2024 Vision Research Seminar Series

Jan. 11, 2024: Elizabeth Zuniga-Sanchez, Ph.D.

Seminar Title: Deciphering the Developmental Mechanisms of Retinal Circuit Assembly
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Elizabeth Zuniga-Sanchez is an assistant professor in the Department of Ophthalmology, with a joint appointment in the Department of Neuroscience at Baylor College of Medicine.

Seminar Summary: Normal vision relies on a precise number of different neuron subtypes coming together to form a functional circuit. However, the molecular basis of how different neuron subtypes become incorporated into a developing circuit remains understood. Our lab seeks to identify the key molecules responsible for proper neural circuit assembly using the mouse retina as a model system. In the mouse retina, bipolar neurons are interneurons that transmit visual information from photoreceptors to ganglion cells. To date, there are 15 different types of bipolar neurons that differ based on their gene expression profiles, morphology, and connectivity. During development, bipolar neurons are born in excess and, through programmed cell death, a specific number of each bipolar subtype remains to give rise to the retinal circuit. Although bipolar development has been well-described, little is known about the molecular mechanisms that mediate bipolar subtype integration. In this seminar, I will present data on how a non-clustered Protocadherin expression code may be responsible for assembling the precise number of each bipolar subtype into a developing circuit. Through this work, we aim to uncover general principles of how different neuron subtypes are assembled during development.

Feb. 8, 2024: Yang Sun, M.D., Ph.D.

Seminar Title: Inositol Metabolism and Eye Diseases
Time: 3 p.m., in-person only; Cullen Eye Institute Auditorium, NC202, 6565 Fannin St., Houston, TX

Speaker Bio: Dr. Yang Sun is a clinician-scientist in ophthalmology and a Professor and Vice Chair, Academic Affairs, of Ophthalmology at Stanford University and Byers Eye Institute. He is the Laurie Kraus Lacob Faculty Scholar at Stanford Child Health Research Institute. Dr. Sun received his BA in Biophysics from Johns Hopkins University, followed by MD and PhD degrees from Washington University School of Medicine. He completed

Ophthalmology residency at Stanford University and a prestigious Heed fellowship at the University of Michigan, Ann Arbor. Dr. Sun was an Assistant Professor at Indiana University, where he was promoted to an Associate Professor with tenure, before returning to Stanford University. He has been continuously funded by the National Eye Institute and the Veterans Administration. Dr. Sun's research in glaucoma has also been funded by the American Glaucoma Society, Lowe Syndrome Association, Knights Templar Eye Foundation, and Matilda Ziegler Foundation. Dr. Sun holds several U.S. patents on novel regulators of eye pressure and is the primary investigator on a number of glaucoma clinical trials. He is a member of Stanford BioX faculty, and he was elected as a member of the American Society of Clinical Investigators.

Seminar Summary: Phosphoinositides are involved in many cellular processes regulating various cellular functions, including signal transduction, membrane trafficking, and cell growth. Enzymes that control phosphoinositide levels are essential for normal development. Mutations in phosphoinositide 5-phosphatases can cause Lowe syndrome, Joubert syndrome, and Marinesco-Sjogren syndrome. We will discuss the role of these 5-phosphatases in congenital glaucoma, cataract and retinal degeneration.

March 21, 2024: Igor Butovich, Ph.D.

Seminar Title: A Concept of Meibogenesis
Time: 3 p.m. via Zoom or in person

Speaker Bio: Dr. Igor Butovich is an associate professor of ophthalmology at UT Southwestern Medical Center. His research focuses on the causes of, and finding the best treatment for, dry eye syndrome.

Seminar Summary: The goal of this seminar, "A Concept of Meibogenesis," is to discuss lipid homeostasis of the ocular surface in the norm and pathology. Meibogenesis is defined as an array of Meibomian gland-specific biosynthetic reactions, and corresponding regulatory and signaling mechanisms, that lead to formation of a lipid-rich holocrine secretion called meibum. Meibum is believed to form a protective layer that isolates the surface of the eye from detrimental environmental factors, and improves vision by changing the refractive properties of the cornea, though other possible functions of meibum are discussed in the literature as well. Meibum is comprised primarily of extremely long chain and branched compounds that belong to various lipid classes such as wax esters, cholesteryl esters, and a range of other complex lipids. In healthy age- and sex-matched subjects, the lipid composition of meibum is very conservative and changes only minimally from subject to subject. However, a MG pathology called MG dysfunction results

in dramatic quantitative and/or qualitative changes in meibum production, negatively affecting the ocular surface physiology, vision, and quality of life in general. MGD is a major contributing factor to a widespread condition called Dry Eye syndrome. The molecular mechanisms of the onset and progression of MGD are currently poorly understood, but believed to be of a multifactorial nature. In this seminar, we will discuss the history and recent advances in the area of MG biochemistry and physiology, as well as major bioanalytical approaches that have been developed to study meibogenesis in humans and experimental animals.

April 11, 2024: Rinki Ratnapriya, Ph.D.

