2023 Vision Research Seminar Series

Jan. 12, 2023: Yuqing Huo, M.D., Ph.D.

Seminar Title: Glycolysis in Retinal Angiogenesis and Subretinal Fibrosis
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Huo is a professor of cellular biology and anatomy, director of the Vascular Inflammatory Program, Vascular Biology Center, Medical College of George, Augusta University. He obtained medical training and served as an internal medicine physician and cardiologist for three years in China. Subsequently, He pursued Ph.D. graduate training at the Medical School of Peking University (China), obtaining expertise in eNOS/nitric oxide biology and endothelial inflammation. He pursued postdoctoral training in Dr. Klaus Ley's laboratory at the University of Virginia, learning in vivo microscopic approaches to study leukocyte/platelet/vascular interactions in mice. Dr. Huo primary research interests are to study how leukocytes and vascular cells interact to participate in cardiovascular disease and obesity/metabolic disease.

Over the past 10 years, Dr. Huo expanded his research to the retinopathy field. By collaborating with his colleagues in the James and Jean Culver Vision Discovery Institute at MCG of Augusta University, his group studied the molecular mechanism underlying the role of adenosine receptor 2A (A2aR) and adenosine kinase (ADK) in the regulation of ocular angiogenesis and has found that A2aR/adenosine-mediated glycolysis/VEGFR2 in endothelial cells plays a critical role in pathological retinal angiogenesis. His group also demonstrated that PFKFB3-mediated endothelial glycolysis is critical for angiogenesis, especially for the development of oxygen-induced retinopathy (OIR) in mice. Furthermore, his group also revealed that a glycolysis-dictated reciprocal activation between retinal endothelial cells and microglia/macrophages is critical for retinal/choroid angiogenesis. This study was featured in NIH/NEI. This research work reveals an important role of glycolysis in the development of pathological angiogenesis and fibrosis in the ocular system.

Seminar Summary: Disorders such as angiogenesis and fibrosis in retinas and choroids involve participation of vascular cells, immune cells as well as mesenchymal cells. For these cells, glycolysis is one of the major cellular metabolic pathways. PFKFB3 (6-phosphofructo-2-kinase/fructose-2, 6-bisphosphatase isoform 3) is a critical enzyme for activation of glycolysis in vascular cells and leukocytes. It catalyzes the synthesis of fructose-2,6-bisphosphate (F2, 6P2), which is the most potent allosteric activator of 6-phosphofructo-1-kinase (PFK-1), a rate-limiting enzyme for glycolysis. We generated mice

with a deficiency of Pfkfb3 in endothelial cells or myeloid cells and used these mice to study how glycolysis in ECs and myeloid cells is involved in pathological angiogenesis and fibrosis in murine models of oxygen-induced retinopathy (OIR) and laser-induced choroidal neovascularization (CNV). These studies reveal a critical role of the glycolytic pathway in the development of these retinal disorders. Additionally, these studies also indicate that inhibiting glycolysis is a promising strategy in the treatment of these diseases.

Feb. 9, 2023: Zheng Jiang, Ph.D.

Seminar Title: Spontaneous Glial Cell Activities in Healthy and Glaucomatous Mouse Retinas
Time: 3 p.m. via Zoom

Speaker Bio: I have 18 years of experience in retina physiology research. During my doctoral training in Dr. King-Wai Yau's lab at Johns Hopkins University, I discovered a novel phototransduction pathway in M2- and M4-ipRGCs, which is mediated by cyclic nucleotide and HCN channels. This finding reveals a complex heterogeneity in phototransduction among ipRGCs and, more importantly, breaks a general dogma about the segregation of the two phototransduction motifs in the animal kingdom. I joined the Department of Ophthalmology at Baylor College of Medicine as an assistant professor in 2019. My laboratory is focusing on two major directions: i) understanding phototransduction mechanisms and potential applications of melanopsin transduction pathways; ii) studying the electrophysiological properties of retinal ganglion cells in normal and diseased retinas. Along the scientific journey, we discovered a novel electrical activity in retinal glial cells and two new defects in an early-stage glaucoma model.

