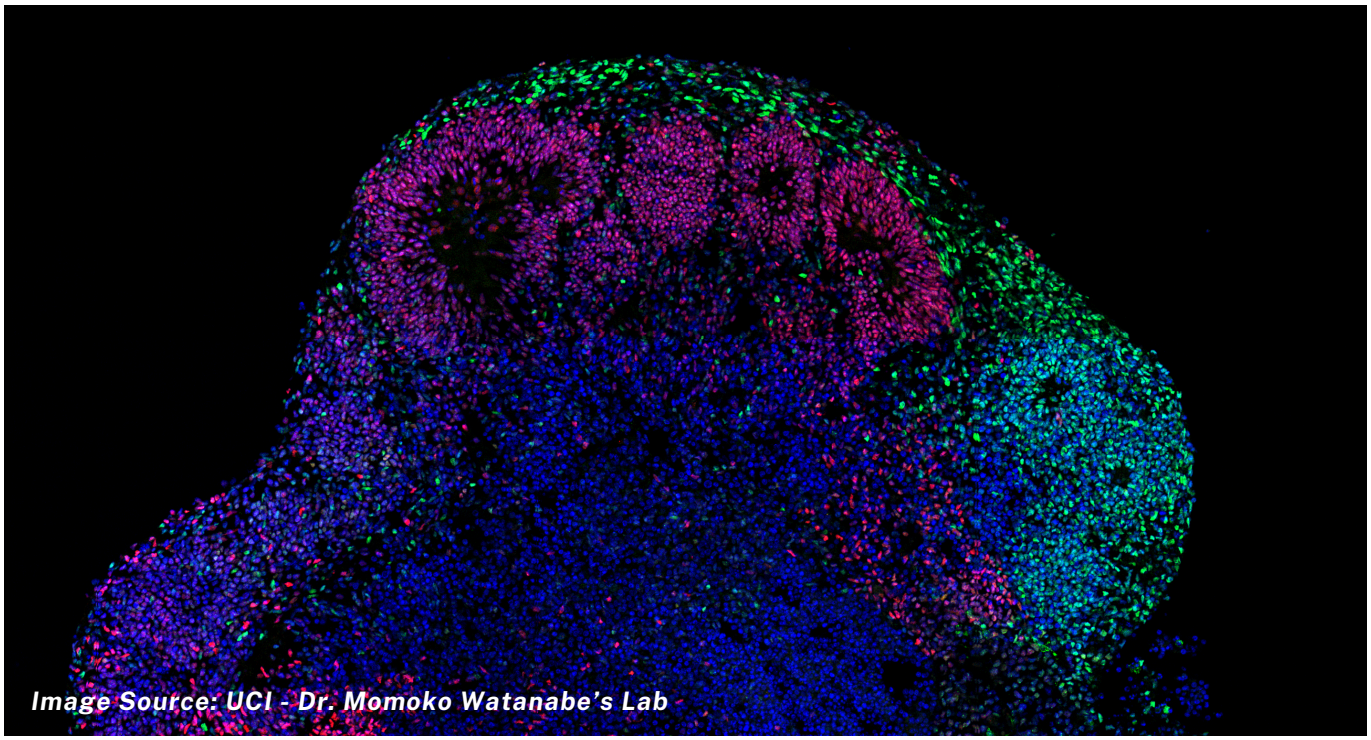
UC Irvine
Sue & Bill Gross
Stem Cell Research Center

13TH ANNUAL STEM CELL SYMPOSIUM



UCI Stem Cell Research Center
Sue & Bill Gross Hall
February 25th, 2026
9:00 AM - 7:00 PM

UC Irvine Sue & Bill Gross
Stem Cell Research Center

Symposium Agenda

Registration & Breakfast — **8:30 - 9:00 AM**

Introduction by Brian Cummings, Ph.D. — **9:00 - 9:10 AM**

Session 1: Engineering Neurogenesis - Moderated by Quinton Smith, Ph.D.

Molly Shoichet, Ph.D. - University of Toronto — **9:10 - 9: 50 AM**
"Regenerating the Brain"

Lisa A. Flanagan, Ph.D. - UC Irvine — **9:50 - 10: 30 AM**
"Human Neural Stem Cell and Endothelial Cell Reciprocal Communication Governs Cell Function"

Yuan Chen Tsai, Ph.D. - UC Irvine, Watanabe Lab — **10:30 - 10:50 AM**
"Morphogen-Guided Neocortical Organoids Recapitulate Regional Areal Identity and Model Neurodevelopmental Disorder Pathology"

Morning Break - *Boardroom* — **10:50 - 11:10 AM**

Session 2: Hematopoietic Gene and Cell Therapy - Moderated by Angela Fleischman, M.D., Ph.D.

Piyanuch Kongtim, M.D., Ph.D. - UC Irvine — **11:10 - 11: 50 AM**
"Overcoming the HLA barrier to Hematopoietic Stem Cell Transplantation"

Donald B. Kohn, M.D. - UC Los Angeles — **11: 50 - 12: 30 PM**
"Gene Therapy for Blood Cell Diseases"

Lunch Buffet - *Boardroom* — **12:30 - 1:30 PM**

Session 3: - Moderated by Daniela Bota, M.D.

Vivian Gama, Ph.D. - Vanderbilt University — **1:30 - 2:10 PM**
"The Coordination of Mitochondrial and Peroxisomal Fission Establishes Cell Fate During Neurogenesis"

Katja Piltti, Ph.D. - UC Irvine, Anderson Lab — **2:10 - 2:30 PM**
"C1q-BAI1 Regulation of Neural Stem Cell Quiescence, Activation and Metabolic Rewiring"

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Symposium Agenda

Munjal Acharya, Ph.D. - UC Irvine — **2:30 - 3:10 PM**
"Stem Cell-Derived Extracellular Vesicles to Alleviate Cancer-Related Cognitive Impairments"

Afternoon Break - *Boardroom* — **3:10 - 3:30 PM**

Session 4: Cell Therapies for Motorneuron Injury and Disease- Moderated by Aileen Anderson, Ph.D.

Ghazaleh Eskandari-Sedighi, Ph.D. - UC Irvine, Blurton-Jones Lab — **3:30 - 3:50 PM**
"Protective Human Microglia in a Chimeric Mouse Model of Alzheimer's Disease"

Robert Hunt, Ph.D. - UC Irvine — **3:50 - 4:30 PM**
"What is an Interneuron"

Clive Svendsen, Ph.D. - Cedars-Sinai — **4:30 - 5:10 PM**
"Treating Neurological Diseases Using iPSC-Derived Astrocyte Progenitors Engineered to Secrete Growth Factors"

Closing Remarks by Brian Cummings, Ph.D. & Michael Hicks, Ph.D. — **5:10-5:15 PM**

Poster Session
Roaming Dinner & Bar - *Boardroom & 4th Floor Main Enterence* — **5:15 - 6:30 PM**

Awards Ceremony — **6:30 - 7 PM**

- Clinical Research Coordinator Training Program
- GMP Facility Operations Training Program
- CIRM Training Grant
- Alpha Clinic Clinical Trial Investigator Training Program
- GMP Professional Training Program
- Student Poster Session Awards & Oral Presenters Recognition

Non-UCI Affiliated Attendees: *Park-By-Plate Link*
Event Code: 13SCSS
Please submit your car information to avoid ticketing

Session 1: Engineering Neurogenesis

INTRODUCING OUR SPEAKERS

Molly Shoichet, Ph.D. - University of Toronto

Molly S. Shoichet is University Professor and Pamela & Paul Austin Chair in Precision and Regenerative Medicine at the University of Toronto. She served as Ontario's first Chief Scientist and has been awarded numerous honours including Fellow, Royal Society (UK), Fellow, National Academy of Engineering (USA), and NSERC Herzberg Gold Medal – Canada's highest award for science/engineering, Officer of the Order of Canada, among many others. Dr. Shoichet's research focuses on innovative 3D cell culture models for drug discovery, and drug and cell delivery strategies to overcome central nervous system-related pathologies. She is a prolific entrepreneur, co-founding multiple spin-off companies, and a passionate advocate for translational research and science communication.

Lisa Flanagan, Ph.D. - UCI Irvine

Dr. Lisa Flanagan is Professor and Vice Chair for Academic Affairs in the Department of Neurology at the University of California, Irvine (UCI), with joint appointments in Biomedical Engineering and Anatomy and Neurobiology. Dr. Flanagan's research combines cell biology and bioengineering to decipher neural stem cell fate potential and optimize treatment of neurological conditions. Her overall goal is to better understand stem cell function during brain development and to maximize repair of the central nervous system after debilitating conditions such as stroke. Before joining UCI, Dr. Flanagan completed her Ph.D. at University of California, San Diego and post-doctoral training at Harvard Medical School in Boston, Massachusetts. . She received the National Science Foundation CAREER Award, serves on the Editorial Board for Scientific Reports, has served as Co-Editor for Electrophoresis, received the AES Electrophoresis Society Mid-Career Award, is a fellow of the Center for the Neurobiology of Learning and Memory, and has organized multiple international scientific conferences. Dr. Flanagan is passionate about diversity and inclusion; she served on the external advisory board for the University of Texas at Dallas ADVANCE program, won the Carol Connor Award for her efforts to create a more equitable faculty environment, and received the UCI School of Medicine Universal Faculty Mentoring Award.

Yuan-Chen Tsai, Ph.D. - UC Irvine, Watanabe Lab

Yuan-Chen (YC) Tsai is a postdoctoral fellow in Dr. Momoko Watanabe's laboratory at the University of California, Irvine. She earned her BSc in Biomedical Sciences and MSc in Neuroscience from University College London, United Kingdom, and completed her PhD in Neuroscience in Dr. Shiva Tyagarajan's lab at the University of Zurich, Switzerland. Her doctoral research focused on elucidating the distinct roles of $GABA_A$ receptor subtypes and their scaffolding protein gephyrin in regulating neuronal activity in the mouse cortex. In her postdoctoral work, she applies human stem cell-derived brain organoids to model Fragile X syndrome (FXS) and studying the inhibitory neurons in healthy and FXS organoids, contributing to our understanding of this neurodevelopmental disorder.

Session 2: Hematopoietic Gene and Cell Therapy

INTRODUCING OUR SPEAKERS

Piyanuch Kongtim, M.D., Ph.D. - UC Irvine

I am a dedicated clinician-scientist with over 10 years of experience specializing in hematopoietic stem cell transplantation (HSCT), cellular immunotherapy, and immune modulation strategies to improve outcomes for patients with hematologic malignancies and immune-related conditions. My research aims to optimize transplant protocols through the development and validation of novel conditioning regimens, donor selection algorithms, and graft-versus-host disease (GVHD) prevention techniques. I have been actively involved in designing and leading investigator-initiated clinical trials employing innovative cellular therapies, including virus-specific T-cells, natural killer (NK) cell infusions, and donor lymphocyte administrations, targeting post-transplant infections, relapse, and immune reconstitution challenges.

Throughout my career, I have contributed to advancing the understanding of the immunobiology underpinning haploidentical and unrelated donor stem cell transplantation, with an emphasis on reducing transplant-related morbidity and mortality. I have developed and validated prognostic models to assist clinicians in personalized transplant decision-making, integrating clinical, cytogenetic, and immune parameters.

