OHSU Medical Scientist Training Program 2026 Retreat

OHSU MSTP

Medical Scientist Training Program

2026 Retreat

Friday, August 21, 2026

Vey Auditorium • Doernbecher Children's Hospital

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Welcome

On behalf of the 2026 MSTP Retreat Planning Committee, welcome. We are delighted to bring our physician-scientist community together for a day dedicated to science, mentorship, and connection. The pages that follow showcase the remarkable breadth of research underway across our program — spanning molecular mechanisms of disease, engineering and imaging innovation, and translational and clinical discovery. We are grateful to our keynote and featured speakers, the mentors who guide this work, and above all, our trainees, whose curiosity and dedication fill this booklet. We hope you leave today inspired by the discovery and the community that defines our program.

— The 2026 MSTP Retreat Planning Committee

2021 Matriculating Cohort

Kelly Abshire • Eric Cramer • Hannah Jaeger • Jessica Keating • Kayla Maanum • Amara Pang • Katherine Pelz • Elias (Eli) Wisdom • Xammy Wrynla

Retreat Agenda

Vey Auditorium, Doernbecher Children's Hospital

Time	Activity
10:45–11:15 am	Check-in
11:15–11:30	Opening Ceremony & Introduction to Incoming Cohort
11:30–11:45	Leadership Address (SoM) — Dr. Nathan Selden, MD, PhD
11:45–12:45 pm	Keynote Speaker — Dr. Gül Dölen, MD, PhD (UC Berkeley)
12:45–1:40	Lunch & Group Photo
1:45–2:00 pm	State of the Program Address — Dr. Yabing Chen, PhD
2:00–3:00 pm	Student Talks — Taitea Dykstra, Rin Yang, Peter Tran, Malik Seals
3:00–3:40 pm	Community-Building / Information-Sharing Small Groups
3:45–4:00 pm	Leadership Address (UME) — Dr. Ben Schneider, MD
4:00–5:00 pm	Student Talks — Mady Tung, TJ Ekstrom, Jaime Contreras, Amanda Zucker
5:00–6:00 pm	Poster Session (see Poster Index for numbers)
6:00–8:00 pm	Dinner & Fun Activities

Poster Index

Poster 1 — Steven Adamou
Modulation of P2X7R Activity with Nanobodies

Poster 2 — Hyuntae Byun
Music exposure enhances resistance to Salmonella infection by promoting healthy gut microbiota

Poster 3 — Rohan Chaudhari
Adoptive T cell transfer suppresses endogenous tumor-specific CD8 T cell recovery following lymphodepletion

Poster 4 — Owen Doyle
Characterizing Retinal Artery Pulsatility in Aortic Stenosis with Doppler Optical Coherence Tomography

Poster 5 — Bianca Hoang-Dang
Subthreshold Visual Motion Modulates People's Perception of Others' Attention: Evidence from Intracranial sEEG Recordings

Poster 6 — Sam King
Machine-Learning Phenotypic Clustering of Coronary Artery Bypass Grafting ERAS Patients

Poster 7 — Samuel H. Kim
α-Synuclein Regulates DNA Double-Strand Break Repair and Chromatin Accessibility in Parkinson's Disease and Melanoma

Poster 8 — Jack Henry Kotnik
Recombinase-Orthogonal Monosynaptic Rabies Virus Tracing Tools for Intra-Brain Synaptic Network Comparisons: A Case Study of SYNGAP1 Haploinsufficiency

Poster 9 — Hanna E. Minns
Intracranial Electrical Fields for the Treatment of Glioblastoma

Poster 10 — Kevin Mueller
Investigating Factors Associated With Respiratory Syncytial Virus Vaccination and Breakthrough Infection Among Patients With Systemic Autoimmune Rheumatic Diseases

Poster 11 — Luke Whitcomb
GDF15-induced Wasting in Cardiac, but Not Skeletal, Muscle Is Mediated by Reduced Caloric Intake in C57BL/6J Mice

Poster 12 — Jing Xie
Investigating Structural and Functional Connectivity Networks in Stress-Related Infant Neural Connectomes

Director's Welcome

Dr. Yabing Chen, PhD, MBA, FAHA
Interim Director, OHSU MD/PhD Program
Welcome to the OHSU MSTP Annual Retreat. Thank you to our student leaders, administrators, speakers, faculty, and staff whose dedication makes this event possible. It is a pleasure to come together as a community to share science, learn from one another, and strengthen the connections that support the growth of our physician-scientists.
As the most important advances often emerge when diverse perspectives come together, I encourage you to engage beyond your own field, ask bold questions, and explore opportunities for collaboration across disciplines and training stages.
I hope you find this retreat inspiring, energizing, and rewarding. As we work to advance science and improve human health, let's remember: "If you want to go fast, go alone. If you want to go far, go together."

Meet the Incoming Cohort

Entering MSTP students, 2026

Katarina (Kate) Augustyn

M1
Katarina (Kate) Augustyn earned a B.S. from the Massachusetts Institute of Technology in 2025. Their research interests include cancer biology, immunology, and stem cell biology, and they are interested in clinical areas such as regenerative medicine, oncology, and orthopedics.

Jessica Cope

M1
Jessica Cope earned a B.A. from UC Berkeley in 2024. Their research interests include the structural biology of pulmonary infection, and they are interested in pulmonology and critical care.

McKenna Finley

M1
McKenna Finley earned a B.A. from Lewis & Clark College in 2023. Their research interests include cancer biology, hematopoiesis, and stem cell biology, and they are interested in clinical areas such as hematology, medical oncology, pathology, and palliative care.

Dylan Flink

M1

Dylan Flink earned a B.S. from the University of Minnesota–Twin Cities in 2023. Their research interests include decision-making and its neural circuits, and they are interested in neurology and psychiatry.

Meet the Incoming Cohort continued

Elle Kass

M1
Elle Kass earned a B.A. from Connecticut College in 2021. Their research interests include neuroscience, and they are interested in child and adolescent psychiatry.

Ridhi Patil

M1
Ridhi Patil earned a B.S. in Biomedical Engineering from UT Austin in 2024. Their research interests include translational immunology, cancer, immunotherapy, and neuroimmunology, and they are interested in clinical areas such as oncology, rheumatology, and OB/GYN.

Augustine Vanlianuk

M1
Augustine Vanlianuk earned a B.S. with Honors from the University of Michigan–Ann Arbor in 2023. Their research interests include gene expression and neurobiology in neurodegenerative disease, and they are interested in the diagnosis and management of neurodegenerative disease.

M.D./Ph.D. Student Leadership

2026-2027

Admissions Liaisons

Sam King, Peter Tran

APSA Institutional Representative

Eric Cramer

M.D./Ph.D. Committee Student Representatives

Kelly Abshire, Taitea Dykstra, Jack Henry Kotnik, Eli Wisdom

Peer Mentorship Leader

Amara Pang

Student Administration Liaison

Luke Whitcomb

Community Engagement Liaisons

Ashley Anderson, Kayla Maanum, Rodaba Rahim, Mady Tung, Simone Woodruff

Keynote Speaker

Dr. Gül Dölen, MD, PhD
University of California, Berkeley
"The Emerging Neurobiology of Psychedelics: Critical Periods, Metaplasticity, and Extracellular Matrix Remodeling"
Dr. Gül Dölen's research explores critical periods, psychedelics, and the social brain. Her lab has shown that psychedelics may act as a "master key" for reopening critical periods — windows of heightened neural plasticity — a property that may help explain their therapeutic promise across a wide range of psychiatric conditions.
A physician-scientist, Dr. Dölen completed MD–PhD training at Brown University and the Massachusetts Institute of Technology, where her doctoral work on fragile X syndrome identified a potential therapeutic target. She went on to postdoctoral training with Dr. Robert Malenka at Stanford University, where she showed that oxytocin and serotonin act together in the nucleus accumbens to make social interaction rewarding.
Dr. Gül Dölen is a Professor and the Bob & Renee Parsons Endowed Chair in the Department of Neuroscience, the Department of Psychology, the Berkeley Center for the Science of Psychedelics, and the Helen Wills Neuroscience Institute at the University of California, Berkeley. She also maintains an Adjunct Professorship in Neuroscience and Neurology at the Johns Hopkins University School of Medicine. Her honors include the Joukowsky Family Foundation Outstanding Dissertation Award, the Conquer Fragile X Rising Star Award, the Angus MacDonald Award for Excellence in Undergraduate Teaching, the Society for Social Neuroscience Early Career Award, the Searle Scholars Award, and the Johns Hopkins University President's Frontier Award.

