in PWCI Following an Arts-based Intervention** | ***Ayse Uneri***

Background: Alzheimer's disease (AD) affects emotional and social function. The insular cortex (Salience Network) integrates internal and external cues, supporting social behavior and cognition. In the IMOVE study, it was recently found that social engagement has a positive effect on cognitive performance. Here, we investigated whether functional connectivity within insular subnetworks relates to immediate memory performance in people with cognitive impairment (PWCI).
Methods: IMOVE was a randomized, controlled 2x2 factorial design study which recruited people aged 60-85 years old and adjudicated as having mild cognitive impairment (MCI) or early-stage AD (NCT03333837). Participants were split into one of four study conditions for 12 weeks: movement alone, social alone, movement group, and usual care control group. Seed-based functional connectivity analysis used an 8mm spherical region of interest (ROI) placed in the left ventral anterior insula (LvAI, MNI space: −33, 13, −7). A correlation between the time series from the ROI and time series in each remain brain voxel was performed in each participant. A Gaussian spatial smoothing kernel (8mm x 8mm x 8mm FWHM) was applied to the resulting map, followed by an r to z transform. Simple linear regression was used to examine average z-scored connectivity between LvAI and the whole brain with age, sex, education, and cognitive status (MCI or early-stage AD) as covariates. Statistical maps were thresholded $p < 0.05$ using a cluster extent correction for multiple comparisons. Statistical analyses were performed in SPM12.
Results: Increased immediate memory scores were correlated with increased connectivity with LvAI and parahippocampal gyri, lingual gyri, and left precentral gyrus, and decreased connectivity with inferior parietal lobule bilaterally, and right angular gyrus.
Discussion: Improved immediate memory performance after intervention, regardless of study arm, was linked to increased connectivity between LvAI and areas implicated in memory, spatial awareness, and movement.

80. **Inhibition of HMGB1 Restores Cognitive Deficits and Epigenetic Loss of Cholinergic Neurons following Adolescent Binge Alcohol Exposure** | ***Shivani Paresh Vaidya***

Neuroinflammation is a central feature of many neurological and psychiatric disorders, including alcohol use disorder (AUD). Using a well-established rat model of adolescent intermittent ethanol (AIE) exposure, we investigated how adolescent binge drinking leads to persistent adult cognitive impairment and long-lasting molecular changes in the brain. Consistent with prior findings, AIE produced sustained deficits in cognition, increased neuroinflammatory signaling, and reduced expression of forebrain cholinergic (ChAT+) neuronal markers. Importantly, previous work suggests that this suppression of cholinergic phenotype reflects epigenetic silencing rather than neuronal loss, highlighting the potential reversibility of these effects. To understand broader transcriptomics changes, we performed bulk RNA sequencing of forebrain tissue. AIE resulted in persistent downregulation of cholinergic genes, including *ChAT, VAChT, Ngfr, and Ntrk1*, alongside a shift toward a pro-inflammatory transcriptional profile. This included increased expression of HMGB1-related inflammatory genes (Hmgb1, Hmgb2l1, Cxcr4), enhanced glutamatergic signaling (Vglut1/Slc17a7), and reduced GABAergic markers (Gad1, Gad2), suggesting an excitatory–inhibitory imbalance. These findings were supported by increased *Vglut1* mRNA and protein

expression in the basal forebrain following AIE. Notably, increased VGLUT1 expression was also observed in post-mortem brain tissue from individuals with AUD, supporting the translational relevance of these findings. Given prior evidence implicating HMGB1 as a key mediator of ethanol-induced neuroinflammation and epigenetic dysregulation, we tested whether targeting this pathway could reverse AIE-induced changes. Pharmacological inhibition of HMGB1 using glycyrrhizic acid restored cholinergic gene expression, normalized *Vglut1* levels, reduced neuroinflammatory signaling, and improved cognitive function in adulthood. Together, these findings demonstrate that adolescent alcohol exposure induces persistent but reversible epigenetic reprogramming of basal forebrain circuitry via HMGB1-dependent neuroinflammation. Importantly, these results identify HMGB1 signaling as a clinically relevant and potentially druggable target for preventing or reversing long-term cognitive deficits associated with adolescent binge drinking and AUD.