My work has also focused on establishing consensus guidelines for donor selection, antibody testing, and cellular therapy applications in high-risk transplantation settings. I have a strong track record of collaborative research, multidisciplinary team leadership, and a commitment to translational science that bridges laboratory findings with clinical applications. Through my ongoing research efforts, I aim to refine transplant methodologies further, enhance immune reconstitution, and develop effective cellular therapies to improve survival and quality of life for patients undergoing stem cell transplantation.

Donald B. Kohn, M.D. - UC Los Angeles

Donald B. Kohn MD is a Distinguished Professor at the University of California, Los Angeles in the Departments of Microbiology, Immunology & Molecular Genetics (MIMG) and Pediatrics. He is a pediatric bone marrow transplant physician and is a member of UCLA's Broad Stem Cell Research Center and Jonsson Comprehensive Cancer Center. He performs laboratory and clinical studies of gene therapy for blood cell diseases, especially inborn errors of immunity and hemoglobinopathies. His research is focused on developing improved methods for adding or editing genes in human hematopoietic stem cells and evaluating these approaches in early phase clinical trials.

Session 3: Neuroprotective Strategies for Stem Cell Fate and Survival

INTRODUCING OUR SPEAKERS

Vivian Gama, Ph.D. - Vanderbilt University

Since joining Vanderbilt, Dr. Gama's work has focused on the molecular principles governing organelle remodeling as a driver of cellular transitions during neurogenesis. Dr. Gama's research has pioneered the use of pluripotent stem cell systems to understand the pathophysiology of rare, incurable mitochondrial and peroxisomal diseases, potentially uncovering new therapeutic targets. Several federal grants, including an R35 ESI MIRA, an established investigator R35 MIRA award from the NIGMS, and a Brain Initiative Grant from the NIMH, have funded her research program. In 2023, she was selected as a Chancellor Faculty Fellow, in recognition of her research and mentoring. Her research and personal background motivate and inspire her interactions with trainees, particularly in adopting a holistic approach to mentorship that considers each member's background and specific needs, enabling them to achieve their goals and succeed over the long term.

Katja Piltti, Ph.D. - UC Irvine, Anderson Lab

Dr. Katja M. Piltti is a Research Professional at the University of California, Irvine, whose interdisciplinary expertise spans molecular stem cell biology, behavioral neuroscience, and GMP-compliant manufacturing. Her work integrates mechanistic insight with translational rigor to overcome barriers to the clinical implementation of stem cell–based therapies. Dr. Piltti earned her Ph.D. in Doctoral Program in Biomedicine and Physiology from the University of Helsinki, Finland, and completed postdoctoral training in Physical Medicine and Rehabilitation, and in Memory Impairments and Neurological Disorders at UC Irvine.

Munjal Acharya, Ph.D. - UC Irvine

Dr. Munjal Acharya's research is focused on the neurobiological mechanism(s) and mechanism-based mitigation strategies to alleviate radiation and cancer-related cognitive impairments (CRCI). Dr. Acharya has uncovered a glia-dependent pathophysiological mechanism of radiation-induced cognitive dysfunction. In addition, Dr. Acharya has developed human stem cell-based regenerative strategies to remediate the brain from the unintended side effects of cranial irradiation and chemotherapy. His research has delineated the paracrine mechanism (exosomes) of stem cell transplantation-mediated recovery of the injured brain. His recent work on BDNF augmentation to reverse chemobrain is poised to advance to clinical translation.

Dr. Acharya's Ph.D. was focused on sub-cellular membrane dysfunction in the epileptic brain (M. S. University of Baroda, India). His interest in neuroscience continued as a postdoctoral scholar at Duke University Medical Center (NC) to study the efficacy of stem cell grafting to treat epilepsy.

Session 4: Cell Therapies for Neurological Disorders

INTRODUCING OUR SPEAKERS

Ghazaleh Eskandari-Sedighi, Ph.D. - UC Irvine, Blurton-Jones Lan

Dr. Ghazaleh Eskandari-Sedighi has done her PhD studies on protein misfolding diseases of the nervous system at University of Alberta, Canada. She then pursued a postdoctoral training in the same institution, focusing on glycobiology and neuroimmunology. She is currently a postdoctoral fellow at UCI MIND, working under supervision of Prof. Mathew Blurton-Jones. Her research is focused on leveraging novel stem cell models to understand microglial-based mechanisms of resilience to Alzheimer's disease.

Robert Hunt, Ph.D. - UC Irvine

I have been an active member of the Department of Anatomy & Neurobiology at UC Irvine since joining the faculty in 2015 and director of the Epilepsy Research Center since 2021. My lab focuses on conditions of brain development and injury where a treatment does not yet exist. We are creating new models of complex neurological disorders, developing cellular and molecular tools that enable precise manipulation or repair of the brain and recording high-speed dynamics of specialized neurons derived from human stem cells. Ultimately, we hope to discover precisely how the nervous system is changed in neurodevelopmental disorders or by traumatic brain injury, and to use this information to create new therapies. Our research has been funded by NIH, NSF, CIRM, DoD and private sources, including a K99/R00 Pathway to Independence Award from the National Institute of Neurological Disorders and Stroke. Here at UCI, the lab also participates actively in the Interdepartmental Neuroscience Program, Epilepsy Research Center, Center for Autism Research and Translation, Stem Cell Research Center and the Center for the Neurobiology of Learning and Memory.

Clive Svendsen, Ph.D. - Cedars Sinai

Dr. Clive Svendsen received his PhD from the University of Cambridge in England. In 2000, he moved to the University of Wisconsin as Professor of Neurology and Anatomy and founded their Stem Cell and Regenerative Medicine Center. In 2010, Dr. Svendsen moved to Los Angeles and founded the Cedars-Sinai Board of Governors Regenerative Medicine Institute, which currently has over 30 faculty members. Dr. Svendsen maintains a large lab that focuses on using patient-derived induced pluripotent stem cells (iPSCs) to model neurological diseases including Spinal Muscular Atrophy, Parkinson's Disease and ALS. His lab also combines iPSCs and organ-chip technologies for enhanced multicellular models. The other focus of Dr. Svendsen's lab involves cutting-edge clinical trials that use combinations of neural progenitor cells along with growth factors. He is the Sponsor for a current Phase 1/2a clinical trial delivering neural progenitor cells to the subretinal space as a treatment for Retinitis Pigmentosa. Additionally, he was the Sponsor for the first-ever clinical trial delivering neural progenitors engineered to release GDNF to the spinal cord of ALS patients, which met the trial endpoint of safety. He is also the Sponsor for an ongoing trial delivering these same cells to the motor cortex of ALS patients.

Menú

Please be mindful of those who are dietary restrictions & allergies. Thank you!

All food will be served in the boardroom, directly behind the Conference Center.

BREAKFAST

Coffee, Tea, & Water (Iced & Hot)
Mini Muffins, Danish, & Scones Served with Butter & Jam - V
Assorted Bagels (VG) with Butter, Cream Cheese (V), & Jam
Seasonal Fresh Fruit Platter
Nature's Bakery Bars - VG, GF, Nut Free

Additional Coffee, Tea, & Water will be available throughout the morning

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BUFFET LUNCH - ASIAN ACCENTS

Sweet Soy Sause - V
Sweet & sour Source - VG
White Rice - VG
Peanut Lime Ramen Noodle Salad - VG
Teriyaki Salmon with Lemon Green Beans

General Tso's Chicken
Vegtable Egg Rolls - V
General Tso's Tofu
Fortune Cookie

Lemonade
Water

All baked goods are made in a facility the uses nuts | Items will be labeled
V - Vegetarian | VG - Vegan | GF - *Gluten Friendly* | DF - Dairy Free

Menú

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AFTERNOON BREAK

Chips, Trail Mix, Assorted Mini Cookies & Brownies

ROAMING DINNER - ASIAN INSPIRED

- Thai Mango Salad - Mango, Bell Pepper, Scallions, Moxed Greens, Sweet Coconut, Yuzu Vinaigrette - VG & GF
- Sesame Salad - Mandarin Oranges, Napa Cabbage, Shredded Carrot, Cucumber, Crispy noodles, Sesame-hoisin dressing - V & DF
- Coconut Curry Chicken Skewer - DF & GF
- Sweet Tahi Chili Vegetable Skewers - VG
- Vegtable Fried Rice - V & FG
- Noodle Vegtable Stir Fry - V
- Edamame Dumpling - VG
- Ahi Tuna Poke Cucumber - DF & Gluten Free

Lemonade & Cucumber-Infused Iced Water

BAR

Ballast Point IPA	Point Noir	Champagne
Corona Extra	Chardonnay	Allagash White Ale

All baked goods are made in a facility the uses nuts | Items will be labeled

V - Vegetarian | VG - Vegan | GF - *Gluten Friendly* | DF - Dairy Free

Poster Presenters

1. **Abiageal Keegan** - *"Microdystrophins Partially Rescue Deficits in Duchenne Muscular Dystrophy iPSC-Cardiomyocytes." (not presenting)*
2. **Vaidehi Gandhi** - *"Autocrine C1q as a regulator of microglial state."*
3. **Bella Fleming** - *"Elucidating dysfunction in hippocampal development in Fragile X Syndrome using patient-derived brain organoids and multiome-sequencing.*
4. **Elaine Lai -** "*Investigating the effects of AAV transduction in Duchenne Muscular Dystrophy iPSC-cardiomyocytes."*
5. **Rosty Brichko** - *"Dendrites of Older Adult Neurons Take Longer to Regenerate"*
6. **Nicolette McClure** - *"Huntingtin Protein Interactors: Cell-Type Specific Interactors"*
7. **Zachary Pope** - *"Unmasking DNMT3A: More Than a Methyltransferase"*
8. **Daniel Ortiz** - *"Transient mRNA delivery of full-length dystrophin in iPSC-derived cardiomyocytes for Duchenne muscular dystrophy."*
9. **Wei Song** - *"Circadian Control of Intestinal Wnt Signaling Governs Stem Cell Function and Differentiation"*
10. **Casey Hudson** - *"Human neural stem cell-derived extracellular vesicles ameliorate breast cancer chemobrain."*
11. **Madhy Garcia Garcia** - *"Extracellular Vesicle–Mediated Modulation of Microglia via the NF-κB Pathway: Mechanistic Insights into Neuroinflammatory Regulation."*
12. **Vi Dang** - *"Transcriptomic analysis of glycosylation genes in chemotherapeutic-resistant glioma cells."*
13. **Tzu Chia (Nini) Liu & Marwah Ghouli** - *"Identifying vessel promoting microRNA from human neural stem and progenitor cells."*
14. **Chanel De Smet & Michelle Baez** - *"Glucocorticoid conditioning increases human regulatory T cell frequency in virto"*
15. **Zeina Elrachid** - *"C1q drives neural stem cell quiescence by regulating cell cycle and metabolism through BAI1"*
16. **Natalie Celt** - *"Spatially Heterogeneous Bioprinted Model of the Myocardial Infarction Border Zone for Assessing Patient-Specific Disease Trajectories and Therapeutic Outcomes"*
17. **Harrison Jeong** - *"Light-Processed Hydrogels for Delivering Spatial Patterning Cues to Tissue Engineered Systems"*
18. **Marie Wheeler** - *"Using Stem Cells to Identify Convergent DNA Methylation Abnormalities in Human Growth Disorders"*
19. **Veiva Piner** - *"Fas Ligand-Conjugated-Microparticles as a Tool to Induce Long-Term Immune Tolerance for Allogeneic Neural Stem Cell Transplantations in Chronic Cervical Spinal Cord Injury"*
20. **Cameron Fraser** - *"Influence of Initial Tumor Cell Dose on Growth Dynamics and Cellular Architecture of Glioblastoma Xenografts in NSG Mice"*