Featured Speakers

Dr. Nathan Selden, MD, PhD

Leadership Address — School of Medicine

Dr. Nathan Selden, MD, PhD, is Dean of the School of Medicine, President of the OHSU Practice Plan, and Executive Vice President of OHSU.

Dr. Selden was appointed Dean on February 21, 2024. Prior to that time, he served for 8 years as Chair of the Department of Neurological Surgery. He continues to hold the Campagna Endowed Chair in Pediatric Neurosurgery. Dr. Selden's clinical practice focuses on surgery for childhood epilepsy, brain tumors, and congenital disorders. In 2006, he performed the first ever transplantation of neuronal stem cells in a human patient.

An internationally known academic neurosurgeon, Dr. Selden has authored over 200 peer-reviewed publications, edited a neurosurgical textbook series, and — with Nigel Nicholson, Dean Emeritus of Reed College — wrote a book in 2019 entitled "The Rhetoric of Medicine: Lessons on Professionalism from Ancient Greece".

Dr. Selden also holds multiple national leadership roles. He is the immediate past-president of the Society of Neurological Surgeons, the oldest neurosurgical society in the world. He has also served as a Director and Vice-chair of the American Board of Neurological Surgery and as President of the Congress of Neurological Surgeons. He was the founding national director of the neurosurgery boot camp courses and chaired the group that designed national training outcome measures — or milestones — for the United States. In 2013, he received the "Courage to Teach" Award from the Accreditation Council of Graduate Medical Education, which accredits all residency and fellowship training programs nationwide.

Raised in Portland, Dr. Selden is an avid hiker and skier. He obtained a bachelor's degree at Stanford University, a PhD in neuroscience at Cambridge University — where he was a British Marshall Scholar — and a Medical Degree from Harvard Medical School. Dr. Selden then trained in neurological surgery at the University of Michigan, followed by a fellowship in pediatric neurosurgery at Northwestern University, before returning home to Oregon and joining the OHSU faculty in 2000.

Dr. Ben Schneider, MD

Leadership Address — Undergraduate Medical Education

As an educational leader, Dr. Ben Schneider focuses on Undergraduate Medical Education (UME) and serves as Associate Dean of UME at Oregon Health & Science University (OHSU). In this role, he oversees all aspects of the MD program, including outreach, admissions, curriculum, academic progress, student affairs, and learner assessment.

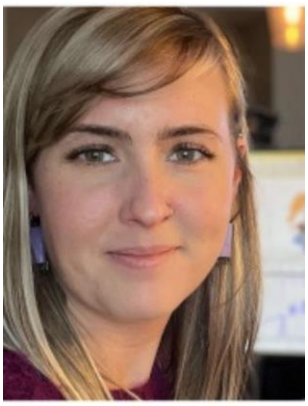
He began leading OHSU's Career and Residency Advising in 2013 and was Assistant Dean, UME Student Affairs from 2015 until he became the Associate Dean of UME in 2025. He brings extensive experience in UME and GME education, the transition to residency, curriculum transformation, accreditation, student progress, mistreatment prevention, and interprofessional education. He previously served as Medical Director of the OHSU PA program and continues to collaborate closely with the program.

Clinically, Dr. Schneider is a family physician who enjoys caring for entire families by providing comprehensive care to adults and children. He is a patient advisor and educator, meeting people where they are and recommending the best possible care. Whether the focus is disease prevention, health maintenance, or the management of acute or chronic conditions, he helps patients understand their options and make informed decisions.

Outside of medicine, Ben enjoys spending time with his wife and their three children. He especially values time enjoying the natural bounty that Oregon has to offer.

Student Speakers

Oral presentations



Investigating the Role of Androgen Receptor Signaling in CD8 T Cells in Multiple Sclerosis

Taitea Dykstra • G2

Taitea Dykstra is an MD/PhD student originally from Seattle, WA entering her second year of PhD training in the Program in Biomedical Sciences at OHSU in the laboratory of Dr. Amy Moran. Her research focuses on how endocrine signaling shapes neuroimmune responses, with a particular interest in how androgen receptor signaling regulates CD8 T cell fate during neuroinflammation and its implications for multiple sclerosis and brain tumors. She hopes to pursue a career as an academic neurosurgeon and physician-scientist studying the intersection of neuroimmunology, endocrinology, and neuro-oncology to develop more precise therapies for neurological disease. Outside the lab, she is an avid knitter who is almost always planning her next sweater project, and the one after that.

Fluorescence Guided Surgery for IDH-Mutant Brain Tumors

Rin Yang • G2
Rin Yang is a 2nd year graduate student from New York who is currently in the Biomedical Engineering Program working in the labs of Drs. Summer Gibbs and Melissa Wong. They are interested in studying surgical technologies for brain tumors and understanding how malignant cells navigate the blood brain barrier. Outside of the lab, Rin enjoys watching birds and can often be found carrying crow snacks.

Impact of Macrophage Polarization on the Metabolic Landscape of Colorectal Tumor-Immune Hybrids

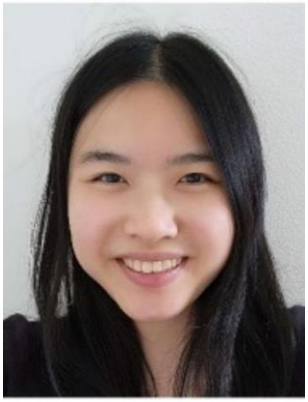
Peter Tran • G1

Peter Tran is a 3rd-year MD/PhD student from Long Beach, CA, beginning his PhD in the Graduate Program for Biomedical Science. Co-mentored by Drs. Melissa Wong and Aaron Grossberg, Peter studies how macrophage identity shapes tumor-immune hybrid cells, focusing on their metabolic plasticity and malignant behavior. He hopes to bridge his research interest in cancer immunometabolism with his clinical interests in otolaryngology, dermatology, or allergy/immunology pursued through academia and/or industry.

Tumor Intrinsic Nerve Recruitment Impairs Anti-Tumor Immunity in PDAC

Malik Seals • G2

Malik Seals is a G2 in the OHSU MD/PhD program, originally from Columbus, Mississippi. His thesis research investigates the molecular mechanisms by which pancreatic tumor cells recruit sympathetic nerves into the tumor microenvironment and how this process influences anti-tumor immunity. Looking ahead, he envisions his career at the intersection of science, medicine, and policy, whether in academia or industry, with a long-term commitment to advancing our understanding of the complex bidirectional communication between the nervous and immune systems. One fun fact is that at his peak, he had outranked 94% of all ranked players worldwide on mobile Call of Duty.