Seminar Summary: Retinal glial cells play an important role in the maintenance of normal retinal biology. Müller cells are the principal glial cells of the vertebrate retina and span the entire depth of the retina from the outer limiting membrane to the inner limiting membrane. Importantly, despite the critical role of retinal glial cells in supporting normal RGC physiology, it remains unknown whether these cells and/or their interactions with RGCs participate in early-stage glaucoma. Our new approach uses a cutting-edge physiological recording system to monitor extracellular potentials from freshly dissociated retinas. In normal adult mouse retinas, we discovered a glial spontaneous slow voltage fluctuation (SSVF) that has never been reported before. We further demonstrated that the source of SSVFs is likely to be Müller cells. By using a custom algorithm to automatically detect and align these glial and RGC events, we can now efficiently study glial-RGC interactions with spatial and temporal precision on a large scale. Our preliminary results show a novel glial

functional defect in the early stages of a glaucoma mouse model, suggesting that glial cell hyperactivity is a major factor in early glaucoma pathogenesis.

March 23, 2023: Dong Feng Chen, M.D., Ph.D.

Seminar Title: Harnessing Immune Balance to Combat Glaucoma
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Dong Feng Chen, M.D., Ph.D., is an associate professor of ophthalmology at the Schepens Eye Research Institute of Massachusetts Eye and Ear and the Department of Ophthalmology, Harvard Medical School. She was trained in the laboratory of Nobel Laureate, Professor Susumu Tonegawa at MIT, before joining the faculty of Harvard Medical School. Her laboratory researches the mechanisms controlling neurodegeneration and regeneration in the eye and brain, and they were the first to report full-length optic nerve regeneration from the eye to the brain in genetically engineered post-born mice. Recently, they uncovered an unexpected link among microbiome, autoimmune T cell responses, and neuron and vision loss in glaucoma. These findings received news commentary in Nature Review Immunology and EyeWorld, etc., highlighting the potential for paradigm shifts in diagnosis, management and treatment of glaucoma and other neurodegenerative diseases in the eye and brain.

Seminar Summary: Glaucoma affects 80 million people worldwide and is a leading cause of irreversible blindness, yet the underlying causes of vision loss are not fully understood. One reason for this is that the eye has traditionally been considered an immune privileged site, which means that there has been little understanding of the involvement of the adaptive immune system, including T cells, in the initiation and progression of the disease. During this presentation, Dr. Chen will describe her team's journey from developing an inducible mouse model of glaucoma to uncovering the role of commensal microbiota-sensitized Th1 cells, as well as the interaction with the innate immune system (specifically microglia), as the root cause of neurodegeneration in glaucoma. Lastly, Dr. Chen will critically discuss the translation studies of their work and the potential implications for the future diagnosis, management and treatment of glaucoma.

April 13, 2023: Ross Poché, M.D., Ph.D.

Seminar Title: Awakening the Regenerative Potential of the Mammalian Retina
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Ross Poché is an associate professor of integrative physiology at Baylor College of Medicine. He received his bachelor's degree from the University of New Orleans and Ph.D. from Baylor College of Medicine. His research focuses on transcriptional and epigenetic mechanisms regulating retinal progenitor cell proliferation and differentiation.

Seminar Summary: One of my lab's long-term goals is to elucidate the transcriptional and epigenetic mechanisms regulating retinal progenitor cell proliferation, differentiation, and regeneration, leading to new therapeutic interventions to restore sight. Toward that end, projects aimed at characterizing mouse mutants suffering from defects in retinogenesis are ongoing. One specific aspect of our research is to identify new strategies to promote Müller glial (MG) cell-mediated retinal regeneration in response to photoreceptor damage. Here, we are interested in determining whether the mouse retina retains latent regenerative potential akin to other vertebrates, such as the zebrafish, and whether we can genetically "awaken" that potential to restore sight. The talk will highlight the discoveries made regarding Hippo pathway regulation of damage-induced Müller glial cell reprogramming to a proliferative, progenitor-like state. I will also present preliminary data describing an approach to isolate native Müller glia and rod proteomes in response to damage.

May 11, 2023: Roxana Radu, M.D.