Poster Presenters

21. **Nolan Origer -** *"Investigating the Impact of Adhesome Modulation on Induced Pluripotent Stem Cell Genome Stability."*
22. **Daniella Lu** - *"Modeling ASXL1-Driven Clonal Hematopoiesis in Human Stem Cells."*
23. **Sarah Soobin Lee** - *"Therapeutic Induction of Regulatory T Cells through DRAK2 Inhibition and Neural Stem Cell Stimulation for Multiple Sclerosis Treatment."*
24. **Satya Karri** - *"The Effects of Feeding and Fasting on Epidermal Stem Cells."*
25. **Onwodi Ifejeokwu & Manuel Robledo** - *"Mapping Mitochondrial Dysregulation in Glial-Networks of Alzheimer's Disease Brains."*
26. **Olga Jaime** - *"Capturing the Myogenic Waves of hPSC Development with Moscot."*
27. **Kevin Sanchez** - *"Redirecting ATXN3 Alternative Polyadenylation to Rescue Stress Induced TDP-43 pathology in TDP-43M337V iPSC-MNs"*
28. **Dina El Tahlawy** - *"From Risk to Remedy: Rescuing APOE4-Mediated Deficits in iPSC-Based Therapeutics for Alzheimer's Disease."*
29. **Nolan Huck** - *"Modeling Spinocerebellar Ataxia Type 7 Cone-Rod Dystrophy in Human Retinal Organoids."*
30. **Magdalene Seiler, Ph.D.** - *"Generation of a new rat model of retinal degeneration with TdTomato-Pcp2 expression."*
31. **Hajime Ozaki** - *"Hydrogel-Engineered Morphogen Gradients Spatially Induce Posterior Organizers in Human Cerebral Organoids."*
32. **Jean Paul Chadarevian** - *"iPSC-Microglia (iMG) replacement for the treatment of GRN-related frontotemporal dementia."*
33. **Pallabi Pal** - *"MicroRNAs targeting Valosin-containing protein improve molecular defects in cell model of multisystem proteinopathy"*
34. **Alexii Villamar** - *"Inclusion of IL-15 Cytokine Improves CD8+ T cell Viability in Ex Vivo Graft Conditioning Protocol."*
35. **Wilber Santiago Perez** - *"Treg-Mediated Suppression of Neuroinflammation Restores Cognitive Function Following Cranial Radiation Therapy."*
36. **Iceis Hurtado** - *"Maximizing exosome secretion rate at the single cell level in human neural stem cells."*

Poster Presenters - Abstracts

Abiageal Keegan - #1

Duchenne Muscular Dystrophy (DMD) is a severe, muscle-wasting genetic disorder that ultimately leads to heart failure. DMD is caused by the lack of dystrophin expression, a myocyte stabilizing protein. The disease is difficult to target by current gene therapy methods as the dystrophin transcript spans 14 kb, far exceeding the 4.7 kb packaging limit of AAV. Another major challenge is that dystrophic animal models do not recapitulate the cardiomyopathy observed in patients. To circumvent this challenge, we use cardiomyocytes (CMs) differentiated from human induced pluripotent stem cells (iPSCs) to model the disease. DMD iPSC-CMs exhibit functional deficits characteristic of dystrophic cells. This platform enables investigation of the therapeutic efficacy of various gene therapy strategies in multiple genetic backgrounds. Synthetic variants of dystrophin, called microdystrophins, have advanced to clinical trial. Microdystrophins contain key domains of dystrophin and have been successful in rescuing disease characteristics of the skeletal muscle. Because it takes several years for cardiac complications to develop, the duration since gene therapy administration in patients has not been long enough to assess clinical benefit. To determine the efficacy of microdystrophin gene therapy, we compared three microdystrophin variants in DMD iPSC-CMs. We also tested a dystrophin variant, minidystrophin, which is larger than the microdystrophins in clinical trials. We found that microdystrophins partially rescue disease phenotypes; however, the results are variable among genetic backgrounds. We conducted bulk RNA-sequencing and found that none of the gene therapies altered the global transcriptional profiles of the DMD iPSC-CMs to resemble a healthy profile. We show that minidystrophin better rescues DMD phenotypes, including improved calcium handling and viability. These findings suggest microdystrophins may have limited efficacy in DMD cardiomyocytes and that delivering larger dystrophin variants may be a better strategy to improve DMD patient outcomes.

Vaidehi Gandhi - #2

Microglia are the resident immune cells of the central nervous system (CNS) that adopt heterogeneous states to maintain homeostasis.1 However, in CNS injury, they adopt a sustained, proinflammatory state that inhibits regeneration.1 Understanding mechanisms that drive maladaptive activation is critical to developing neuroprotective therapies. C1q is a key activator of proinflammatory microglia1,2that drives transcriptional and functional changes.2 While traditionally secreted, C1q also acts intracellularly in neurons3 and T cells.4 Similarly, transforming growth factor-ß siignals intracellularly in an autocrine manner to epigenetically5 promote quiescence.6 Our lab found the first evidence of endogenous (autocrine) C1q in the nucleus of non-apoptotic cells and upregulation of chromatin-remodeling transcripts following exogenous (paracrine) C1q exposure in iPSC-derived microglia (iMicroglia),In prep suggesting a parallel intracellular role for C1q.. Neutralizing C1q significantly reduces iMicroglial inflammatory gene expression upon LPS exposure,In prep suggesting that C1q is necessary to respond to inflammatory stimuli. Microglia are the primary producers of C1q in the CNS and upregulate C1q expression in response to stimuli, including paracrine C1q;1this suggests that microglial C1q may regulate activation state through an autocrine mechanism.7 However, current C1q-neutralization approaches cannot distinguish between paracrine and autocrine effects, nor do they test intracellular/nuclear signaling. To address this gap, I generated C1q KO iPSC lines using CRISPR RNP technology and differentiated them into iMicroglia. Here, I present a novel finding that autocrine C1q directly modulates microglial behavior, transforming our understanding of neuroinflammation.

Poster Presenters - Abstracts

Bella Fleming - #3

Fragile X syndrome (FXS) is the leading inherited monogenetic cause of autism spectrum disorders (ASD) through the silencing of the Fragile X Messenger Ribonucleoprotein 1 (FMR1) and loss of functional FMR1 protein (FMRP). To understand the molecular and cellular mechanisms of FXS, we performed multiome snRNA-sequencing and ATAC-sequencing on the cerebral cortices of embryonic FMR1-KO mice and their wild-type (WT) littermates. Our preliminary data demonstrated that the cortical hem (CH), the transient organizer for the hippocampus, was unexpectedly most affected. The CH had many differentially expressed genes and displayed an upregulation in c-Myc and Wnt signaling pathways, critical for cell proliferation and cortical posteriorization. We hypothesized that changes in the CH in FXS lead to developmental defects in the hippocampus, at both the molecular and cellular levels, contributing to FXS pathologies. The hippocampus is known to play an important role in learning, memory, and cognition which are all altered in FXS. We established FXS patient-derived induced pluripotent stem cells (iPSCs) to create CH and hippocampal-enriched organoids. Using our human-tissue based platform, by immunochemical, RT-qPCR, and Western blot analyses, we confirmed the upregulation of c-Myc and Wnt signaling players, including CDK4, FZD8, and HDAC2, revealed by the murine multiome-sequencing. We will further investigate hippocampal development by characterizing distinct cellular compositions. Together, understanding the early cellular and molecular pathways that underlie the defects in FXS pathologies is essential for accurately targeting the disease pathology and determining the optimal timing for interventions in future therapeutic applications.

Elaine Lai - #4

Duchenne muscular dystrophy (DMD) is an X-linked muscle wasting disease that affects every 1 in 5,000 males. Symptoms include loss of ambulation, respiratory problems, and cardiac complications with heart failure being the leading cause of death for DMD patients. Dystrophin is a 427 kDa protein encoded by a coding sequence that spans 11 kb. Dystrophin connects the actin cytoskeleton of muscle cells to the extracellular matrix and protects cells from contraction-induced injury. DMD is caused the lack of dystrophin expression. Thus, restoration of dystrophin expression holds promise in delaying the onset of heart failure. Gene therapy using adeno-associated virus (AAV) is the most efficient method to deliver genes systemically to the skeletal muscles, diaphragm, and the heart. A major limitation of AAV gene therapy is that the packaging limit is 4.7 kb. Even though AAV demonstrates high tropism in preclinical models, high doses of AAV is required in patients for adequate expression. High dosing can lead to serious adverse events due to activation of the immune response. Cell-intrinsic responses to AAV treatment could lead to tissue inflammation, cell death, or limit transduction efficiency. In this study, I use cardiomyocytes differentiated from human induced pluripotent stem cells (iPSC-CMs) to study DMD in the molecular context of human cells. We observe hallmarks of disease, including poor calcium handling and lower force of contraction, in DMD iPSC-CMs. To investigate the pro-inflammatory signals after AAV treatment, I transduced iPSC-CMs with a gene encoding GFP under the control of a muscle specific promoter in an AAV6 capsid. I performed bulk-RNA sequencing to capture the progression of the innate immune response. By investigating cell autonomous responses to AAV, we can identify potential targets to mitigate adverse effects associated with AAV gene therapy.

Poster Presenters - Abstracts

Rosty Brichko - #5

Neuronal dendrites undergo age-related structural changes that may contribute to circuit and synaptic dysfunction before neurons die. While dendrites can regenerate after injury in aging animals, regeneration has been thought to become increasingly limited with older age. However, prior studies tracked adult regeneration for a limited time period. This study assesses whether older adults are delayed in initiating regeneration and the extent to which they regenerate when given more time. Here, we show that older adult Drosophila melanogaster begin regeneration at a similar time as younger adults and continue to regenerate their dendrites for weeks after injury. While regeneration in older animals is more significant than previously appreciated, injured wild-type adults do not fully recover total dendrite length and area coverage compared to controls, regardless of age at injury. Manipulating insulin signaling in middle-aged adults boosts dendrite regeneration. Together these findings demonstrate an increased ability of neurons to regenerate after injury in older adult animals more than was previously shown, and a potential avenue to investigate how insulin metabolism can enhance regeneration in older adults.