81. Next Generation Antifungals: A Novel Platform for Black Shank Control | *Alejandro Valdes*

Fungal pathogens significantly limit crop productivity, and increasing resistance to existing fungicides threatens effective disease management. Black shank, caused by Phytophthora nicotianae, is a highly destructive disease that highlights the urgent need for new, sustainable antifungal solutions. This project, supported by a Flash Grant from the North Carolina Biotechnology Center (NCBC), represents a collaboration between the Pierce Lab (synthetic organic chemistry) and the Lux Lab (plant pathology) at NC State to develop nextgeneration crop protection agents. The Pierce Lab has designed a novel class of antifungal compounds based on a proprietary heterocyclic scaffold ("Core Tech."), while the Lux Lab provides expertise in biologically relevant pathogen evaluation. Building on promising preliminary results from industry screening, we synthesized and evaluated an expanded library of Core Tech analogs to explore structure activity relationships (SAR) and optimize performance. In vitro testing against crop-relevant pathogens revealed that several lead compounds demonstrated exceptional activity against black shank, outperforming a commercial gold-standard fungicide at 1 and 10 ppb. Additionally, solubility studies showed at least a 2-fold improvement, suggesting enhanced formulation potential. These results highlight the promise of our scaffold as a next-generation antifungal platform. Topperforming compounds are being advanced to in planta evaluation in the Lux Lab to validate efficacy under greenhouse conditions. In parallel, we are assessing the environmental profile of these compounds, including degradability and potential impacts on soil and water systems, and initial toxicological studies. Together, this work supports the development of effective and environmentally responsible crop protection agents.
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82.* B Cells Contribute to Restricting Klebsiella Pneumoniae in the Gut and in Preventing Systemic Dissemination and Expansion | *Juan David Valencia Bacca

Klebsiella pneumoniae (Kpn) is an increasingly urgent public health threat driven by multidrug-resistant and hyper-encapsulated strains that disseminate systemically from the gastrointestinal (GI) tract. Although intestinal colonization frequently precedes invasive disease, the immune mechanisms that control early Kpn expansion and dissemination remain incompletely characterized. In particular, the role of B cells during initial infection is unclear. Here, using an oral infection model without antibiotic pre-treatment, we examined how B cells and antibodies shape Kpn colonization dynamics and disease outcome. B cell–deficient (μMT) mice exhibited WT-like fecal shedding and similar initial colonization bottlenecks, but subsequently developed uncontrolled bacterial expansion in the gut and extraintestinal tissues, leading to increased dissemination and mortality. Lineage tracking with a barcoded Kpn library and the STAMPR pipeline revealed that B cells do not suppress initial seeding, but instead constrain post-seeding clonal expansion within the gut and periphery. To define the antibody

mechanisms underlying this phenomenon, we analyzed mice selectively deficient in mucosal IgA transport or secreted IgM. pIgR$^{-/-}$ mice exhibited increased intestinal and systemic bacterial burdens but survived infection, whereas mice unable to secrete IgM (μS$^{-/-}$) displayed normal GI colonization yet succumbed to disease. Strikingly, activation-induced cytidine deaminase–deficient mice (AID/Cre), which lack class-switched antibodies but retain germline-encoded IgM, maintained WT-like colonization levels and were fully protected from disseminated infection. Together, these findings demonstrate that B cells protect against Kpn not by preventing colonization, but by limiting post-seeding expansion and systemic dissemination. While mucosal IgA restrains early intestinal growth, natural, germline-encoded IgM is essential for survival following oral Kpn infection. These results identify post-seeding expansion as a critical determinant of disease outcome and establish natural IgM as a key component of host defense against invasive Kpn infection. Harnessing natural IgM biology, either through vaccination strategies that preserve germline broad specificity or through IgM-based therapeutics, may offer a promising approach to protect vulnerable populations against multidrug-resistant Kpn strains.

83. Integrating Wearables and Low-Cost Environmental Sensors to Map Health and Exposure Across DURHAM (Distributed Urban Residential Heat & Air Quality Monitoring) | *Danielle Wagner*

Though climate and air quality research are often isolate, they have many overlapping source-related concerns and potential for exposure-related mitigation, including traffic-related ozone and $PM_{2.5}$ emissions and highway-centered heat sources. Hot DURHAM (Disparities in Urban Residential Air quality & Heat monitoring) is a pilot study investigating measurable effects of heat and air quality over the course of a year using low-cost environmental sensors and Oura ring biometrics among a pilot cohort (n=13) in the Durham, NC.

Since initiating in June of 2025, outdoor temperatures variations across several sites in Durham have been estimated to vary by as high as 4.5°C (7°F) in the summer and 2.3°C (4°F) in the winter, confirming earlier estimates predicted using Weather Underground citizen stations. Variations in frequency of high emission events paired with indoor $PM_{2.5}$ response to extreme outdoor values indicate a vast variation of household operation, which may impact chronic exposure to higher PM levels. The study is intended to continue through 2026 to capture seasonal variations.

Preliminary investigations between household indoor and outdoor environmental metrics ($PM_{2.5}$, CO_2, and temperature) and Oura physiological data (e.g. resting heart rate, body temperature, sleep duration, breathing rate) have been used to contextualize individual responses to occupant and ambient events. Upcoming work includes further assessing correlations between exposure and health, as well as gauging the effects of occupant-informed interventions to influence each of these metrics. These interventions will be based on anecdotes and feedback from surveys, including individualized environmental summary reports, real-time environmental dashboards, and portable filters with suggested placement by source emissions.