Seminar Title: What is the Role of ABCA4 in the Retinal Pigment Epithelium?
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Roxana Radu, M.D., is an assistant professor of ophthalmology at the UCLA Stein Eye Institute and Department of Ophthalmology, David Geffen School of Medicine at UCLA. She possesses extensive education in both clinical and basic-research medical sciences and specific expertise in retinoid biochemistry, which she acquired during her postdoctoral training with Dr. Gabriel Travis. Dr. Radu has established a translational research program that aims to address pressing unmet needs for experimental models of macular degeneration, for which no therapies currently exist. Her group has developed disease models, including mouse lines and human iPSC-derived RPE cultured cells, to elucidate the underlying mechanisms of photoreceptor cell loss in Stargardt disease (STGD1), a juvenile maculopathy, and its relation to age-dependent macular degeneration (AMD). The recent discovery that the ABCA4 gene responsible for STGD1 is expressed and functional in RPE cells has changed the "status quo" of STGD1 pathophysiology. Moreover, Dr. Radu reported for the first time a link between innate immunity dysfunction and STGD1, providing evidence of bisretinoid-mediated complement dysregulation via the alternative pathway in RPE cells carrying an AMD risk allele for the

complement factor H (CFH) gene. Current efforts focus on deciphering the intersection of vitamin A-lipid metabolic pathways to understand the biological significance of lipid deposition in RPE cells and identifying key molecular targets for potential therapies for ABCA4-maculopathies.

Seminar Summary: In recent years, the retinal pigment epithelium (RPE) has emerged as a promising cellular target for treating degenerative diseases of the macula. This region supports color vision at high spatial and temporal resolutions, which are essential for many daily activities. Macular degeneration causes the RPE to become dysfunctional and eventually die, leading to photoreceptor degeneration and central visual loss. Currently, there are no therapies for non-exudative macular degenerations such as STGD1 and the dry form of AMD. In this presentation, Dr. Radu will discuss the underlying mechanisms of RPE dysfunction and cell death relevant to STGD1 and AMD. The discovery of ABCA4 expression in RPE cells, in addition to photoreceptors, has led to the development of new models to investigate the RPE cell-autonomous drivers of pathology for these diseases. Dr. Radu will explore the biological processes at the intersection of the complement system, retinoid-lipid metabolism, and mitochondrial bioenergetics and their implications for potential therapeutics.

June 15, 2023: Vivien Coulson-Thomas, Ph.D.

Seminar Title: Hyaluronan (HA) Prevents Age-related Meibomian Gland Dysfunction
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Vivien J. Coulson-Thomas is an Associate Professor in Vision Science. Dr. Coulson- Thomas completed post-doctoral training in glycosciences and neurobiology at the University of Cambridge in the United Kingdom, and in ophthalmology at the University of Cincinnati. She earned her B.S. in Biomedicine and her MSc and PhD in molecular biology from the Federal University of Sao Paulo. Throughout her education, Dr. Coulson-Thomas earned various awards including the JBC/Herb Tabor Young Investigator Award from the Journal of Biological Chemistry in 2014, British Society of Matrix Biology Young Investigator Award in 2015, the award for excellence in Research, scholarship and creative activity from the University of Houston in 2022, and most recently the Endre Balazs & Janet Denlinger Award from the international society for hyaluronan sciences. She has over 25 years' experience in the field of glycosciences, and over 15 years' experience working with the Ocular Surface, with almost 50 published peer-reviewed papers. Her research focuses on studying how the extracellular matrix regulates the development, homeostasis and pathology of the ocular surface, for which she currently has two RO1 grants from NEI. Most

recently, her lab is working on understanding how changes in the extracellular matrix with aging affect dry eye disease.

Seminar Summary: The prevalence of dry eye disease (DED) ranges from ~5 to 50%, with ~85% of all cases being caused by Meibomian gland dysfunction (MGD). As humans and mice age, their Meibomian glands (MGs) undergo age-related changes resulting in MG atrophy and dropout, named age-related-MGD (ARMGD). The etiology of ARMGD remains elusive, which makes developing therapies to prevent ARMGD extremely challenging. We previously demonstrated that hyaluronan (HA) regulates MG morphogenesis and homeostasis, with an increase in HA leading to an increase in both the number of meibocytes and acini, and, consequently, enlarged glands. We are currently investigating the role of HA in the aging MG, and its therapeutic potential for preventing ARMGD. For this, hyaluronan synthase (Has) knockout mice were aged and compared to age-matched wt mice. Our data shows that at 1 year, Has1-/-Has3-/- mice present significantly enlarged MGs, compared to age-matched wt mice and compared to all adult mice. At 2 years, wt mice present severe MG atrophy and dropout, while age-matched Has1-/-Has3-/- mice present healthy glands. As wt mice age, they present a loss of HA surrounding the MG and changes in the composition of the HA matrix, which is correlated with MG atrophy. A loss of HA surrounding the MG in wt mice precedes MG atrophy. In contrast, Has1-/-Has3-/- mice present a significant increase in HA deposition and, consequently, do not present MG atrophy. A decrease in HA synthesis in Has1-/-Has3-/- mice, via administration of a chemical inhibitor, is enough to cause MGD. Taken together, our data shows that increasing the HA matrix surrounding the MG can prevent ARMGD in mice.