Nicolette McClure - #6

Huntington's disease (HD) is a devastating genetic neurodegenerative disorder characterized by progressive cognitive, psychiatric, and motor impairments. It is caused by an abnormal CAG repeat expansion (≥40) in the huntingtin (HTT) gene, resulting in a mutant protein (mHTT) with an expanded polyglutamine tract. Developing an effective treatment for HD requires a comprehensive understanding of HTT's normal functions and how they are disrupted by mutation. Although HTT is ubiquitously expressed, selective degeneration of medium spiny neurons (MSNs) in the striatum and cortical atrophy are hallmarks of HD, while other regions such as the cerebellum remain relatively unaffected. Emerging evidence also implicates non-neuronal cells—astrocytes and microglia—in disease progression, as transcriptional and morphological abnormalities in these cell types have been observed. HD pathology extends beyond the brain, affecting peripheral tissues including the heart and gut. These findings suggest that HTT may have cell-type-specific functions that underlie the selective vulnerability seen in HD. HTT is essential in numerous biological pathways and is thought to act as a protein scaffold mediating multiple cellular processes. However, its precise molecular functions remain incompletely understood. Its role as a scaffold is facilitated by extensive protein–protein interactions, many of which may be altered by the mutant form of the protein. Previous studies, along with recent data from our lab, identify RNA-binding proteins (RBPs) as prominent HTT interactors. RBPs play key roles in gene expression regulation through control of RNA splicing—a process that enables one gene to produce multiple mRNA and protein isoforms. Notably, transcriptional dysregulation and splicing abnormalities, including the appearance of cryptic exons, have been reported in HD, suggesting that mHTT may perturb RNA processing through altered RBP interactions. We hypothesize that subsets of HTT-interacting partners, and consequently HTT functions, are cell-type specific, leading to selective vulnerability in HD. To test this, we are using transcriptomic and proteomic approaches to identify HTT/mHTT interactors and RNA changes across diverse cell types, both neural and peripheral—including MSNs, cortical neurons, astrocytes, microglia, cardiomyocytes, and intestinal epithelial cells. To enable this, we generated a novel set of isogenic induced pluripotent stem cell (iPSC) lines (18Q/50Q) with an in-frame fusion of biotin ligase (TurboID) to HTT or mHTT, allowing proximity labeling of their protein interactors. These lines, produced by the SCRC iPSC Core, have been successfully differentiated into all target cell types. Mass spectrometry analyses have been completed for MSNs, cortical neurons, astrocytes, and microglia. In MSNs, proteins enriched in TurboID-18Q suggest roles in cytoskeletal dynamics and vesicular trafficking, while those enriched in TurboID-50Q implicate translational control and signaling pathways. Early cortical neuron data reveal enrichment of RNA-binding and ribosomal proteins for both normal and mutant HTT. RNA sequencing for MSNs and cortical neurons is ongoing, alongside proteomic analysis of astrocytes and microglia. This work will elucidate cell-type-specific HTT functions within the brain and peripheral tissues, offering new insight into why certain cells are more vulnerable to mutation. Ultimately, it may reveal therapeutic targets for treating HD as a multisystem disorder.

Poster Presenters - Abstracts

Zachary Pope - #7

DNMT3A, a de novo DNA methyltransferase, plays a central role in gene regulaEon. SomaEc DNMT3A mutaEons are frequent in Clonal Hematopoiesis of Indeterminate PotenEal (CHIP) and Acute Myeloid Leukemia (AML), and have also been linked to elevated cardiovascular disease risk. Germline DNMT3A mutaEons are the primary cause of TaPon-Brown–Rahman syndrome, a developmental disorder characterized by generalized overgrowth, macrocephaly, and intellectual disability. While DNMT3A's enzymaEc role in DNA methylaEon is well characterized, studies in mice suggest addiEonal non-canonical funcEons — including RNA splicing and telomere regulaEon — that may contribute to disease independently of methylaEon. These roles remain poorly understood in human systems, and tradiEonal knockout models cannot separate enzymaEc from non-enzymaEc effects. To address this, we developed a human embryonic stem cell model with an inducible FKBP12F36V degradaEon tag (dTAG) at the endogenous DNMT3A locus, allowing temporal control of DNMT3A protein levels. Combined with catalyEcally inacEve mutants, this system enables direct invesEgaEon of DNMT3A's gene regulatory funcEons independent of DNA methylaEon acEvity. By dissecEng these mechanisms, our work aims to clarify how DNMT3A contributes to normal development and disease, including CHIP and AML.

Daniel Ortiz - #8

Duchenne muscular dystrophy (DMD) is a rare X-linked neuromuscular disorder characterized by progressive muscle weakness, which leads to severe skeletal muscle degeneration and heart failure in young men. This progression is caused by a mutation in the dystrophin gene, which results in the lack of dystrophin in muscle fibers, impairing their ability to contract properly. Therapeutic strategies currently face limitations due to the large size of the full-length coding sequence of dystrophin (11 kb). Viral vectors, like adeno-associated virus (AAV), can only package truncated versions of dystrophin that encode one-third of the full-length protein. While these truncated versions may compensate for a complete absence of dystrophin, their effects on the heart have not been well established as mouse models do not exhibit cardiac problems until a geriatric age. To overcome these limitations, we investigated the therapeutic efficacy of delivering mRNA encoding full-length dystrophin in cardiomyocytes (CMs) differentiated from human induced pluripotent stem cells (iPSCs) with dystrophin mutations. Importantly, DMD iPSC-CMs exhibit hallmarks for disease including arrhythmia, poor force of contraction, and poor viability. This strategy will provide insight into whether delivery of transient mRNA is sufficient to address cardiac complications without inducing an immunogenic response, which is a safety concern with AAV vectors.

Poster Presenters - Abstracts

Wei Song - #9

The circadian clock, the body's biological pacemaker, coordinates essential physiological processes over the 24-hour day. Disruption of circadian rhythms, through environmental factors such as night shift work, has become increasingly prevalent in modern day society and has been named a probable carcinogen by the International Agency for Research in Cancer. We have found that circadian disruption accelerates colorectal cancer (CRC) progression by perturbation of Wnt signaling. Regulation of Wnt signaling is crucial to maintain the intestinal stem cell (ISC) niche and secretion of Wnt ligands is clock controlled. However, the mechanism of how the circadian clock regulates stemness in the normal intestinal epithelium and how this process impinges on Wnt signaling remains unclear. To better understand stemness rhythms in the intestine, we utilize an ex vivo intestinal organoid system that recapitulates the small intestinal niche. We found that intestinal stemness exhibits a 24-hour rhythm using an organoid formation assay as a functional stemness readout. To understand the effects of clock disruption on intestinal stemness, we disrupted the circadian clock environmentally using two models: a shift disrupted (SD) paradigm where light cues are manipulated which models night shift work, and an inverted feeding paradigm where feeding rhythms is perturbed. Upon environmental circadian rhythm disruption, intestinal stemness rhythms are disrupted and stemness output is suppressed. Additionally, using an intestine specific genetic deletion of core clock gene Bmal1, we found that genetic clock disruption phenocopies environmental disruption paradigms. Concurrently, Wnt target expression and Wnt -/- small intestinal monolayers and organoids are suppressed. ligand secretion in Bmal1 Deletion of Bmal1 specifically in ISCs dampens stem cell proportions. Taken together, our findings suggest that the circadian clock regulates Wnt signaling, a key intestinal stem cell niche factor, and disruption of the clock is detrimental to intestinal stem cell renewal and differentiation potential.

Casey Hudson - #10

About 75% of 3.8 million breast cancer survivors in the U.S. are suffering from chemobrain or cancer-related cognitive impairments (CRCI) that significantly impact survivors' quality of life. Chemobrain is characterized by memory loss, impaired recall, executive function deficits, and decreased processing speed and attention. We previously tested the efficacy of human neural stem cell-derived extracellular vesicles (hNSC-EVs) to alleviate radiation therapy-induced CRCI. In this study, we aimed to test the neuroprotective capabilities of hNSC-EVs in a syngeneic, immunocompetent female mouse breast cancer chemobrain model and demonstrated its mechanism of action. We performed behavioral testing and fluorescent IHC analyses to evaluate the impact of chemotherapy and the benefit of a systemic EV treatment on cognitive function, neuroinflammation, neuronal activity, and synaptic integrity. Breast cancer-bearing mice exposed to adjuvant chemotherapy (Adriamycin and cyclophosphamide) showed impaired learning and memory, memory consolidation, and executive function compared to chemotherapy-treated mice that received the EVs. IHC showed a significant increase in microglial activation, and significant decreases in synaptic density and neuronal plasticity-related IEG in breast cancer-bearing mice receiving chemotherapy. Conversely, EV-treated mice brains showed improvements in synaptic integrity and neuron function, and reductions in gliosis. MicroRNA sequencing identified three major miRNA candidates, Let-7, miR-9, and miR-21, with potential target pathways in chemobrain. We plan to elucidate the mechanism of action of functional EV cargo (miRNA)-mediated neurocognitive recovery through intra-cranial AAV-PHP.eB vector expressing miRNA. These results present a regenerative strategy to ameliorate chemobrain that could improve the QOL of millions of cancer survivors.

Poster Presenters - Abstracts

Madhy Garcia Garcia - #11

As the most prevalent form of dementia and a leading cause of death among the elderly, there is an urgent need not only to develop a treatment for AD but also to focus on preventing this devastating disease. To this end, my primary research involves exploring ways to reduce the inflammatory response of microglial cells using stem cell-derived models. Microglia, which constitute 10% of the cells within the central nervous system, serve as the brain's immune system. In post-mortem tissue, these cells are found surrounding amyloid plaques, underscoring their significant role in AD pathology. It is believed that, in the early stages of AD, microglia mount an immune response to amyloid-beta (Aβ). However, as the disease progresses, their ability to clear Aβ diminishes significantly, and their phagocytic capabilities eventually cease during the disease's final stages. In their ramified state, microglia induce an inflammatory response by secreting pro-inflammatory cytokines, transitioning from a resting-like state to a neurotoxic state. However, a sustained ineffective response to external stimuli can lead microglia to overproduce an inflammatory response, thereby contributing to the neurodegeneration process. Neurons and microglia continuously communicate to achieve a wide range of functions, particularly through bidirectional communication via extracellular vesicles (EVs). Within the AD context, researchers have detected pathogenic proteins tau and Aβ inside EV cargo, leading to speculation that this could be an additional mechanism for the disease's spread throughout the brain. Through my research, I am investigating how EVs derived from healthy neurons can be used to prevent the robust inflammatory response observed in AD patients by targeting microglial cells and maintaining them at homeostasis-like signatures.

Vi Dang - #12

Glioblastoma, astrocytoma, and oligodendroglioma comprise a class of aggressive and deadly brain tumors called diffuse gliomas. Around 20,000 glioma cases are diagnosed yearly in the US alone. The current standard chemotherapy treatment, temozolomide (TMZ), is insufficient as the 5-year survival rate of glioblastoma patients is as low as 8%. This is due to the presence of TMZ-resistant cells within tumors that lead to chemoresistance and tumor recurrence. Thus, it is critical to characterize the molecular profile of TMZ-resistant cells to determine means of targeting them for more effective treatment. Preliminary data from our lab show that glycosylation could be an important dynamic regulator of TMZ resistance. Glycosylation, the post-translational addition of glycans (sugars) to proteins and lipids, regulates the function of many membrane proteins including drug transporters, growth factor receptors, and adhesion proteins. Our lab has developed an innovative dielectrophoretic-based method to sort cells based on electrophysiological membrane properties that are influenced by glycosylation. We used this method to successfully enrich TMZ-resistant populations from various glioma types and patient-derived tumors for downstream transcriptomic characterization using glycosylation gene microarrays, qRT-PCR, and single-cell RNA sequencing. My data show that TMZ-resistant glioma cells exhibit transcriptomic differences in glycosylation genes, suggesting that these cell-surface sugars may serve as novel biomarkers or targets for glioma treatment. Future studies will examine how these unique glycosylation properties of resistant glioma cells can be manipulated to improve response to chemotherapy treatment and thus glioma patient outcomes.