Transcatheter Aortic Valve Material Thrombogenicity Is Driven By Platelet Activation

Mady Tung • G3

Mady Tung is a 4th-year MD/PhD Candidate at Oregon Health & Science University. They grew up in the suburbs of Dallas/Fort Worth, Texas, and they moved to Los Angeles to complete their undergraduate degree in Biomedical Engineering at the University of Southern California. Currently, they are continuing their study of Biomedical Engineering in the lab of Dr. Monica Hinds, where they investigate host responses to blood-contacting cardiovascular devices with the aim of developing safer, more effective biomaterials. In the future, they hope to apply their growing knowledge of biomaterials to the study of theranostic nanoparticles in tandem with their clinical interests in diagnostic and interventional radiology. In their free time, they enjoy swimming, organizing collaborative creative projects for charity, and looking through cat adoption websites.

Phenotypic Analyses of the Immune Microenvironment Across the Dysplasia-to-Colorectal Cancer Disease Progression

TJ Ekstrom • G3

TJ Ekstrom is a 4th-year MD/PhD student who studies how stromal cells assist in regulating intestinal stem cell state during early development, homeostasis, and disease. TJ plans to continue this line of research as a gastroenterologist in the future. Outside the lab, TJ loves to bake, watch horror movies, and travel to new places.

Title: The functional role of FX in pancreatic ductal adenocarcinoma

Jaime Contreras • G1
Jaime Contreras earned a B.S. from the University of California, Los Angeles in 2018 and is now a 1st-year graduate student in the Lau Lab.

Investigating Metastatic Potential with CHCs

Amanda Zucker • G4

Amanda Zucker grew up in New York and completed her undergraduate degree in cell and molecular biology at Binghamton University. Amanda spent three years at Memorial Sloan Kettering Cancer Center studying genetic heterogeneity of metastasis in pancreatic cancer prior to joining the MD/PhD program at OHSU. She is now in her 5th year of the program, working in the Wong and Gibbs laboratories to study mechanisms driving metastatic potential of circulating hybrid cells in pancreatic cancer. Long-term, Amanda is interested in building a career as an oncologic surgeon-scientist. A fun fact about Amanda is that she spent a year and a half volunteering with a marine rescue treating injured seals and sea turtles.

Abstracts

Oral Presentations

ORAL PRESENTATION

Investigating the Role of Androgen Receptor Signaling in CD8 T Cells in Multiple Sclerosis

Taitea Dykstra[1,2], Fanny Polesso[2], Reed Hawkins[2,3], John Cheney[2], Amy Moran[2]

1. *Medical Scientist Training Program, Oregon Health & Science University, Portland, OR, USA*
2. *Department of Cell, Developmental, and Cancer Biology, Oregon Health & Science University, Portland, OR, USA*
3. *Current affiliation: Fred Hutchinson Cancer Center, Seattle, WA, USA*

Multiple sclerosis displays a striking but complex sex bias: women are substantially more likely to develop disease, whereas men often experience faster progression and greater disability. This pattern suggests that sex-dependent signals influence distinct phases of disease rather than acting uniformly as protective or pathogenic factors. Androgen receptor (AR) signaling is known to regulate CD8 T cell differentiation in chronic immune settings, but its role during central nervous system autoimmunity remains poorly defined.

Using mice with CD8-specific deletion of AR, loss of AR signaling was found to alter disease course in a mouse model of MS and shift the differentiation trajectory of pathogenic CD8 T cells. Complementary chromatin accessibility data further point to AR-dependent regulation of genes governing T cell fate. This work seeks to define endocrine regulation of adaptive immune cell fate as a previously unrecognized mechanism governing neuroinflammation.

ORAL PRESENTATION

Fluorescence Guided Surgery for IDH-Mutant Brain Tumors

Rin Yang[1,2,] Kyle Milnes[1], Gourav Kumar[1], Kai Tao[1,3,] Gauri S. Malankar[1], Stephen Bowden[4], Melissa Wong[3,5], Lei G. Wang[1,3], Summer L. Gibbs[1,3]

1. *Department of Biomedical Engineering, Oregon Health & Science University, Portland, OR*
2. *School of Medicine, Oregon Health & Science University, Portland, OR*
3. *Department of Cell, Developmental and Cancer Biology, Oregon Health & Science University, Portland, OR*
4. *Department of Neurosurgery, Oregon Health & Science University, Portland, OR*
5. *Knight Cancer Institute, Oregon Health & Science University, Portland, OR*

Gliomas are the most common type of primary brain tumors, comprising 30% of central nervous system (CNS) tumors and 80% of all malignant brain tumors. Gliomas harboring isocitrate dehydrogenase (IDH) mutations are generally associated with slower, more indolent growth, likely due to metabolic reprogramming, with approximately 80% of diagnosed low grade gliomas carrying an IDH mutation. However, because these tumors unpredictably undergo malignant progression, prognosis for patients with an IDH-mutant glioma still range from only months to several decades of survival. Investigation of this wide range of outcomes has revealed that larger postoperative residual tumor volumes are associated with shorter progression-free survival (PFS) and overall survival (OS) in patients with grade II and grade III gliomas. Notably, total resection of IDH-mutant gliomas with R0 margins is in <15% of patients, which not only abrogates the benefits of surgery but also increases likelihood of disease recurrence. This surgical challenge is due to the diffuse infiltrative nature of IDH-mutant gliomas, which results in lack of clear borders that complicate efforts for conservation of brain tissue especially in existing workflows using existing intraoperative imaging tools.

Fluorescence guided surgery (FGS) utilizes machine assisted visualization of tissue- and disease-specific contrast agents to highlight tissues of interest, offering real-time visualization intraoperatively. However, there is not currently a contrast agent that is suited for the resection of IDH-mutant gliomas. Due to lack of blood brain barrier disruption in these tumors, existing clinically approved contrast agents including sodium fluorescein, indocyanine green (ICG), and 5-aminolevulinic acid (5-ALA) do not provide IDH-mutant glioma-specific contrast. We are developing fluorescent probes specific for IDH-mutant glioma resection to fill this unmet clinical need.

Since 2008 when IDH-mutations were discovered to be oncogenic drivers, they have been leveraged as targets for therapeutics. In 2024, Vorasidenib, an IDH mutant targeting inhibitor was FDA approved for the treatment of IDH-mutant gliomas. These inhibitors offer a potential platform from which to develop a probe for FGS in IDH-mutant glioma resection when conjugated to our novel small molecule fluorophores, termed OregonFluor (OF), which are cell membrane permeable permitting ready labeling of intracellular targets in live cells and tissue such as mutant IDH. Our OF dyes are compatible with FGS systems that are currently used in operating rooms, which allows for ease of clinical translation of our FGS strategy for IDH-mutant gliomas. We have synthesized a library of IDH-mutant inhibitors labeled with our OF dyes and demonstrated their specificity for the IDH mutation. We anticipate these tools could improve surgical control of IDH-mutant gliomas, positively impacting surgical resections and overall patient outcomes.

ORAL PRESENTATION

Impact of Macrophage Polarization on the Metabolic Landscape of Colorectal Tumor-Immune Hybrids

Peter Tran
Grossberg / Wong Lab, Oregon Health & Science University

Despite advances in chemotherapy and immunotherapy, metastatic colorectal cancer (CRC) remains largely incurable, underscoring the need to identify novel drivers of disease progression. Recent studies have identified that tumor and immune cells within the tumor microenvironment (TME) undergo cell-cell fusion to generate tumor-immune hybrid cells. Hybrid cells harbor the transcriptional profiles of both parental lineages, yet little is known how the macrophage polarization identity of these hybrids dictate metabolic programming and malignant behavior. Characterizing the macrophage polarization-dependent biology of hybrid cells represents a critical yet unexplored frontier, as these cells have been shown to correlate with worsening disease prognosis and may represent an underappreciated mechanism driving therapeutic resistance and metastatic progression in CRC. Here, we investigate macrophage polarization states and associated metabolic profiles in hybrid cells using bulk RNA sequencing and Seahorse XF metabolic analysis to evaluate the functional consequences of polarization-dependent metabolism on proliferation, invasion, and phagocytic behavior. We hypothesize that M2-polarized hybrids exploit oxidative and fatty acid metabolic programs to sustain proliferation and invasion while M1-polarized hybrids retain glycolytic and phagocytic features. Defining polarization-dependent metabolic programs in hybrid cells may expose a clinically targetable mechanism that can disrupt hybrid cell-driven progression in CRC.