July 20, 2023: Rui Chen, Ph.D.

Seminar Title: Single-cell Multi-omics Atlas of the Human Retina from Development to Disease
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Rui Chen is a professor of molecular and human genetics at Baylor College of Medicine. He received a bachelor's degree from Tsinghua University, China and a Ph.D. degree from Baylor College of Medicine. After completing postdoctoral training, he joined the Department of Molecular and Human Genetics as an assistant professor, associate professor and full professor. He is the Director of Center of Single Cell Omics at Baylor College of Medicine and has extensive experience in single cell omics profiling.

Seminar Summary: Single cell genomic technologies are revolutionizing basic and translational research in many medical fields, including ophthalmology. I will provide an

update on the generation of the version 1 single cell atlas of the human retina as part of the human cell atlas (HCA) effort, which includes transcriptomics and open chromatin profiles of over 100 cell types from the retina. In addition, findings from single nuclei multi-omics profiling of developing human fetal retina will be discussed. Finally, to facilitate access to the data source by the community, information about the database and the interactive cell atlas browser will be presented.

Aug. 10, 2023: Mrinalini Hoon, Ph.D.

Seminar Title: The Mechanisms Underlying Assembly of Retinal Circuits
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Mrinalini Hoon is an assistant professor at the University of Wisconsin-Madison Department of Ophthalmology and Visual Sciences. She is also the director of the University of Wisconsin-Madison School of Medicine's electron microscopy facility. She earned her bachelor's degree in Physiology from Calcutta University and has a Ph.D. in neuroscience from the International Max Planck Research School at the University of Goettingen, Germany. Thereafter, she completed her postdoctoral training with Dr. Rachel Wong at the University of Washington. Her lab is currently funded by grants from NIH/NEI as well as grants from other research foundations. Her research program employs a multi-faceted toolkit to determine the mechanisms that regulate the formation, maturation and maintenance of functional circuits in the mammalian retina.

Seminar Summary: Processing through retinal circuits underlies visual function. Yet we know little about the mechanisms that establish precise connections between retinal cell types. By combining murine transgenic tools with single cell electrophysiology and high-resolution light and electron microscopy, we are studying the mechanisms that regulate the establishment of inner retinal synapses, specifically the inhibitory synapses at bipolar cell terminals that regulate visual information transfer. We find that a specific early GABA receptor type plays a key role in the establishment and function of these synapses. Additionally, the maturation of these synapses is controlled by visually driven activity. Thus, distinct molecular and activity-dependent mechanisms shape the assembly of retinal microcircuits. Understanding the mechanisms that regulate circuit formation is crucial to determining pathways that are perturbed during disease and degeneration conditions.

Sept. 14, 2023: Jijie Pang, M.D., Ph.D.

Seminar Title: Retinal Mechanical Sensation and Scotopic Light Signaling
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Jijie Pang is an associate professor in the Department of Ophthalmology at Baylor College of Medicine. She earned her M.D./Ph.D. degree at Xi'an Jiaotong University, China. Thereafter, she completed her postdoctoral training at Baylor College of Medicine. Her work focuses on retinal visual signaling in physiological and pathological conditions. She characterizes retinal photoreceptors, bipolar cells, amacrine cells and ganglion cells with light-evoked activities and single-cell immunofluorescence. Based on such neuronal identities, she further studies the communication between photoreceptors and bipolar cells and synapses among bipolar cells, amacrine cells and ganglion cells, primarily by using whole-cell patch-clamp techniques, in conjunction with genetic engineering, electron microscopy and immunocytology. Built on these physiological data, her study further explores roles of mechanical signals in normal retinal visual pathways and in pathogenesis of glaucoma, as well as other retinal diseases related to physical stresses.