Poster Presenters - Abstracts

Tzu Chia (Nini) Liu & Marwah Ghouli - #13

Human neural stem and progenitor cells (hNSPCs) and human endothelial cells (hECs) interact during early central nervous system development, wherein hECs undergo vasculogenesis, angiogenesis, and lumen formation—processes essential for establishing a functional vascular network that supplies oxygen and nutrients to the developing brain. In adulthood, hNSPCs may also contribute to vascular repair following brain injury, such as stroke or traumatic brain injury (TBI). Our laboratory found that hNSPC-secreted factors, particularly extracellular vesicles (EVs), stimulate vasculogenesis and lumen formation within a 3D neurovascular scaffold that recapitulates the brain's mechanical properties. Given their low immunogenicity, ability to cross the blood–brain barrier, and amenability to molecular engineering, hNSPC derived EVs represent promising therapeutic agents to drive vascular regeneration after stroke or TBI by delivering regulatory cargo to endothelial cells. We therefore hypothesize that hNSPC-derived EVs contain molecular cargo that promotes vasculogenesis and lumen formation, and we focus on microRNAs (miRs) because they make up 50% of the noncoding RNA cargo within EVs and have been found to be critical in angiogenesis in normal development and post-injury repair. To identify candidate miRs, we compared the vasculogenic potential of two primary brain-derived hNSPC lines, two neuralized induced pluripotent stem cell (iPSC)- derived hNSPC lines, and three umbilical cord-derived endothelial colony-forming cell hEC lines. Functional assays in our 3D neurovascular scaffold show that hNSPC derived EVs enhance vasculogenesis relative to hEC-derived EVs. EV size and concentration were measured with nanoparticle tracking analysis and EV identity was validated through Western blot for EV markers Alix, CD81, CD9, and Calnexin. Uptake of hNSPC-derived EVs into hECs was validated by visualization of fluorescently labeled hNSPC-derived EVs within hECs using high-resolution microscopy. To identify vessel promoting miRs, we extracted RNA from hNSPC- and hEC-derived EVs and used differential expression analysis to determine miRs enriched in hNSPC-derived EVs—the EV population that demonstrated greater vasculogenic activity—followed by interrogation of miR–target interaction databases and literature review to prioritize candidates associated with vascular function. We identified candidate vessel promoting miRs that are more highly expressed in hNSPC-derived EVs relative to hEC-derived EVs. Future studies will evaluate the effects of the top candidates on vasculogenesis by treating hECs in our neurovascular assays with EVs loaded either with miR mimics or inhibitors. By identifying key vessel promoting miRs in hNSPC-derived EVs, we aim to elucidate their role in endogenous vessel formation, which could advance our understanding of hNSPC-hEC interactions and enable the precise engineering of EV/exosome therapies for vascular repair after injury.

Chanel De Smet & Michelle Baez- #14

Hematopoietic Cell Transplantation (HCT) is a therapy applied to treat various blood cancers. An advantage of allogeneic-HCT is the anti-tumor response known as graft versus tumor, which is carried out by alloreactive CD8+ cytotoxic T cells. A major complication of allogeneic HCT is graft-versus-host disease (GVHD) wherein donor immune cells attack host tissues leading to serious complications. To treat GVHD after its onset, patients are given glucocorticoids (GCs) to dampen the immune response. Still, GC treatment is often not enough to prevent patients from succumbing to GVHD, so the development of GVHD prevention strategies are critical to make HCT a safer cancer therapy. CD4+ FoxP3- conventional T cells (Tcons) are at the forefront of GVHD development. Allogeneic Tcons produce waves of inflammatory cytokines resulting in tissue damage. Regulatory T cells (Tregs) work to suppress the immune response by inhibiting Tcon proliferation and are important for graft tolerance. We published an ex vivo graft conditioning protocol using a GC named fluticasone propionate (FLU), that resulted in an increased overall survival and reduced GvHD severity in a mouse allograft. We demonstrated that was due to the increased ratio of Tregs to Tcons after the conditioning process which is sustained in vivo for at least 10 days post transplant. In order to increase the clinical relevancy of this protocol, we cultured human peripheral blood mononuclear cells (hPBMCs) with a cocktail of glucocorticoids and cytokines. Our results indicate that GCs in combination with Bcl-2 inhibitors and cytokines yields significant reductions in Tcon viability and increased frequencies of Tregs in vitro. This is an important first step in translating our mouse findings to human cells and ultimately testing in a xenograft model.

Poster Presenters - Abstracts

Zeina Elrachid- #15

C1q levels in the CNS are elevated by inflammation and neurovascular trauma, yet the consequences of C1q on the neural stem cell (NSC) regeneration response remain poorly understood. We report the novel finding that C1q can drive NSC quiescence, a reversible state of cell cycle arrest that is primarily characterized by decreased proliferation and metabolic function, and investigate the mechanisms by which C1q mediates this effect. We have recently identified novel C1q receptor candidates that enable direct receptor-mediated regulation of NSC behavior. One of these is Brain Angiogenesis Inhibitor 1 (BAI1), which has no previously discovered role in NSC. Here, we establish a direct BAI1-dependent role for C1q in NSC quiescence.

To investigate the role of C1q in NSC function, we exposed NSC to purified human C1q at physiological concentrations ranging from 0.1nM to 300nM, then assessed NSC proliferation and metabolism as outputs of quiescence. To measure proliferation, we performed BrdU and Edu incorporation assays on C1q-treated NSC. We then assessed the effects of C1q on metabolic function by measuring the NADH/NAD+redox ratios and mitochondrial morphologies of C1q-treated NSC. To determine the role of BAI1 in the effect of C1q on NSC, we generated a BAI1 knockout (KO) NSC line using CRISPR/Cas9. We then tested the effects of BAI1 KO on proliferation, metabolism, and C1q binding to intracellular p32/gC1qR, a mitochondrial protein. To further investigate C1q interactions with BAI1 and p32, we utilized a pull-down assay to validate C1q interactions with BAI1 and p32 individually and in complex.

These data show that C1q exposure decreases NSC proliferation and induces a metabolic shift from oxidative phosphorylation to aerobic glycolysis (Warburg effect). BAI1 KO reverses these effects of C1q, identifying BAI1 as a critical mediator of C1q-driven NSC quiescence. With this, we show that BAI1 mediates C1q internalization, promotes an increase in intracellular C1q-p32 interactions, and decreases functionally available p32 as one mechanism of action. Decreased availability of p32 within the cell results in altered proliferation and metabolism, highlighting a novel mechanism by which BAI1 mediates C1q-driven NSC quiescence.

Natalie Celt- #16

Acute myocardial infarction (MI) often results in irreversible structural and functional damage to cardiac tissue. While pharmaceutical interventions can mitigate some of the pathological remodeling that follows MI, they fall short in regenerating healthy myocardium. Induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) offer a promising therapeutic alternative by potentially halting or reversing post-MI remodeling. However, their clinical application remains limited due to patient-specific safety concerns and variability in therapeutic outcomes. Notably, the post-MI heart develops spatial heterogeneity across three distinct zones, each with differing mechanical properties, which can significantly affect iPSC-CM engraftment and function.

This work presents the fabrication of a biomimetic model of post-MI cardiac tissue that replicates the variability of tissue anisotropy and stiffness across patients. This model aims to serve as a pre-screening platform for evaluating iPSC-CM therapeutic efficacy under conditions that reflect the mechanical complexity of infarcted myocardium. In parallel, we introduce a polymeric force sensor capable of detecting spatial heterogeneity in cardiomyocyte force generation in situ. Unlike current methods—such as traction force microscopy, which requires extensive processing, or bulk-assessing techniques like muscular thin films and micropillars—this sensor enables more dynamic and localized measurement of contractile performance.

Current results validate the successful replication of region-specific stiffness representative of the three characteristic zones observed during myocardial infarction (MI) remodeling, namely, the remote, border, and infarct zones. iPSC-derived cardiomyocytes (iPSC-CMs) seeded onto these regions exhibit distinct morphological and behavioral responses consistent with their mechanical environments, ranging from cardiac maturation markers and contractile function.

Together, this work establishes a novel platform for modeling myocardial infarction and offers a more precise method to assess the functional integration of stem cell therapies in mechanically heterogeneous cardiac tissue.

Poster Presenters - Abstracts

Harrison Jeong- #17

Gradients of soluble biochemical factors are ubiquitously observed under natural physiological conditions, mainly due to the critical roles they play in biological processes like tissue morphogenesis. However, tissue engineering technologies that rely on the delivery of growth factors to in vitro models are often limited to their addition to media for 2-D cell culture. It is also challenging to establish gradients in a way that truly recapitulates a 3-D spatial presentation of morphogens. In collaboration with the Watanabe Lab at UCI, we seek to mimic morphogen gradients secreted by neural signaling centers, such as the anterior neural ridge and roof plate of the telencephalon, in order to generate cortical organoids as in vitro models with high fidelity cell diversity and topographic organization (or 'arealization') as the in vivo conditions. Herein, we present a biomaterial-focused approach where the gradients within hydrogels generated from digital light processing (DLP) enable a controlled diffusion of morphogens to produce different cortical areas in organoids. We hypothesize that network density/stiffness gradients across the morphogen reservoir to the organoid site, as established by the light projection patterns used to cure photocrosslinkable polymers during 3-D printing, will allow for directed morphogen diffusion gradients sufficient for inducing organoid arealization in vitro. The stiffness gradients within the DLP-printed hydrogels are enabled by the ability to vary light intensity via a directly specified parameter (z-axis) or grayscale photomasks (xy-plane). A high-throughput and -precision DLP-based, 3-D printing approach will be used to produce micro architectured hydrogels with spatially defined distribution of antagonistic morphogens for cortical organoids. Here, we showcase the material selection process and the design iterations that we tested to reach our final model.

We believe that our platform could revolutionize the state-of-the-art for engineering other in vitro tissue models, such as for vascularized cardiac models or cutaneous wounds, that require proper biochemical gradients. We aim to push the project further by studying an antagonistic 2-morphogen system that is increasingly more representative and can induce arealization of different regions of the brain organoid.

Marie Elizabeth Strauss Wheeler- #18

Loss-of-function mutations in DNMT3A, a DNA methyltransferase, or NSD1, a histone methyltransferase, cause overgrowth syndromes. Conversely, disruption of the DNMT3A domain that binds NSD1-deposited H3K36 dimethylation (H3K36me2) results in growth restriction. To investigate the molecular basis of these opposing growth outcomes, we generated isogenic human embryonic stem cells carrying growth syndrome–associated mutations in DNMT3A and NSD1. Unexpectedly, both overgrowth- and growth restriction–associated DNMT3A mutations led to DNA hypomethylation in a shared subset of active enhancers, implicating H3K36me2 in directing enhancer methylation maintenance. In contrast, bivalent promoters—marked by both active and repressive histone modifications—showed divergent DNA methylation changes: hypermethylation in growth restriction-associated DNMT3A mutants and hypomethylation in overgrowth-associated DNMT3A or NSD1 loss-of-function mutants. These findings identify locus-specific DNA methylation defects as a common molecular feature and nominate dysregulated DNA methylation at bivalent promoters as a potential driver of abnormal growth phen

Poster Presenters - Abstracts

Veiva Piner- #19

Human fetal neural stem cell (hNSC) transplantation has demonstrated success in improving recovery in immunodeficient models of chronic cervical spinal cord injury (ccSCI) in humans (Levi et al., 2019). However, clinical translation of hNSC transplantation has yet to address immune-rejection concerns associated with allogeneic hNSC grafts. Thus, this study employs a combined hNSC plus Fas-ligand-conjugated microparticle (FasL-MP) injection to the injury site to promote localized immune tolerance. FasL is intended to induce apoptosis in activated immune cells known as T-cells at the injury site. The MP delivery system ensures that the Fas-ligand is immobile, thus promoting localized immune tolerance without suppressing systemic immunity or compromising hNSC viability or function.