ORAL PRESENTATION

Neurexin-1 Marks a Tumor Cell Subpopulation Concentrated at the Sympathetic Nerve Interface in Pancreatic Ductal Adenocarcinoma

Malik Seals[1,2,] Ariana Sattler[3,4], Gulsu Sener[4], Gordon Mills[3,4], Ece Eksi[3,4]

1. *Medical Scientist Training Program, Oregon Health & Science University, Portland, OR, USA*
2. *Department of Integrated Cancer Biology, Program of Biomedical Science Graduate Program, Oregon Health & Science University, Portland, OR, USA*
3. *Department of Cell, Developmental, and Cancer Biology, Oregon Health & Science University, Portland, OR, USA*
4. *Oregon Health & Science University Knight Cancer Institute, Portland, OR, USA*

Sympathetic innervation promotes tumor progression and immune evasion in pancreatic ductal adenocarcinoma (PDAC), yet the molecular mechanisms by which tumor cells actively recruit sympathetic nerve fibers into the tumor microenvironment (TME) remain undefined. The neurexin (NRXN)-neuroligin (NLGN) trans-synaptic adhesion axis, active at central synapses, represents a candidate co-opted recruitment mechanism: NRXN1 ectodomain shedding by ADAM10 generates a soluble ligand that engages NLGN1 on peripheral axons. We hypothesized that a discrete subpopulation of NRXN1-expressing PDAC tumor cells drives sympathetic nerve recruitment, with downstream consequences for intratumoral lymphocyte infiltration and formation of tertiary lymphoid structures.

Using multiplex immunofluorescence (mIF) imaging on orthotopic KPC tumors paired with spatial proximity analysis across 23,204 single cells in four regions of interest, we identified a discrete population of NRXN1+ epithelial tumor cells (ECAD+NRXN1+) concentrated at the tumor-nerve interface. These cells localized a median of 19.1 μm from the nearest TUBB3+/NLGN1+ sympathetic nerve fiber, compared to bulk ECAD+ tumor cells (64.1 μm; Mann-Whitney U, $p<0.001$), consistent with contact-associated rather than constitutive NRXN1 upregulation. In a pancreas-localized sympathetic denervation model (Dbh-Cre × Rosa26-iDTR KPC mice), diphtheria toxin-mediated ablation of sympathetic fibers produced a near doubling of intratumoral CD3+ T lymphocyte density relative to innervated controls (0.296 vs. 0.132 counts/mm2; $p=0.006$, $\eta 2=0.87$). Sympathectomized groups also formed mature TLS.

To test functional necessity, we are generating CRISPR-Cas9 NRXN1 knockout KPC lines for orthotopic implantation, quantifying sympathetic nerve density, axonal outgrowth, lymphocyte infiltration, and TLS formation as primary outcomes. Cross-validation in human PDAC tissues from the Oregon Pancreas Tissue Registry will stratify nerve density and lymphoid aggregation by NRXN1 status. This will enable us to determine whether intratumoral NRXN1 expression and nerve proximity covary in humans, thereby establishing translational relevance for a novel therapeutic target along this neural-tumoral-immune communication axis. These findings identify NRXN1-mediated sympathetic nerve recruitment as an upstream driver of immune evasion in PDAC and position the NRXN1-NLGN1 axis as a tractable neuroimmune target in this refractory malignancy.

ORAL PRESENTATION

Thrombogenicity of Transcatheter Aortic Valves and the Valve Biomaterial Components

M. Tung, M.T. Hinds, D.E.J. Anderson
Department of Biomedical Engineering, Oregon Health & Science University, Portland, OR, USA
Statement of Purpose: Aortic stenosis is a common valvular disorder in which the aortic valve thickens and calcifies, resulting in impaired function. Transcatheter aortic valve replacement (TAVR) is a minimally invasive treatment; patients who undergo TAVR are often placed on lifelong anticoagulation against thromboembolic events, but long-term anticoagulant use may cause bleeding complications, so new strategies are needed to reduce TAVR-related thrombosis. We aimed to better understand the thrombogenicity of the biomaterial components of currently used TAVR valves, which are commonly composed of decellularized porcine pericardial tissue (leaflets and skirt) and cobalt chromium (CoCr) stents (frame). Blood-contacting biomaterials are generally thrombogenic via the intrinsic coagulation pathway, but the extent to which porcine pericardium and CoCr, individually and in combination, activate this pathway is unknown. We hypothesized that pericardium and CoCr activate the intrinsic pathway in an additive manner, resulting in greater thrombogenicity when combined.
Methods: Ex vivo studies were performed in two male non-human primates (Papio anubis) implanted with an exteriorized chronic, arteriovenous, femoral shunt. Thrombus formation was assessed in four devices: (1) porcine pericardium, (2) CoCr frame, (3) pericardium wrapped around a CoCr frame, and (4) a miniaturized valve device (CoCr frame with pericardium skirt and leaflets). Stents were exposed to whole blood at 150 mL/min with a 100 U/kg heparin bolus and 150 U/kg/hr infusion. Platelets and fibrinogen were labeled with 111In and 125I; platelet attachment was quantified by gamma camera for 60 min, and fibrin incorporation was measured as endpoint data.
Results/Discussion: Devices comprising both pericardium and CoCr frame showed increased platelet accumulation compared to pericardium or frame alone. Pericardium alone showed comparable accumulation to the combination groups in the first 20 minutes but less overall, though differences among these groups were not significant. Platelet accumulation on the frame alone was both delayed and significantly less than on the combination devices. Fibrin accumulation was similarly increased on combination devices, though not significantly. These results indicate pericardium and CoCr may be additively thrombogenic, suggesting they activate the intrinsic coagulation pathway via different mechanisms. Ongoing in vitro studies assess Factor XII and platelet activation; Factor XII is activated by negatively charged molecules such as collagen (present in pericardium), whereas CoCr is electrically neutral, so its thrombogenicity may be driven by a different mechanism.
Conclusions: Pericardium and CoCr combined are more thrombogenic than either biomaterial individually. Ongoing studies will confirm the thrombogenicity mechanisms in vitro using contact-pathway inhibitors and platelet activation assays, informing both future TAVR valve design and post-TAVR anticoagulation strategies.