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84. Wireless Multimodal Wearable Sensor for Plant Monitoring and Stress Diagnosis | *Jin Xu*

Nearly half of the global population experiences food insecurity, underscoring the urgent need for advanced agricultural technologies. As the primary source of food production, plants are highly susceptible to a wide range of abiotic and biotic stresses, which can severely compromise yield and quality. Wearable plant sensing technologies have recently emerged as a promising approach for precision agriculture by enabling continuous, in situ monitoring of plant physiological states. However, current systems remain limited by restricted sensing modalities, inefficient data transmission, and inadequate analytical capabilities. Here, we present a multimodal wearable sensing platform for plants that enables continuous and high-fidelity monitoring of key physiological

parameters, including temperature, humidity, and three representative classes of volatile organic compounds with high selectivity, alongside critical microenvironmental factors such as light intensity and carbon dioxide concentration. The device features a bookmark-inspired mechanical architecture that ensures conformal and stable integration with the abaxial leaf surface across diverse plant species and leaf morphologies. This integrated platform enables comprehensive, organ-specific sensing of plant physiological dynamics, facilitating the identification and differentiation of multiple abiotic and biotic stress conditions. The acquired data are wirelessly transmitted through a hybrid communication system combining local Bluetooth connectivity with real-time cloud streaming for remote access. Furthermore, an integrated machine learning framework is employed for advanced data analytics, enabling accurate stress classification, early disease detection, and real-time decision support for precision agriculture.

85. **Fanconi Anemia Protein FANCJ Regulates Repair of DNA-Protein Crosslinkâ€“stalled Replication Forks** | ***Akbar Zainu***

DNA-protein crosslinks (DPCs) are cytotoxic lesions where a protein becomes covalently linked to DNA, forming bulky adducts that impair DNA replication. Exposure to environmental electrophiles and carcinogens, particularly formaldehyde from tobacco smoke, incomplete combustion contributes to DPC formation. Additionally, clinical chemotherapeutic agents, such as decitabine, Cisplatin etc induce DPCs. Impaired DPC repair is linked to progeroid disease Ruijs-Aalfs syndrome and to broader genome-instability phenotypes relevant to cancer predisposition.
Our recent work implicated the Fanconi anemia (FA) pathway, a mediator of DNA interstrand crosslink repair, in DPC repair. However, mechanism of FA-mediated DPC repair, its interactions with other pathway and overall contribution to DPC resolution remain unknown. FANCJ is a DNA helicase and critical downstream effector of FA pathway. Germline mutations in FANCJ confer increased susceptibility to ovarian, breast cancer and FA. FANCJ directly interacts with breast cancer susceptibility protein, BRCA1. Although *in vitro* studies suggest an indirect role for FANCJ in DPC repair, underlying mechanism of how FANCJ mutations drive repair and disease pathogenesis remain poorly understood. Here, we investigate *in vivo* the mechanistic role of FANCJ in DPC repair.
Using CRISPR/Cas9 gene editing, I created mouse-ES cell lines with different mutant alleles of FANCJ. I found that: 1 C-terminus FANCJ-BRCA1 interaction is critical for DPC repair. 2. ATPase activity of FANCJ is not required for DPC repair. 3. Using a site-specific barrier reporter system simulating DPC, I showed that FANCJ suppresses homologous recombination (HR) repair at stalled forks. Importantly, FANCJ-mediated HR suppression is mediated by BRCA1. Given the central role of HR dysregulation in genome-instability and cancer, these results suggest that FANCJ restrains BRCA1-driven hyper-HR that could lead to deleterious outcomes. Collectively, these findings establish FANCJ as a key regulator of genome-stability at DPC stalled replication forks.
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86. **List Randomization for Prevalence Estimation of Sensitive Behavioral Data Among Women with HIV of Reproductive Age in Lilongwe, Malawi** | ***Karen Diepstra***

Background: Self-reported data related to sexual behavior is subject to reporting biases, such as social desirability bias. List randomization, which enables prevalence estimation without requiring that respondents disclose their answer to potentially sensitive questions, is one method that may mitigate the impact of such biases. We examined the list randomization strategy among women with HIV (WWH) in Malawi.
Methods: In the Family Planning and Antiretroviral Therapy (FP-ART) cohort study, participants were randomized (1:1) to answer five blocks of true/false statements via

either list response or direct response. Each block contained one sensitive true/false statement and three non-sensitive statements. Participants randomized to direct response were directly asked each statement as a classic true/false question. Participants randomized to the list response method were instead asked "How many of these 4 sentences are true?" for each block, and the prevalence and prevalence difference (PD) estimates were derived from this data.
Results: There were 386 WWH who enrolled in FP-ART, of whom 196 (50.8%) were randomized to direct response and 190 (49.2%) to list response; 2,448 main FP-ART study visits were included. The self-reported prevalence of using a condom during last vaginal sex was 29.3% among list response compared to 32.9% among direct response visits (PD: -3.7%; 95% CI: -11.9%, 4.6%) (Figure 1). The proportion who reported that their HIV status was disclosed to all current sex partners was 59.0% for list response versus 58.9% for direct response visits (PD: 0.0%; 95% CI: -12.7%, 12.8%).
Conclusion: We did not find evidence that responding to sensitive questions using the list method versus direct response elicited greater reporting of potentially stigmatizing data (i.e., higher prevalence of perceived negative statement or lower prevalence of perceived positive statement). However, list randomization may be a useful method for eliciting sensitive behavioral data that should be explored in other settings.
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