To study the safety and efficacy of the FAsL-MP treatment, hNSCs were co-cultured in-vitro with FasL-MPs to assess the effects on 1) differentiation lineage fate 2) cell death 3) cell proliferation 4) CD 133 expression (stemness marker) 5) CD 95 expression (FasL receptor)

FasL-MPs are expected to have no significant impact on any parameter listed. This would demonstrate that FasL-MPs do not cause any adverse effects on the stem cells themselves, and could thus be used as a promising treatment. In parallel, activated and non-activated human T-cells were co-cultured in-vitro with FasL-MPs. FasL-MPs are expected to induce apoptosis in activated T-cells and have no effect on non-activated T-cells. This would validate the treatment's intended mechanism of action, showing that FasL selectively induces localized cell death in activated immune T-cells.

Together, these findings show that combined FasL-MP and hNSC treatment of ccSCI is a promising therapeutic strategy. Future in vivo studies are warranted to address treatment longevity, efficacy, and safety.

Cameron Fraser- #20

Glioblastoma (GBM) is the most aggressive form of malignant brain tumor with a high annual incidence of 10,000 new cases per year and median survival of less than 24 months. Standard xenograft models used to develop novel therapies to meet this need often use excessively large cell numbers to initiate tumor formation yielding compact, uniform masses that are not representative of GBM in situ. To address this, we implanted D54-MG human glioma cells in various doses in NOD scid gamma (NSG) mice to test the impact on tumor development. In vivo bioluminescent imaging was performed throughout animal survival. Brains were collected for histological and immunofluorescent analysis to assess tumor volume, cell organization, and immune cell localization. High-dose transplants resulted in well-demarcated tumors with less macrophage and neutrophil infiltration. Low-dose transplants resulted in consistent tumor initiation with smaller initial tumor volumes and greater overall immune cell infiltration. Despite prolonged survival in the low-dose cohort, terminal tumor volumes were larger than those observed in high-dose animals. These findings demonstrate that initiating GBM xenografts with fewer implanted cells produces tumors with distinct growth kinetics and histopathology that more closely resemble the infiltrative and heterogeneous nature of clinical GBM. This refinement has implications for improving the physiological relevance of preclinical models and for evaluating therapies targeting tumor-immune interactions.

Poster Presenters - Abstracts

Nolan Origer- #21

Induced pluripotent stem cells (iPSCs) have revolutionized fields such as regenerative medicine, disease modeling, and drug discovery. However, they still present challenges for large-scale adoption including high costs, low reprogramming efficiencies, and genomic instability during reprogramming. These genomic abnormalities, including copy number variations (CNVs) and point mutations, can negatively impact downstream applications of iPSCs in treatment and modeling of neurological disorders. While advances in genomic sequencing have improved detection of these abnormalities, effective strategies to prevent their occurrence remain underdeveloped.

The optimization of iPSC technologies has previously leveraged biophysical cues, mechanotransduction, and mechanosignaling to improve reprogramming efficiency. Investigations in this domain typically involve modifications of culture substrates or the targeted regulation of genes and proteins involved in cellular responses to the microenvironment. However, the effects of these manipulations on chromosomal stability during reprogramming have not yet been explored.

In this investigation, we focused on genes that participate in cell-cell and cell-extracellular matrix interactions (collectively termed the “adhesome”) during iPSC generation. Preliminary results from an shRNA screen targeting 103 genes revealed a top candidate, SHROOM3, whose knockdown increased reprogramming efficiency in primary and secondary reprogramming models. We further investigate the effects of SHROOM3 knockdown on genomic stability in the search to provide a more efficient and higher genetic fidelity iPSC generation method.

Leveraging our existing reprogramming time course single-cell RNA sequencing data, we sought to understand the impacts of SHROOM3 knockdown on genomic stability. To assess the accumulation of point mutations and short insertions and deletions over the course of reprogramming, we used and compared two computational mutation calling pipelines. According to these inferences, control knockdown cells acquired 5,390 (scAllele) and 6,995 (SComatic) new variants during reprogramming, whereas SHROOM3 knockdown cells acquired only 898 and 1,251 new variants, respectively. This reduction in variant burden suggests that SHROOM3 knockdown may protect cells from reprogramming-induced mutagenesis.

To further investigate this potential protective effect, we employed an orthogonal, qPCR-based method to assess CNVs in our iPSCs generated in each condition at the eight most common sites for karyotypic abnormalities in PSCs. Our results revealed copy number gains in the control knockdown condition, with 6 of 8 loci showing significant deviations from diploid levels (average copy number: 2.84). In contrast, the SHROOM3 knockdown condition exhibited minimal CNVs with only 4 of 8 loci altered and an average copy number of 1.93, closely matching the diploid control DNA. Importantly, the autosomal CNV distribution in SHROOM3 knockdown iPSCs was not statistically different from the control DNA, suggesting near-native chromosomal integrity at these sites.

Our findings present SHROOM3 as a potential regulator of genome integrity during reprogramming in addition to a factor for improving reprogramming efficiency. Preliminary pathway analysis using our single-cell RNA sequencing data suggests this shift may be linked to increased expression of native antioxidants and upregulation of DNA repair pathways. These results highlight the potential of adhesome interactions to modulate genomic stability and overcome this negative byproduct of reprogramming.

Poster Presenters - Abstracts

Daniella Lu- #22

Age is the dominant risk factor for many chronic diseases, yet the mechanisms linking aging to disease susceptibility are poorly understood. One key process implicated in age-related disease is the accumulation of somatic mutations in hematopoietic stem and progenitor cells (HSPCs), leading to clonal expansion of these advantageous mutations. This phenomenon, known as clonal hematopoiesis of indeterminate potential (CHIP), has been associated with an increased risk of adverse outcomes, including cardiovascular disease, myeloid malignancies, and increased all-cause mortality. Among recurrent CHIP-associated genes, ASXL1 is one of the most clinically significant yet mechanistically unresolved drivers.

ASXL1 encodes a chromatin regulator that modulates gene expression through epigenetic mechanisms, including histone modifications and chromatin remodeling. In both CHIP and myeloid malignancies, ASXL1 mutations are predominantly heterozygous frameshift or nonsense mutations clustered within the last two exons, resulting in escape from nonsense-mediated decay and the production of stable C-terminally truncated proteins. Despite this, most functional ASXL1 studies rely on complete gene knockout or overexpression of mutant alleles, primarily in murine models, which do not recapitulate the physiologic consequences of heterozygous truncations in human cells. These limitations hinder our ability to understand whether ASXL1 mutations act through loss-of-function, dominant-negative, or gain-of-function mechanisms, and how these alternations reshape epigenetic landscapes during human hematopoietic differentiation.

To address these gaps, my work aims to model ASXL1 truncation in a precise and physiologic manner by generating isogenic human embryonic stem cells (hESC) harboring a heterozygous, CHIP-relevant nonsense mutation. This approach enables direct comparison of wild-type and mutant ASXL1 function within a controlled human genomic background while maintaining the ability to differentiate these cells into hematopoietic progenitors and other relevant lineages. Using this system, I will characterize how ASXL1 truncation alters histone modification profiles, chromatin accessibility, and transcriptional programs across early hematopoietic development. Together, these studies will establish a human stem cell-based model for dissecting ASXL1 mutation biology and will provide mechanistic insight into how ASXL1-driven epigenetic dysregulation promotes clonal expansion and predisposition to early myeloid transformation. Elucidating these mechanisms is critical for understanding the adverse clinical impact of ASXL1 mutations and for identifying therapeutic vulnerabilities in ASXL1- mutant disease.

Sarah Soobin Lee- #23

Multiple sclerosis (MS) is a chronic autoimmune disease characterized by inflammatory demyelination driven by autoreactive T cells and dysfunction of regulatory T cell (Treg) and their control over autoreactive T cells. Current therapies make patients vulnerable to infection and cancer during treatment, emphasizing the need for safer approaches. DRAK2 (DAP-kinase-related apoptosis-inducing kinase 2) is a protein of the death-associated protein kinase (DAPK) family, which is mainly expressed in B and T lymphocytes, where it functions as a negative regulator of T cell activation threshold. Previous works on DRAK2 have demonstrated that Drak2-/- mice are resistant to experimental autoimmune encephalomyelitis (EAE) without any defect in T cell recruitment to CNS upon infection, with an increase in Tregs in the immune system. Our lab results have shown that DRAK2 deficiency causes alterations in cell metabolism, which in turn may favor Treg expansion. Moreover, studies on neural stem cells (NSCs) in treating autoimmune diseases discovered that NSC transplant into mice also stimulates Treg differentiation in vivo which reduces signs of neuroinflammation in mice with EAE. Our studies have revealed that hNSCs from induced pluripotent stem cells also induce a large number of Tregs in both healthy and MS patient PBMC cultures. Using both methods together, DRAK2 inhibition and NSC stimulation, results have shown that NSC co-culture with mouse T cells from Drak2-/- show much larger expansion of Tregs in vitro. Eventually, the results from the studies suggest that DRAK2 can be a novel therapeutic target, bridging mechanistic studies with a human MS and stem cell context while uncovering the role of immunometabolism in generating Tregs as an innovative way to treat MS.

Poster Presenters - Abstracts

Satya Karri- #24

Food intake regulates metabolism throughout the entire body, with hormones and metabolic organs like liver and fat coordinating this response. How skin, and in particular epidermal stem cells, respond to food intake is less understood. Previous studies have shown that fasting alleviates symptoms of inflammatory skin diseases like psoriasis and atopic dermatitis. And calorie deprivation has been shown to promote longevity and counter skin aging. Using a combination of single cell, bulk, and spatial transcriptomics, we identified key gene expression differences across diverse cell types in mouse skin during feeding and fasting. Unexpectedly, the gene encoding the rate-limiting enzyme in ketogenesis, Hmgcs2, is upregulated in the epidermis and hair follicle during fasting. This finding was unexpected because during fasting, the liver converts free fatty acids into ketone bodies that are transported to diverse organs and used as fuel. To investigate the function of Hmgcs2 in the epidermis, we knocked it out in the epidermis. We discovered that loss of Hmgcs2 rescued the normal fasting-induced decrease in epidermal stem cell proliferation, suggesting that Hmgcs2 is responsible for reducing proliferation in the epidermis and hair follicle during fasting. Interestingly, feeding and Hmgcs2 loss leads to increased Wnt4 expression in the epidermis, suggesting that HMGCS2 regulates epidermal stem cell proliferation through the Wnt pathway, a well-known regulator of epidermal stem cell proliferation. We identified insulin as a mediator of feeding-induced repression of Hmgcs2 epidermal expression. Using single cell ATAC-seq and CUT&RUN assays, we mapped three feeding-fasting-regulated gene-regulatory regions in the Hmgcs2 gene: two upstream enhancers and the promoter. Fasting induces binding of FOXO1 and FOXA1 to the promoter of Hmgcs2, suggesting that those regulatory elements are the primary regulators of Hmgcs2 in skin. Considering insulin is known to repress FOXO binding in the nucleus, this would further support our claims about insulin as a potent inhibitor of Hmgcs2 expression. Overall, this suggests that food intake results in a spike in insulin which downregulates epidermal Hmgcs2 expression by decreasing FOX factor binding, thereby contributing to decreased proliferation in the epidermis and hair follicle. Together, these findings support recent research suggesting that ketogenesis outside the liver plays a role in signaling the fasting state to regulate diverse organs.