ORAL PRESENTATION

Phenotypic Analyses of the Immune Microenvironment Across the Dysplasia-to-Colorectal Cancer Disease Progression

TJ Ekstrom[1], Cody Rounds[2], Jocelyn Jones[2], Molly Thomas[1,3], Gregory Baker[2,4,5], Summer Gibbs[2,5], Melissa Wong[1,5]

1. *Department of Cell, Developmental & Cancer Biology, Oregon Health & Science University, Portland, OR*
2. *Department of Biomedical Engineering, Oregon Health & Science University, Portland, OR*
3. *Division of Gastroenterology and Hepatology, Oregon Health & Science University, Portland, OR*
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Inflammatory bowel diseases (IBD) affect 2.4 to 3.1 million people in the United States and confer a 2.5-fold increased risk of developing colorectal cancer relative to the general population. Colitis-associated colorectal cancer (CA-CRC) often develops from focal areas of colonic dysplasia, which are screened for by colonoscopy. Despite earlier detection of cancer at younger ages, patients exhibit poorer prognoses compared to patients who develop spontaneous CRC. While colonoscopy remains the gold-standard screening tool for CRC risk stratification, its utility is constrained by cost, accessibility, and patient compliance. Therefore, improving our understanding of the tissue immune microenvironment of IBD-associated dysplasia and determining whether these signatures are present in peripheral blood could transform the early diagnosis and detection of patients at high risk for CA-CRC. To address this question, we investigated whether discrete immune phenotypes could differentiate IBD patients with and without dysplasia in tissue, and whether the identified signatures are detectable in peripheral blood. We constructed a panel of directly conjugated, photocleavable antibodies targeting canonical immune and epithelial markers and employed multiplexed cyclic immunofluorescence (cyCIF) to profile cell phenotypes within the immune microenvironment of tissue from IBD patients with inflamed chronic colitis, low-to-high grade dysplasia, and CA-CRC as well as patient-matched normal adjacent controls. Leveraging this training cohort, cyCIF images were assembled and background-normalized prior to training a variational autoencoder on pixel-level imaging data using MORPHAEUS software to infer cell states within the tissue and blood. Our findings demonstrate an enrichment of immune populations at dysplastic sites compared to patient-matched non-dysplastic sites. Notably, we identified immune neighborhood sub-types within the tissue microenvironment that shift over the disease axis. These results validate our ability to detect cell-type-specific compositional differences in IBD-associated dysplasia using a 10-marker cyCIF panel and MORPHAEUS machine learning. Future work will expand the cyCIF panel to incorporate stromal and epithelial stem cell markers of dysplasia. Additionally, we will recruit a larger patient cohort to systematically assess changes in the tissue microenvironment across the disease axis and evaluate the potential for stratifying dysplasia from CA-CRC in peripheral blood based on the identified immune-based signatures.

ORAL PRESENTATION

The functional role of FX in pancreatic ductal adenocarcinoma

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Fucosylation, the post-translational modification of proteins and lipids with L-fucose, can regulate crucial immune and organ developmental processes. This process can rely on the de novo conversion of GDP-L-fucose from the sugar GDP-D-mannose by the enzyme FX. Increasing studies have demonstrated that aberrant fucosylation can contribute to the pathogenesis of cancers including melanoma and breast cancer, yet roles of fucosylation in pancreatic ductal adenocarcinoma (PDAC) remain largely unclear.

Over the past several years, our laboratory has reported that dietary administration of L-fucose in mice suppresses melanoma and breast tumors triggering antitumor immune responses characterized by enhanced dendritic cell and T cell activities.

Interestingly, publicly available bulk RNA sequencing data of human PDAC tissue has revealed that the enzyme FX is highly upregulated and correlates with poorer survival outcomes. This suggests that the capacity to convert GDP-mannose to GDP-L-fucose elicits tumorigenic effects, although the underlying mechanism(s) and tumor-promoting functional contributions are unclear. Thus, our lab has focused determining the functional role(s) of FX in PDAC pathogenesis.

Here, we investigated the function of FX in PDAC cells that could potentially shine light into developmental, functional and therapeutical roles to combat PDAC. To this end, we knocked down FX in human and mouse PDAC cells. We observed in colony formation assay that loss of FX in PDAC cells increase cell proliferation. In contrast, treating PDAC cells with mannose reduced PDAC cell proliferation—an effect that is par;ally rescued by knockdown of FX. Together, our data support the novel and intriguing concept that the availability of mannose and the ability to convert GDP-D-mannose into GDP-L-fucose is a tumor-suppressive and potentially therapeutically actionable mechanism in PDAC.

We have planned further studies to elucidate how FX paradoxically correlates with poorer patient survival yet suppress PDAC growth in vitro. As FX may mediate tumorigenic capacity through other cellular behaviors at the cost of proliferation, we will study if FX promotes other functions including motility and therapy resistance

ORAL PRESENTATION

Investigating Metastatic Potential with Circulating Hybrid Cells

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Pancreatic ductal adenocarcinoma (PDAC) with basal-like features and the related histologic subtype pancreatic adenosquamous carcinoma (PASC), collectively termed basal-squamous PDAC, are highly aggressive malignancies lacking prospective noninvasive early detection methods. Currently, definitive diagnosis requires retrospective molecular and histologic characterization of resected tissue after patients have received initial, ineffective chemotherapy. To address the critical need to understand the underlying biology driving basal-squamous progression, we combined a murine basal-squamous model with patient-matched tumor and blood. We identified neoplastic-immune hybrid cells in tissue and circulating hybrid cells (CHCs) in peripheral blood in basal-squamous PDAC. We classified hybrid cells and CHCs as squamous or glandular (p40/CK5 or CK8, respectively) to compare these populations during metastatic progression. In patient specimens, squamous hybrids comprised a higher percentage than glandular hybrids, and the percentages of each were relatively similar between the primary tumor and peripheral blood, demonstrating that CHCs are a promising noninvasive biomarker for phenotyping the primary tumor. Additionally, squamous CHCs had increased levels of total and activated epidermal growth factor (EGF) receptor. Upregulation of EGF signaling in squamous hybrid cells indicates a potential mechanism driving basal-squamous tumor aggressiveness and the possibility of selective therapeutic targeting to treat these tumors.

Poster Presentations

POSTER 1

Modulation of P2X7R Activity with Nanobodies

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The P2X class of receptors are non-selective cation channels sensitive to extracellular ATP. P2X7Rs are unique among P2XRs because they require relatively higher concentrations of ATP (micromolar) to become activated, do not desensitize, and contain a unique cytoplasmic domain responsible for activating downstream inflammatory pathways. Given P2X7Rs are expressed on nearly all cells involved in both innate and adaptive immunity, it is unsurprising that they are implicated in mediating inflammatory conditions such as atherosclerosis and Alzheimer's Disease. Despite this wide pathogenic profile, no drugs targeting any P2XRs have been brought to market highlighting a need to better understand receptor modulation. Although several nanobodies have been reported to modulate P2X7R function, mechanistic insight into how these molecules influence receptor activity remains limited. Bridging this knowledge gap would facilitate the rational design of biologic therapeutics targeting purinergic signaling pathways.

To address this gap, we used single-particle Cryo–EM to define the epitope landscape of three distinct nanobodies bound to the human P2X7Rs. These structural data were complemented by bio-layer interferometry to assess the binding kinetics of the nanobodies. We identify multiple binding postures across the nanobody panel, revealing distinct mechanisms of receptor modulation. These structural differences correlate with cell-based assays demonstrating how specific epitope engagement translates into altered channel activity. Together, this study provides the first structural framework for understanding how biologics can differentially modulate P2X7R activity and establishes mechanistic principles for the rational design of species-selective therapeutics targeting this receptor.