Seminar Summary: In recent decades, a growing number of studies have reported mechanical-sensitive channels (MSCs) in retinal neurons. Our recent studies observed the expression of several types of MSCs in the inner and outer retinal neurons and first reported the pressure-evoked current and voltage response in photoreceptors and bipolar cells. The data have demonstrated that outer and inner retinal neurons are functionally mechanosensitive. Traumatic retinal injury and glaucoma are retinal disorders closely related to pressure. Our current studies funded by DoD focus on the role of MSCs in pressurized air wave-induced traumatic retinal injury. Traumatic retinal injury and glaucoma often impair the peripheral and paracentral retina. Our previous data have identified the glaucomatous eyeball expansion and pressure-induced malfunction in retinal ganglion cells and rod-drive AII amacrine cells. Our recent data generated a novel equation to describe the ocular mechanical hemostasis. Our recent studies attempt to address the function and variation of rod bipolar cells and ganglion cells, the signal integration among multiple photoreceptors in the secondary rod pathway, and a potential novel rod pathway formed by rod bipolar cells. I primarily use patch-clamping recording approaches in these studies, such as state-of-the-art dual-cell patch-clamping and the most advanced multi-cell patch-clamp techniques.

Oct. 12, 2023: Melanie Samuel, Ph.D.

Seminar Title: Neurons Are Not Alone: Surprising Regulators of Glia and Vessels in the Retina
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Melanie Samuel is an associate professor of neuroscience at Baylor College of Medicine. As a Barry M. Goldwater Scholar, she earned three bachelor's degrees from the University of Idaho and then completed her Ph.D. at Washington University in neuro-immunology with Michael Diamond. As a postdoctoral fellow with Joshua Sanes at Harvard University, she uncovered molecular pathways that determine neural resiliency. Dr. Samuel's interdisciplinary research group aims to decode the molecular regulators of neuron and glia interaction in order to understand mechanisms that may predispose the brain to diseases. Her past awards include those from the Howard Hughes Medical Institute, the Damon Runyon Cancer Research Foundation, the Brain Research Foundation, a Pathway to Independence Award from the NIH, the NIH Director's New Innovator Award, the Norton Rose Fulbright Award, a Mallinckrodt Scholar Award, and several active R01 awards.

Seminar Summary: The Samuel lab seeks to identify and understand the molecular mechanisms that govern information flow in the nervous system to repair these systems in disease. Much attention has been dedicated to solving the brain's 'connectome,' or street map. Equally important is understanding the road signs and signals that keep traffic (information) moving. This process occurs at synapses. These connections give meaning to the map and underlie all cognition, thought, and behavior. Because nearly all cognitive diseases involve declines in synapse function, deciphering synaptic regulators remains one of the most significant challenges in neuroscience. This talk will focus on surprising non-neuronal regulators of synapses and circuit function, microglia and the vasculature, that are often ignored in the context of wiring studies. Understanding the fundamental processes by which microglia and the vasculature regulate synapses will provide new intervention targets for treating neurological diseases, nearly all of which are accompanied by synapse dysfunction and loss.

Nov. 9, 2023: Anna Matynia, Ph.D.

Seminar Title: The Neural Circuits for Light-mediated Behavior Are More than Meets the Eye
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Anna Matynia is an associate professor in vision science at the University of Houston College of Optometry. She received her B.Sc. from Queen's University in Canada and her Ph.D. in cell biology from Baylor College of Medicine. She completed a postdoctoral fellowship in neuroscience at the University of California, Los Angeles in Dr. Alcino Silva's group. Dr. Matynia served as research faculty at the University of California, Los Angeles, at the Jules Stein Eye Institute, where she pioneered research into the neural pathways for photophobia. She currently has an RO1 and U01 grant from NEI, with her research focusing on neural circuits associated with clinically relevant disease or dysfunction in both the retina and cornea. The current funded projects in her laboratory are 1) investigating the role of melanopsin in retinal and trigeminal circuitry underlying photo allodynia (light-induced or -enhanced pain), 2) precision mapping of corneal afferents for blink, lacrimation and nociception, and 3) identification of early retinal biomarkers of neurodegeneration in Alzheimer's Disease.

Seminar Summary: Photoallodynia/photophobia is a clinical condition in which light-induced or -enhanced pain ranges from mild to severely debilitating. The neural pathways mediating photoallodynia were virtually unknown a decade ago. Dr. Matynia will present evidence from clinically relevant models that identifies both retinal and trigeminal contributions to photoallodynia, focusing on the role of melanopsin-expressing neurons. The identification of a specific cell population that contributes to corneal function raised the question of whether other corneal reflex pathways can be attributed to distinct neural circuits. Dr. Matynia will discuss current and future challenges in identifying these pathways.