Onwodi Ifejeokwu & Manuel Robledo - #25

Alzheimer's disease (AD) is characterized by progressive cognitive decline, neuroinflammation, oxidative stress and mitochondrial dysfunction. In AD transgenic mice, inactivation of one APOE allele accelerates the onset of behavioral defects and neuronal deterioration. This partial APOE loss led to a decrease in parenchymal amyloid-beta (Aβ) plaques burden but an increase in cerebrovascular amyloid deposition, highlighting its complex role in AD pathology and limited information about spatial distribution and cellular associations. In this study, we spatially mapped SOD2 expression in postmortem human brain tissues from AD patients and age-matched controls, sourced from UC Irvine's Alzheimer's Disease Research Center (ADRC). Immunohistochemical analyses identified elevated SOD2 expression in GFAP+astrocytes and plaque-associated Iba1+ microglia, in particular around dense, neuritic "cored" plaques. These findings suggest a glial-specific upregulation of SOD2 associated with plaque morphology, indicating a dysregulated mitochondrial response in glial networks contributing to plaque development and neurotoxicity. Additional Bax, a pro-apoptotic mitochondrial membrane associated protein was found to be upregulated in cerebral amyloid angiopathy (CAA)-affected regions, indicating a link between vascular amyloid deposition, mitochondrial dysfunction, and vascular fragility. Building on our previous work identifying mitochondrial-targeted therapeutics to alleviate oxidative stress and inflammation, we evaluated the effects of repurposed drugs on human induced pluripotent stem cell (iPSC)-derived microglia (iMGs). Hematopoetic stem cell (HSC) yield after differentiation was lower, and microglia differentiation was accelerated in APOE4/4 AD lines relative to matched APOE3/3 controls. Treatment with a mitochondrial drug enhanced Aβ42 phagocytosis in control iMGs over a 24-hour period. Future investigations will explore the impact of the APOE4 genotype on microglial phagocytic dysfunction and assess the therapeutic potential of mitochondrial modulators in 5xFAD transgenic mouse model. These findings underscore the pivotal role of mitochondrial dysfunction and glial activation in AD pathology and support the therapeutic potential of targeting mitochondrial pathways to mitigate disease progression.

Poster Presenters - Abstracts

Olga Jaime- #26

Defining transcriptional regulators of early myogenic commitment from human pluripotent stem cells (hPSCs) could improve lineage specific differentiation to skeletal muscle. Analysis of several myogenic factors in human embryos and early hPSC derivations demonstrated that early co-expression of SIX1+PAX3+ was predictive of efficient myogenic induction to skeletal muscle progenitor cells (SMPCs) and myotubes, and inhibition of SIX1 alone significantly reduced myogenic commitment. Performing single nucleus RNA-sequencing (snRNA-seq) revealed that hPSCs give rise to a heterogenous population of cells across time, comprising of not only myogenic subtypes, but also non-myogenic ones. Because SIX1 expression was more specifically associated with the myogenic lineage — initially by PAX3+ progenitors at early timepoints and later by PAX7+ SMPCs and MYH3+ myotubes — we utilized a SIX1:H2B-GFP reporter hPSC line to study SMPC transitions. To capture the transitions of PAX3 to PAX7 SMPCs and their differentiation to myotubes. We collected SIX1-GFP+ SMPCs longitudinally at days 20, 28, and 42 and assayed for expression of PAX3, PAX7, SIX1, and MYH3 by rt-qPCR and immunofluorescence immediately after single cell sorting of GFP+ cells. Despite GFP+ SMPCs expressing PAX3 and PAX7 at day 20, only GFP+ SMPCs at days 28 and days 42 could differentiate into myotubes. As compared to day 20, PAX3 protein expression was not found at day 28 and 42. To identify the genes driving SMPC differentiation at days 28 and 42, but not day 20, we examined the transcription factors that were highly correlated in each transition. Moscot analysis revealed that a cyclic AMP response binding protein 5 or CREB5 distinguished SMPC differentiation potential and that PAX3 cells give rise to myotubes in sufficient quantity prior to the formation of PAX7 cells, replicating the waves of myogenesis observed in development.

Kevin Sanchez - #27

Amyotrophic Lateral Sclerosis (ALS) is an incurable motor neuron disease that manifests as muscle twitching and weakness, rapidly progressing to paralysis and death. In 97% of cases there is mislocalization and aggregation of RNA binding protein TDP-43 in brain and spinal cord motor neurons, suggesting that TDP-43 dysregulation is a critical event in ALS disease pathogenesis. Recently, modulating the site of polyadenylation of the transcript encoded by the Ataxin-3 (ATXN3) gene has emerged as a candidate for therapy development in ALS. We have documented an increased TDP-43 burden after genetic knockdown of ATXN3, a deubiquitinase, in HEK293T cells and SH-SY5Y neuroblastoma cells, likely due to decreased proteasome turnover of TDP-43. We have also found that overexpression of ATXN3 can markedly reduce TDP 43 aggregation in SH-SY5Y cells and human iPSC-derived motor neurons (MNs). These findings are novel, as modulation of ATXN3 expression levels had not been previously known to affect key ALS disease phenotypes in vitro. Here, we demonstrate that 2'MOE-PS antisense oligonucleotides (ASOs) mapping to the ATXN3 distal polyadenylation site (PAS) can reduce the production of long ATXN3 3'UTR isoforms in iPSC-MNs. Because iPSC-MNs inherently lack TDP-43 pathology, we have been using tunicamycin as a stressor to induce TDP-43 dysregulation in iPSC-MNs harboring the familial ALS TDP-43 M337V mutation. Experiments are currently underway to determine if ATXN3 distal PAS-blocking ASOs can rescue ATXN3 expression regulation and TDP 43 proteostasis in TDP-43M337V iPSC-MNs, and also ameliorate ALS disease-relevant phenotypes in TDP-43M337V iPSC-MNs subjected to tunicamycin treatment.

Poster Presenters - Abstracts

Dina El Tahlawy- #28

Induced pluripotent stem cell (iPSC)-derived human neural stem cells (hNSCs) and microglia (iMG) represent promising cellular therapeutics for neurodegenerative diseases, owing to their capacity to elicit neuroprotective and immunomodulatory responses. However, emerging evidence suggests that the genetic background and disease-associated risk factors such as aging of donor cells significantly influence the functional competence of these cellular therapeutics. Alzheimer's disease (AD) is a progressive disease that affects more than six million Americans, with cases projected to rise to 13.8 million by 2060. Despite significant advances in AD research, current therapeutic strategies, including monoclonal antibodies, primarily slow disease progression. Very few interventions aim to replace lost/damaged cells, restore neural function or reverse existing damage. APOE4 is the greatest risk factor for AD, with one copy increasing the risk by three-fold and in homozygous carriers by up to fifteen-fold. Previous studies in aged humanized APOE 4 mice show an accumulation of senescent neurons and dysregulated endosome-lysosome-autophagy (ELA) system in the hippocampus. However, mechanistic insight into these deficits remains limited, in part due to the reliance on rodent models and the absence of patient-specific cellular models. To address this gap, our study leverages human iPSCs obtained from the UC Irvine ADRC core to generate iMGs and hNSCs from three APOE4/4 homozygous patients. RNA-seq analysis revealed increased expression of genes associated with the autophagy–lysosomal pathway and inflammatory cytokine/chemokine signalings; while genes associated with cell cycle progression, DNA replication, and DNA repair were downregulated. In line with these cell cycle defects, when iPSCs were differentiated to hematopoietic stem cells (HPCs), there was a significant reduction in cell yield in the APOE4/4 lines compared to healthy APOE3/3. Additionally, it was observed that APOE4/4 hNSC showed reduced cellular processes, which suggests that APOE4 may be affecting neural differentiation and maturation. These intrinsic cellular deficits associated with APOE4 may contribute to reduced therapeutic efficacy and highlight the importance of considering donor genotype in the development of iPSC-based therapies. Consequently, Differentially Expressed Gene (DEG) files comparing the APOE4/4 to APOE3/3 iMGs were further analyzed using the iLINCS drug perturbation library to identify potential drug candidates that can reverse the transcriptomic profiles. Ongoing studies will focus on identifying pharmacological and genetic interventions capable of rescuing the proliferative, migratory, and phagocytic deficits associated with the APOE4/4 stem cells. Follow up studies will test the performance and efficacy of drug-corrected iMG and hNSC in a 5xFAD mouse model of AD. Our findings underscore the need for a personalized and corrective approach to optimize the clinical translation of iPSC-derived cellular therapeutics for AD and related disorders.

Nolan Huck - #29

Spinocerebellar ataxia type 7 (SCA7) is a neurodegenerative disease uniquely characterized by cone-rod dystrophy, leading to severe vision impairment and blindness. SCA7 results from CAG polyglutamine (polyQ) repeat expansion in the Ataxin-7 (ATXN7) gene, disrupting transcriptional regulation and epigenetic remodeling in retinal photoreceptors. Current understanding of SCA7 retinal degeneration is limited, necessitating advanced models to uncover disease mechanisms. This study utilizes human induced pluripotent stem cell (iPSC)-derived retinal organoids (ROs) to model SCA7 cone-rod dystrophy. These 3D organoids recapitulate the structural and cellular organization of human retina, including rod and cone photoreceptors. SCA7 ROs derived from patient iPSCs demonstrate disease-relevant phenotypes, including transcriptional dysregulation and altered epigenetic landscapes. ROs will be characterized across developmental stages using light microscopy and immunohistochemistry to assess retinal layer formation, photoreceptor differentiation, and ultrastructural morphology. Transmission electron microscopy will provide detailed insights into photoreceptor outer segment integrity and synaptic organization. This work highlights the potential of iPSC-derived ROs to unravel the molecular basis of SCA7 retinal degeneration and to serve as a platform for therapeutic development.

Poster Presenters - Abstracts

Magdalene Seiler, PhD- #30

To study retinal degeneration and connectivity of retinal transplants, we generated a rat with photoreceptor degeneration that has a fluorescent label in specific retinal cells.