POSTER 2

Music exposure enhances resistance to Salmonella infection by promoting healthy gut microbiota

Clara Y. Zhu, **Hyuntae Byun**, Elyza A. Do, Yue Zhang, Ethan Tanchoco, Joris Beld, Ansel Hsiao, Jun Zhu

Music intervention is gaining recognition as a cost-effective therapeutic for improving human health. Despite its growing application, the mechanisms through which music exerts beneficial health effects remain largely unexplored. Here, we show that music can exert beneficial effects in mice through modulating gut microbiome composition. Adult mice were exposed to ambient noise, Mozart's Flute Quartet in D Major, K. 285, or white noise over a three-week period. Afterward, we observed treatment-specific changes in the community of gut commensal bacteria in these animals. Upon subsequent challenge with the bacterial pathogen Salmonella typhimurium, control groups exhibited significant weight loss and increased Salmonella colonization, whereas the Mozart-treated group did not. 16S ribosomal RNA gene sequencing revealed that the Mozart group showed a significant increase in Lactobacillus salivarius, a probiotic known for its antibacterial properties. Further experiments confirmed that L. salivarius mitigated Salmonella infection in mice and that L. salivarius acidified local environments in in vitro culture, thus inhibiting Salmonella growth. Additionally, mice exposed to Mozart consumed more food but showed similar body weight compared to the control groups. Behavioral assessments, including open field and object location tests, revealed that Mozart-treated mice were more active, less anxious, and exhibited enhanced spatial memory. Finally, Mozart exposure was shown to significantly boost colonization of administered L. salivarius and alter gut metabolite profiles. These findings suggest that music exposure fosters healthier gut microbiota, enhancing resistance to bacterial infections and highlighting the potential of music therapy as a novel strategy to combat drug-resistant pathogen infections.

POSTER 3

Adoptive T cell transfer suppresses endogenous tumor-specific CD8 T cell recovery following lymphodepletion

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Adoptive T-cell transfer (ACT), where patients are infused with millions of tumor-specific effector T-cells, has proven to be highly effective in hematologic malignancies and is FDA approved as early as a second-line treatment for refractory disease. Unfortunately, extending the benefits of ACT to solid tumors has been largely hindered with challenges intrinsic to solid tumor microenvironments such as intratumoral heterogeneity, where the ACT target antigen is only expressed in a fraction of the tumor. Engaging the endogenous immune system alongside ACT may be one strategy to circumvent the issue of intratumoral heterogeneity by allowing for a broader, more synergistic T-cell response against the tumor. However, the role of endogenous cells in ACT remains poorly understood, and past clinical and preclinical research suggests that ACT does not engage anti-tumor endogenous responses. In this study, we investigated whether ACT and accompanying lymphodepletion may directly suppress the tumor-specific endogenous T cell response in a Kras/p53(KP)-driven autochthonous mouse model of lung adenocarcinoma expressing defined tumor-specific neoantigens, both ACT-targeted and non-targeted. Lung tumor-bearing mice were lymphodepleted (LD) with a standard dose of 150 mg/kg cyclophosphamide intra-peritoneally with or without transfer of 6 million tumor-specific ACT cells intra-vascularly. Our results demonstrate that LD alone depletes endogenous tumor neoantigen specific CD8 T cells, but these cells largely recover by 3 weeks post-treatment. In contrast, adoptive cell transfer with LD resulted in sustained depletion of endogenous tumor-specific CD8 cells and these cells had reduced expression of effector markers Ki67 (proliferation) and Granzyme B (cytotoxicity). These findings suggest that ACT may be playing a suppressive role against the endogenous tumor-specific T cell response when pre-conditioning mice with cyclophosphamide. Adoptive cell transfer without LD did not result in a significantly decreased population of endogenous tumor-specific CD8 cells, however results were confounded by a significantly lower number of adoptively transferred cells infiltrating into the lung. Additionally, a pooled vaccine targeting both endogenous tumor-specific and transferred CD8 cells and cells preferentially boosted transferred cells while failing to boost endogenous T cells. Further research studying this suppression with lower doses of LD or homeostatic cytokine supplementation (e.g. IL-7/IL-15) could reveal if the suppression is intrinsic to the adoptively transferred cells or cyclophosphamide. Furthermore, future studies into finding ways to overcome this suppression and activate the endogenous immune system, such as neoantigen targeted vaccination, could be critical to unlocking the full potential of ACT.

POSTER 4

Characterizing Retinal Artery Pulsatility in Aortic Stenosis with Doppler Optical Coherence Tomography

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Ultra-high resolution Doppler Optical Coherence Tomography (OCT) holds promise to detect and quantify abnormal hemodynamics in the retina resulting from aortic stenosis (AS). This work investigates retinal arterial pulsatility parameters in clinically significant AS compared to healthy controls.

Healthy and AS participants were scanned with an ultra-high resolution spectral domain OCT with 1.8 μm depth resolution and 250 kHz scan rate. The Doppler OCT scan pattern is a repeated circular scan (D=1.3 mm, 4000 a-scans) in the optic disc repeated 200 times in 3 seconds. The Doppler shift was estimated using a split-spectrum algorithm adapted for the wide-spectrum laser source. The repeated 200 frames were nonrigidly registered. Arteries were detected on the average frame and propagated back to each valid frame. The Doppler phase shift within the vessel mask was summed across frames to construct the retinal blood velocity waveform. The waveform was phase-folded into a single cardiac cycle and smoothed to reduce noise. The systolic peak point (SPP), diastolic peak point (DPP), and diastolic end point (DEP) were detected. Based on the three points, the systolic rise time (tDEP-tSPP, 10%-90% segment), diastolic decay time (tDPP-tDEP), diastolic/systolic peak ratio (DPP/SPP), and resistive index (1-SPP/DPP) were estimated.

13 eyes from 7 patients with aortic stenosis and 7 eyes from 4 healthy participants were enrolled. 4 eyes and 1 participant were excluded due to severe eye motion and aortic regurgitation, respectively. Systolic rise time is significantly longer in participants with aortic stenosis than in healthy participants ($p<0.05$). Further waveform analysis with consideration blood pressure and age is planned.

POSTER 5

Subthreshold Visual Motion Modulates People's Perception of Others' Attention: Evidence from Intracranial sEEG Recordings

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Objective: Viewing static images of agents attending to objects is associated with an implied motion linking agent to object. This signal is coupled with a behavioral motion aftereffect and encoded in motion-processing areas (Guterstam & Graziano, 2020a; Guterstam et al., 2020; Renet et al., 2024). An online study (n=526) found that subthreshold motion streaming from agent to object can manipulate social attention judgments, suggesting a functional role of visual motion in attention-tracking (Guterstam & Graziano, 2020b). This study is the first to characterize this in-lab and reveal its neural correlates.

Methods: Ten epilepsy patients undergoing clinical sEEG monitoring made forced-choice judgments about which of two faces attended more to a central object while a masked 'beam-like' subthreshold motion streamed from one face, either agent-to-object or object-to-agent (Guterstam & Graziano 2020b). Judgements could be congruent or incongruent with the motion's location. High-gamma (70–200 Hz) activity was analyzed across six theory-of-mind ROIs.

Results: Participants were significantly faster at congruent judgements, but only when motion flowed agent-to-object (motion-direction X congruence interaction: -150ms, 95%CI=[-257,-56], $p<0.001$, 10,000 bootstrap iterations); 9/10 subjects showed this pattern. Seven had usable iEEG; in these, congruent versus incongruent trials modulated high-γ activity in 15/92 (16%) ROI electrodes across left STS, MPFC, bilateral TPJ, and right STS (six of seven subjects), none responding in the object-to-agent control.

Conclusion: Subthreshold motion facilitated social attention judgements, accompanied by high-gamma modulation in theory-of-mind regions (STS, TPJ, MPFC), supporting a functional role for visual motion in tracking others' attention and showing that low-level motion signals engage social-cognitive cortex to shape judgements about others' attentional states.

POSTER 6

Machine-Learning Phenotypic Clustering of Coronary Artery Bypass Grafting ERAS Patients

Sam King, Audrey Hyem, Anthony Pohahau, Ashley Chon, Howard K. Song, Phil Jenkins, Julie Doberne

Introduction. Enhanced Recovery protocols after Cardiac Surgery (ERAS) result in shorter ventilator times and shorter ICU and hospital lengths of stay with equivalent outcomes. Qualification criteria for ERAS select for straightforward procedures with low predicted morbidity. Despite this, some patients have post-operative courses resembling those of more complex patients. The purpose of this study was to utilize machine learning techniques to phenotypically cluster patients to ultimately improve patient selection.