Two separate rat models were generated at Envigo, Missouri, and bred to homozygosity at UCI. Gene constructs for floxed TdTomato and Pcp2-Cre were developed at Envigo and injected into rat embryos. First, the floxed TdTomato strain was created on the immunodeficient RhoS334ter-3 rat strain (SD-Foxn1Tg(S334ter)3LavRrrc (RRRC#539)). The F1 generation was received in 2023 and bred to homozygosity (strain SD-Foxn1rnuTg((Rho-S334X)3,CAG-TfTomato)1010Mjsuc, "RNT").. T Although the second gene construct, Pcp2-Cre, could not be created in RD rats, it was successfully injected into Long-Evans (LE) rat embryos. Two Pcp2-cre founders (strain PCP2 Cre-1105 RKI, "Pcp2") were created: one with targeted insertion, and with random insertion. The female founder (targeted insertion) was mated with a LE rat; the male (targeted + random insertion) was mated with a female NIH nude rat (foxn 1+/-). F1 offspring was bred to homozygosity and immunodeficiency. Homozygous rats of both strains were then crossbred to generate TdTomato-Pcp2 RD rats ("RTP rats"). Retinas were processed for histology and immunohistochemistry between the ages of 19-272 days. In pilot experiments, GFP expressing rat retinas and retinal organoids were transplanted to 6 week old "RTP" rats and analyzed 37 and 77 days post-surgery (dps).

TdTomato-Pcp2 RD rats show photoreceptor degeneration similar to the original Rho S334ter-3 rat strain, with less than one row of photoreceptors remaining at the age of 1 month. Retinas with targeted Pcp2 insertion showed TdTomato in retinal interneurons (cone bipolar cells) and cones. Retinas with random Pcp2 insertion exhibited additional TdTomato in many different cells, including RPE, glial, endothelial and lens cells. Pcp2-TdTomato expression was useful to define transplant-host boundaries. The "RNT" strain is being submitted to the RRRC, University of Missouri as future strain #1055.

Hajime Ozaki - #31

Human cerebral organoids derived from pluripotent stem cells provide a powerful model to study early corticogenesis and neurological disorders. Existing three-dimensional (3D) tissue culture systems face challenges in creating precisely controlled morphogen gradients, which are critical physiological factors for cell differentiation, diversity, and spatial arrangement. To overcome this limitation, we developed a multilayered hydrogel system that produced 3D protein gradients. First,

we established hydrogel materials, a Mebiol– hyaluronic acid methacrylate (HAMA) composite bioscaffolds, which were compatible with cortical organoids. Second, we tested different multilayered hydrogels that enabled the generation of protein gradients. In our optimized multilayered hydrogel condition, spatially directed induction of posterior organizers were observed in cortical organoids. Specifically, cortical organoids were positioned above a BMP4-loaded Mebiol–PEGDA hydrogel, allowing the morphogen to diffuse upward and establish a concentration gradient over time. Organoids exposed to BMP4 via hydrogel diffusion exhibited spatially localized expression of posterior organizers including OTX2 and TTR, predominantly on the BMP4-exposed side. In contrast, conventional uniform treatment induced posterior organizers throughout the entire organoid. Together, these findings establish a straightforward yet effective strategy for spatial patterning of human cerebral organoids through diffusion-mediated morphogen gradients. This approach offers next-generation cortical organoids that recapitulate physiological conditions that lead to cell diversity, spatial arrangement, and circuit maturation for a better understanding of neurodevelopment and disease.

Poster Presenters - Abstracts

Jean Paul Chadarevian- #32

Frontotemporal dementia (FTD) is the second most common cause of dementia in individuals under 65. Among the known genetic contributors, progranulin (human gene symbol: GRN) haploinsufficiency is the second most prevalent cause of familial FTD (FTD-GRN). Prior studies have examined various approaches to therapeutically increase brain levels of progranulin. However, biodistribution, immune reactivity, peripheral toxicity, and repeated infusions remain significant challenges. Alternatively, iPSC-microglia (iMG) transplantation could offer a promising new strategy that addresses these limitations by restoring progranulin levels and replacing dysfunctional microglia within the CNS.

To assess the therapeutic potential of human microglia transplantation in FTD-GRN, we generated a xenotolerant, progranulin-deficient model (hGRNR493X/R493X) that allows for the long-term engraftment of human microglia into the brain. Using an inhibitor-resistant approach, G795A-iMG or PBS were transplanted into 7-month-old hGRNR493X/R493X mice after the onset of FTD-related neuropathologies, then treated with CSF1R-inhibitor (CSF1Ri) chow for 2 months, then returned to regular chow. At 10 months, brain tissue and peripheral blood plasma were collected from CSF1Ri-treated and untreated mice for immunohistochemical and biochemical analysis.

Initial analysis of 3-, 6-, and 12-month-old hGRNR493X/R493X mice revealed a progressive increase in lysosomal accumulation, gliosis, and microglial activation. Surprisingly, healthy human microglia transplantation significantly lowered lysosomal content throughout the brain. However, CSF1Ri-mediated microglia replacement was necessary to also reverse widespread astrogliosis and microglial activation. Multiplex biochemical assessment further found microglial transplantation and replacement significantly reduced multiple inflammatory markers within the brain and periphery. Ongoing experiments will further elucidate the impact of human microglial transplantation on other cell populations within the brain.

Together, these results provide preliminary evidence that iPSC-microglia transplantation and replacement could potentially be developed as a novel therapy for FTD-GRN and likely other neurodegenerative diseases.

Pallabi Pal - #33

Valosin-containing protein (VCP) related disease, also known as multisystem proteinopathy 1 (MSP1), is an autosomal dominant disease caused by gain-of-function pathogenic variants of the VCP gene. The disease is associated with inclusion body myopathy, early-onset Paget's disease of bone, frontotemporal dementia, and familial amyotrophic lateral sclerosis. There is currently no treatment for this progressive disease associated with early demise resulting from proximal limb girdle and respiratory muscle weakness. We hypothesize that regulating VCP hyperactivity to normal levels can reduce the disease pathology. Recently, the use of microRNA-dependent post transcriptional suppression of transgene expression has emerged as an effective method to knock down or silence gene expression.

We hypothesize that by knocking down the VCP with microRNA, we will reduce the gain of function to normal values.

We designed and tested the knockdown efficiency of three microRNA (miR-VCP #2, #6, and #8) constructs targeting the human VCP (hVCP) gene. Human embryonic kidney 293 (HEK293T) cells were used due to their human-like posttranslational modification of protein molecules.

The western blot results show mirVCP#2 was the most efficacious in knocking down the WT VCP up to 22%. Next, we evaluated the effect of mirVCP#2 on patient (R155H) iPSC-derived skeletal muscle progenitor cells (SMPCs). MirVCP#2 significantly decreased VCP protein levels by 30% in SMPCs. Additionally, we observed improvements in the autophagy proteins LC3 and p62, as well as a reduction in TDP-43 expression through western blot, which are hallmarks of VCP disease.

Success in these preclinical studies offers promising therapeutic potential for patients with VCP disease.

Poster Presenters - Abstracts

Alexii Villamar- #34

Allogeneic hematopoietic cell transplantation (allo-HCT) is a potentially curative treatment for various blood disorders, including hematologic cancers. A key benefit of allo-HCT is the graft-versus-leukemia (GVL) effect, mediated by allogeneic cytotoxic T cells, which helps eliminate malignant cells. However, these same allogeneic T cells can also cause graft-versus-host disease (GVHD), a major complication characterized by inflammation and tissue damage.To address this, our lab has developed an ex vivo graft conditioning protocol, which involves pretreating donor cells with specific molecules or drugs before transplantation. This approach has shown promise in reducing GVHD severity and extending survival in a mouse model, likely by altering the balance of different T cell subsets. Despite its success in mitigating GVHD, the protocol significantly reduces the viability of cytotoxic T cells—which are crucial for maintaining the GVL effect. To overcome this limitation and sustain anti-tumor immunity, we are exploring strategies to preserve and enhance the viability of these key immune cells. Specifically, we tested a combination of glucocorticoids and cytokines IL-2 and IL-15. Our in vitro studies demonstrate that this cocktail supports the survival and function of CD8+ T cells, suggesting a promising approach to maintain GVL while minimizing GVHD in allo-HCT.

Wilber Santiago Perez - #35

Cranial radiation therapy (RT) is an effective standard of care in preventing brain cancers, but damaging neurodegenerative consequences post-RT triggers the long-term neuroinflammation. This snowballs to the hippocampal and cortical structures, neurons and synapses and eventually leads to radiation-induced cognitive decline (RICD) in patients and survivors. Regulatory T cells (Tregs) have been shown to suppress inflammation by modulating immune responses, maintaining self-tolerance, and restoring homeostasis, all of which could potentially counteract the neuro-inflammatory mechanisms contributing to RICD. In our experimental design, we aimed to isolate and culture Tregs from donor mice and introduce them to irradiated mice using adoptive T cell transfer (AT). 12-week-old WT (C57Bl6) mice were injected with myelin oligodendrocyte glycoprotein (MOG) and pertussis toxin (PTX) to induce Experimental Autoimmune Encephalomyelitis (EAE) which in turn promote a strong inflammatory environment. Tregs were then extracted from the spleens of these donor mice and cultured with IL-2, TGF-β, and retinoic acid. Cranial RT-exposed (9 Gy) mice were then IP injected with either developed Tregs (RT-AT) or PBS (RT-Veh) at 45 minutes post-RT. 4-6 weeks later, cognitive function tests were performed on the mice, including Fear Extinction (FE) and Object Location Memory (OLM), to determine the hippocampal-amygdala circuit and the hippocampal functions, respectively. Treg adoptive transfer in the irradiated mice restore cognition to control levels. Dual-immunofluorescence (IHC) showed reduced microglial activation and increased synaptic integrity in the RT-AT brains compared to RT-Veh. This data demonstrate the neuroprotective ability of adoptive Treg transfer in restoring brain function post-RT and will facilitate translational research to alleviate RICD.

Poster Presenters - Abstracts

Iceis Hurtado- #36

Traumatic brain injury (TBI) affects millions annually, often resulting in chronic cognitive deficits, tissue loss, and neuroinflammation. Transplantation of human neural stem cells (hNSCs) has shown promise as a potential therapeutic approach for TBI. The Cummings lab has shown that transplantation of hNSCs, derived from the Shef6 human embryonic stem cell line (Shef6-NSC), into rat brain tissue following TBI reduces neuroinflammation and improves functional outcomes. Upon transplantation, inflammatory protein expression in the cerebrospinal fluid is reduced and a subpopulation of Shef6-NSC engraft and line the brain's meninges and lateral ventricles, where they primarily remain in a progenitor-like state. As a possible mechanism of action, these cells may be secreting anti-inflammatory signals into the injury microenvironment via exosomes. Studies have shown that exosomes have promising therapeutic potential. The DiCarlo lab at UCLA has developed a novel nanovial technology that would allow for sorting of single cells by their secreted proteins. The surface of nanovials is biotinylated, enabling functionalization with an anti-CD63 capture antibody. After functionalization, nanovials are loaded with single cells and incubated, allowing for surface capture of secreted exosomes. This can be detected by an anti-CD81 antibody, revealing distinct high and low exosome secretors. We hypothesize Shef6-NSCs can be sorted into distinct populations based on their exosome secretion rate. We were able to successfully load the Shef6-NSCs into nanovials which had previously only been validated with mesenchymal stem cells (MSCs). Future work will utilize nanovials to sort high and low exosome secreting populations for downstream analysis, with the goal of maximizing exosome therapeutic output.

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