Methods. 202 ERAS-qualified patients underwent CABG at OHSU 1/2024-9/2025. Outliers (n=5) were removed prior to clustering by calculating multivariate Mahalanobis distance and excluding patients with $p<0.0001$. We then used unsupervised K-means clustering (k=2) of post-operative metrics to obtain clinically distinct phenotypes and visualized results with Principal Component Analysis (PCA). Clusters were compared using Fisher's Exact test for binary flag variables and the Mann-Whitney U test for ordinal variables. P-values were corrected using Benjamini-Hochberg false discovery rate (FDR) correction.

Results. Two distinct clusters were identified from K-means clustering analysis (Silhouette score=0.430). One cluster can be characterized as "Normal Recovery" (n=189), and the other as "Extended Recovery" (n=17). Extended recovery patients had 11.8 times higher ventilator hours ($q<0.001$), 2 times higher Length of Stay Index ($q<0.001$), and 41 times higher Post-op Reintubation rates ($q<0.001$). Notably, age ($q=0.80$) and elective vs urgent ($q=0.90$) were not predictive of extended recovery status.

Conclusion. Unsupervised K-means clustering was able to identify a population of ERAS-qualified patients that had extended recovery and complication rates. These clusters were both defined as distinct through their Silhouette score and their phenotypic features, including increased vent hours and lengths of stay. Identification of this population allows for future risk-stratification efforts to both strengthen the ERAS protocol and provide a better prediction of surgical risks to patients.

POSTER 7

α-Synuclein Regulates DNA Double-Strand Break Repair and Chromatin Accessibility in Parkinson's Disease and Melanoma

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Background: Melanoma and Parkinson's disease (PD) are two clinically distinct and conceptually opposed disorders, one driven by uncontrolled cell proliferation and the other by progressive neuronal loss. However, a surprising epidemiologic association between these two conditions has emerged, wherein melanoma patients are more likely to develop PD, and vice versa. This paradoxical relationship suggests that shared molecular pathways may produce divergent outcomes depending on cellular context. The neuronal protein α-synuclein (αSyn), central to PD pathogenesis, freely diffuses to the nucleus where it binds DNA and interacts with DNA repair and chromatin-modifying proteins, implicating it in the response to genotoxic stress. In PD, αSyn forms insoluble cytoplasmic aggregates in neurons, sequestering αSyn outside the nucleus and leaving cells vulnerable to DNA damage and repair failure. In contrast, αSyn is upregulated in melanocytes from patients with metastatic melanoma, where we hypothesize its nuclear availability may enhance double-strand break (DSB) repair efficiency, promote cell-cycle re-entry, and drive unchecked proliferation. These contrasting roles point to αSyn as a key modulator of genome integrity and chromatin dynamics.

Methods: Isogenic SK-MEL-28 lines (αSyn WT, KO, KI) were exposed to 0 or 5Gy ionizing radiation and fixed at 20min, 2h, and 6h post-irradiation. Western blot and immunocytochemistry quantified repair kinetics and DNA damage response complex architecture using antibodies to γH2AX, MDC1, 53BP1, and phospho-53BP1. To determine how αSyn's nuclear interactome reorganizes after DNA damage, we performed Rapid Immunoprecipitation Mass spectrometry of Endogenous proteins (RIME) on crosslinked, nuclear-enriched lysates after 0 or 5Gy irradiation using multiple αSyn antibodies followed by on-bead digestion and LC-MS/MS. For epigenomic profiling, nuclei were prepared for single-cell ATAC-seq on SK-MEL-28 cells (WT, KO, KI). Libraries were analyzed using ArchR to map chromatin accessibility, identify differentially accessible regions, and assess transcription factor motif enrichment and gene scores at DSB repair and cell-cycle loci.

Results: Loss of αSyn increased baseline DSB burden (γH2AX fluorescence, validated by Western blot), which remained elevated by at least 50% in KO cells through 6h post-irradiation, indicating impaired DSB resolution downstream of γH2AX. Total 53BP1 was similar across genotypes at baseline, but KO cells showed fewer, smaller, and dimmer 53BP1 foci at all time points, and both genotypes unexpectedly showed decreased total 53BP1 after irradiation. Analogously performed MDC1 experiments showed a similar pattern to 53BP1 with decreased nuclear fluorescence in KO cells following DNA damage induction. Together these findings indicate that αSyn facilitates recruitment and spatial organization of the 53BP1 and MDC1 repair machinery during the DSB response. In line with these findings, RIME revealed increased association of αSyn with repair-associated factors MDC1, H2AX, and CIRBP in WT cells and after DNA damage. Single-cell ATAC-seq revealed reduced chromatin accessibility at regulatory regions near SNCA (αSyn) and DNA repair genes (TP53BP1, ATM, BRCA1) in αSyn KO cells, suggesting that αSyn loss reshapes chromatin toward reduced repair capacity and altered cell-cycle control.

Implications: These results implicate αSyn in DSB repair through coordinated effects on repair factor recruitment, protein interactions, and accessibility at repair gene loci. Its loss produces a persistent DSB burden and altered 53BP1, MDC1, and CIRBP associations, consistent with a functional repair deficit. In PD, sequestration of αSyn into cytoplasmic aggregates may deplete this nuclear repair function, providing a mechanistic link to neuronal DNA damage accumulation, while the same function, upregulated in proliferative melanoma cells, may account for the epidemiologic association between the two diseases. Defining αSyn's role in DSB repair may inform therapeutic strategies to preserve genome integrity in PD.

POSTER 8

Recombinase-Orthogonal Monosynaptic Rabies Virus Tracing Tools for Intra-Brain Synaptic Network Comparisons: A Case Study of SYNGAP1 Haploinsufficiency

Jack Henry Kotnik, Austin Schubert, Gregory Chin, Emily Tiedemann, Lamya Ben Ameur, Arpiar Saunders

Normal development of neural circuitry requires carefully coordinated molecular and neural activity programs that guide, stabilize, and maintain synaptic wiring. Mutations that confer risk for neurodevelopmental disorders frequently disrupt synaptic proteins and may alter the formation of synaptic networks across the brain's many neuron types. Rabies virus-based monosynaptic tracing is a powerful strategy to characterize cell type-specific connectivity, yet current methods cannot directly compare presynaptic networks arising from populations of neurons with and without conditional gene deletions in a single brain.

Here, we report a recombinase-orthogonal monosynaptic tracing system that overcomes this limitation. Our approach combines optimized Cre- or Flpo-dependent AAVs that selectively functionalize "starter" neurons to express TVA- or TVB. EnvA- or EnvB-pseudotyped N2c glycoprotein-deleted rabies viruses selectively label presynaptic inputs to these two parallel, genetically defined populations of postsynaptic starter neurons. Subcellular targeting of GFP and RFP reporters further allows unambiguous discrimination among four experimental conditions within a single animal. When paired with transgenic mouse models harboring recombinase-sensitive floxed alleles, this platform enables direct, within-brain comparisons of presynaptic network organization arising from wild-type versus mutant postsynaptic neurons, enabling sensitive and internally controlled analysis of cell autonomous mutational effects. We apply this system to interrogate synaptic network alterations in a mouse model of SYNGAP1-related intellectual disability, in which haploinsufficiency of SYNGAP1 leads to transient defects in neuronal morphology and persistent disruptions in adult cortical processing.

POSTER 9

Intracranial Electrical Fields for the Treatment of Glioblastoma

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Glioblastoma (GBM) is the most common and lethal malignant primary brain tumor, with a median survival under two years. Despite decades of research, outcomes remain poor, underscoring the urgent need for novel therapeutic approaches. One promising direction involves using electrical fields to inhibit tumor growth: Tumor Treating Fields (TTF), which deliver intermediate-frequency electrical fields via scalp electrodes, extend survival by approximately five months. However, this extracranial approach is fundamentally constrained by poor field precision, energy attenuation through skull and tissue, and a burdensome requirement of over 18 hours of daily wear. These limitations could be overcome through intracranial stimulation, in which implanted electrodes deliver localized, high-intensity fields directly adjacent to the tumor. To investigate this approach, we first optimized stimulation parameters in vitro across two murine glioma cell lines, then translated these findings to an orthotopic, syngeneic rodent model of GBM with implanted intracranial electrodes. Electrical stimulation at 200 kHz induced dose-dependent suppression of tumor cell growth in vitro, with higher voltages producing greater inhibition, while in vivo, animals tolerated chronic electrode implantation and stimulation without neurological deficits, and preliminary findings reveal a remarkable difference in tumor burden between stimulated and unstimulated animals. Together, these early-stage results provide an encouraging proof-of-concept that intracranial electrical field delivery is both feasible and effective in a clinically relevant tumor model. Ongoing work is aimed at rigorously optimizing stimulation parameters to maximize safety and efficacy, advancing toward an implantable bioelectrical therapy that could meaningfully improve survival for patients with GBM.

POSTER 10

Investigating Factors Associated With Respiratory Syncytial Virus Vaccination and Breakthrough Infection Among Patients With Systemic Autoimmune Rheumatic Diseases

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Background/Purpose: Respiratory syncytial virus (RSV) vaccines were approved starting in May 2023 and are recommended by the US CDC to adults aged 60 years or older at increased risk for poor outcomes, including immunocompromising conditions or medications. We previously showed that RSV is associated with poor outcomes and high rates of hospitalization in people with systemic autoimmune rheumatic diseases (SARDs), but less is known about RSV vaccine uptake among individuals with SARDs. Therefore, we described the prevalence, associations, and breakthrough infection of RSV vaccination among people with SARDs.

Methods: We performed a retrospective, cross-sectional study in a US tertiary healthcare system. We identified patients with 2 or more SARD codes and who were prescribed a DMARD or oral glucocorticoid as of February 2025 (positive predictive value 95%). We excluded patients who had died or whose last encounter was on or before May 2023 and those less than 60 years of age on the last day of observation or at time of RSV vaccination. The primary outcome was RSV vaccination documented in the electronic health record. We evaluated factors associated with RSV vaccination and used multivariable logistic regression to assess for associations. We then described breakthrough infections with positive testing after RSV vaccination.

Results: We analyzed 10,587 SARD patients aged 60 years or older (median age 71.7 years, 72.4% female, 88.0% White). The most common SARD type was RA (56.8%), and the most common medications were conventional synthetic DMARDs (40.8%). We identified 1,075 people with SARDs (10.2%) who received the RSV vaccine. There was no association of any SARD type with RSV vaccination after adjusting for general population factors. Influenza vaccine receipt in the previous year had the strongest association with RSV vaccination (no vs. yes OR 0.021, 95%CI 0.018 to 0.026). Glucocorticoid users were less likely (OR 0.33, 95%CI 0.23 to 0.49) and interstitial lung disease was more likely (OR 1.53, 95%CI 1.14 to 2.04) to receive RSV vaccination. We identified 9 cases of breakthrough RSV infections, occurring a median of 301 days after vaccination.

Conclusion: Among patients with SARDs aged 60 years or older, 10.2% were documented to receive RSV vaccination. After accounting for general population factors, glucocorticoid users were less likely to receive RSV vaccination. Neither SARD type nor DMARD class, including CD20 inhibitors, were associated with RSV vaccination. Only 2 of 9 documented cases of breakthrough RSV infections were hospitalized and there were no deaths. While our study is limited to a single geographic area and may under-capture RSV vaccinations and breakthrough infections, further research on effectiveness and vaccine-induced SARD flares is needed.

POSTER 11

GDF15-induced Wasting in Cardiac, but Not Skeletal, Muscle Is Mediated by Reduced Caloric Intake in C57BL/6J Mice

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Cancer-Associated Cachexia (CAC), or the loss of skeletal muscle, cardiac, and fat tissue in patients with solid tumors, significantly impedes clinical therapy and impairs patients' quality of life. Growth Differentiation Factor 15 (GDF15) is a cytokine produced by most tissues in response to physiologic stressors and has been shown to mediate CAC through inducing immune modulation, mitochondrial dysfunction, and anorexia. This stated, the specific role of GDF15-mediated caloric reduction in CAC across various tissue types remains unclear. The present study sought to determine whether GDF15 elicits cardiac wasting via its impact on food intake or another mechanism. 24 C57BL/6J mice (all male) were divided into 3 groups (n=8/group): Sham Ad-Libitum (Sham), GDF15 treated (GDF15) or Sham Pair-Fed (PF). Mice were injected subcutaneously with either 8nmol/kg of recombinant human GDF15 or Vehicle for 12 days before sacrifice and organ weight assessment. PF group was fed the gram amount that the GDF15 group consumed, on average, the day previous. Body weight, food intake, and food pellet shredding (a measure of stress) were measured daily. GDF15 injection produced a marked reduction in cumulative food intake and an increase in food pellet shredding. Though a significant reduction was initially seen in GDF15 and PF groups, final mean body weight did not differ across groups. Gastrocnemius muscle and white adipose mass were significantly lower in the GDF15, but not PF, groups compared to Sham. Contrarily, equivalent wasting of cardiac tissue was seen in GDF15 and PF groups. These results suggest that GDF15-mediated heart wasting is dependent on caloric reduction, while wasting in white adipose and gastrocnemius muscle occurs through a calorie-independent mechanism. Future experiments will seek to elucidate the role of sympathetic nervous system activation in calorically-dependent cardiac wasting, and potential heart dysfunction, induced by GDF15.

POSTER 12

Investigating Structural and Functional Connectivity Networks in Stress-Related Infant Neural Connectomes

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Exposure to Early Life Stress (ELS) is often associated with long-term mental and physical health consequences. To date, few studies have focused on the impact of ELS on infant neurodevelopment, which misses an important opportunity to leverage the immense neuroplasticity of this period. Utilizing the Baby Connectome Project (BCP), our goal was to identify both structural and functional brain networks that were significantly correlated with exposure to ELS. To measure early life stress, we used the Major Life Events Questionnaire (MLE), a 20-item questionnaire that reported major life events that occurred in the household within the last 12 months. Two separate models were examined: (1) the total number of life events reported and (2) mean severity of perceived trauma. To assess structural diffusion imaging, we completed correlational tractography and graph theory-based network analysis on 142 participants (50% female, M = 15.4 months). Among the 142 participants, 41 participants (51% female, M = 14.4 months) passed quality assessment procedures and were included in functional connectivity analysis. While we did not identify any networks significantly associated with total number of life events ($p > 0.05$), we did identify 14 nodes and edges that were negatively associated with mean severity of distress ($p = 0.024$, FWER-corrected). Of these, significant network connectivity between the dorsal attention network (DAN) and default mode network (DMN) were identified. Our results suggest that perceived stress of an event had a significant association with DAN-DMN hypoconnectivity. This stress perception-related disruption of DAN-DMN connectivity may confer early risk for psychopathology and is consistent with studies linking trauma and depression with DAN-DMN hypoconnectivity in older children and adults. Further analysis will be focused on linking ELS, structural and functional neural circuitry, and infant behavioral markers to ascertain how early in development these changes occur and identify effective interventions for at-risk individuals.

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