Seminar Title: Using Functional Genomics to Identify the Mechanisms Underlying Age-related Macular Degeneration
Time: 3 p.m. via Zoom or in person

Speaker Bio: Dr. Ratnapriya is an assistant professor in the Department of Ophthalmology. She earned her B.Sc. from Delhi University in India and her Ph.D. in Human Genetics from JNCASR, India. She completed a postdoctoral fellowship in Ocular Genomics at the National Eye Institute in Dr. Anand Swaroop's group, where she utilized next-generation sequencing-based, genome-wide methods to understand the genetic basis of Mendelian and complex neurodegenerative diseases leading to vision loss in humans. She spearheaded a study analyzing the transcriptome and genetics of around 500 donor retinas to establish a reference of expression quantitative trait loci (EyeGEx) to close the knowledge gap between GWAS findings and causal variants, genes, and disease mechanisms. Her research program at BCM focuses on elucidating disease circuitry by extracting valuable information from large genomic, transcriptomic, and epigenetic datasets to address translational and bioinformatic challenges related to retinal and macular degenerative diseases. Additionally, she serves as a faculty mentor for the Data2Knowledge lab at Rice University, facilitating interdisciplinary collaboration among students and faculty to leverage data science for impactful research. She has been recognized with prestigious awards including the NEI Scientific Director's Award, NEI's Fellows Award for Research Excellence, David R. Hinton MD Scholarship, and Research to Prevent Blindness Career Development Award. Her research is presently supported by grants from the BrightFocus New Investigator Award, Research to Prevent Blindness Career Development Award, and Foundation Fighting Blindness Individual Investigator Award.

Seminar Summary: In contrast to the unprecedented success in identifying disease risk variants in Age-related Macular Degeneration by Genome-wide association studies, the

progress of elucidating the functional relevance of genetic findings in AMD has significantly lagged. This is mainly attributed to our limited understanding of the functional impact of associated, non-coding variants on gene function and the molecular mechanisms underlying the disease. Trait and disease-associated variants are enriched in the cis-regulatory elements. Thus, gene expression regulation has emerged as a reliable intermediatory between non-coding risk variants and disease phenotype. We focus on elucidating the disease circuitry by extracting valuable information from large genomic, transcriptomic and epigenetic data to connect AMD-GWAS loci to causal variants, target genes and underlying mechanisms. The long-term goal for this research is to leverage the ever-expanding field of data science and genomics to translate the genetic findings in AMD for improving disease diagnosis, management and therapy.

July 18, 2024: Stephen Pflugfelder, M.D.

Seminar Title: How Does Dry Eye Inflammation Start?
Time: 3 p.m. via Zoom

Speaker Bio: Dr. Stephen Pflugfelder is a professor and James and Margaret Elkins Chair in Ophthalmology. His clinical activity and scientific research focus on corneal diseases, including dry eye syndrome.

Seminar Summary: Ocular surface dryness is a potent danger signal that stimulates CCL2-mediated monocyte recruitment from the blood. Depending on levels of inflammation and conditioning factors in the environment, these cells will transition to regulatory or inflammatory macrophages. Regulatory macrophages maintain immune tolerance by phagocytosing foreign antigens and apoptotic cell products, whereas inflammatory macrophages produce cytokines and chemokines that cause neural sensitization and amplify the immune reaction by activating dendritic cells and resident innate lymphocytes (gamma delta T cells, NK) and priming autoreactive T cells. Genetic factors in systemic autoimmune diseases may heighten monocyte recruitment and production of inflammatory mediators. Certain dry eye therapies can modulate monocytes to regulatory macrophages.

Aug. 8, 2024: Wenbo Zhang, Ph.D.

Seminar Title: The role of cAMP/Epac in Retinal Ischemic Retinopathy
Time: 3 p.m. via Zoom and in person (hybrid)

Speaker Bio: Dr. Wenbo Zhang is a professor of ophthalmology and visual sciences at the University of Texas Medical Branch at Galveston. His research focuses on molecular mechanisms of retinal injury in ischemic retinopathy, such as diabetic retinopathy, retinopathy of prematurity and glaucoma.

Seminar Summary: Ischemic retinopathy, such as diabetic retinopathy, retinopathy of prematurity, glaucoma and retinal vessel occlusions, causes blindness and affects the life quality of millions of patients. Each of these conditions is associated with both retinal neuronal and vascular injury, which have a profound effect on each other. Yet, current management for these conditions fails to directly address the problem of retinal neuronal injury, which occurs at an early stage of the disease, and treatments for retinal neovascularization do not enhance vascular repair. The exchange proteins directly activated by cyclic AMP (Epac) are novel mediators of cAMP, one of the most common second messengers involved in pathophysiological conditions. In our research, we identified that the cAMP/Epac pathway was an interesting potential target for the treatment of ischemic retinopathy.

Sept. 12, 2024: Yang Hu, M.D., Ph.D.

Seminar Title: Neural Repair of Glaucomatous RGC and Optic Nerve
Time: 3 p.m. via Zoom and in-person (hybrid)

Speaker Bio: Dr. Hu received his M.D. from Beijing Medical University, China and did ophthalmology residency in Beijing Friendship Hospital. He then acquired a Ph.D. in neuroscience from Cornell University Medical College and did a postdoc fellowship with Dr. Zhigang He at Harvard Medical School in axon regeneration and neuroprotection. He is a tenured professor at Stanford University Department of Ophthalmology, and his lab focuses on the molecular mechanisms responsible for retinal ganglion cell (RGC) and optic nerve degeneration after injury or diseases, with the goal of building on this understanding to develop effective combined neural repair strategies to promote CNS neuroprotection, axon regeneration and functional recovery. He has been awarded the Douglas Johnson Award for Glaucoma Research from BrightFocus Foundation, the William & Mary Greve Special Scholar Award, the Stein Innovation Award from Research to Prevent Blindness, and Catalyst for a Cure Research Consortium-3 from Glaucoma Research Foundation.

Seminar Summary: Axonopathy is a common early feature of central nervous system (CNS) neurodegenerative diseases. That there is no curative neuroprotective or restorative regeneration therapy for CNS neurodegeneration is a central challenge for human health. My lab emphasizes understanding fundamental molecular mechanisms responsible for

neuronal soma and axon degeneration, while maintaining a consistent focus on clinically relevant scenarios that will allow us to translate lab discoveries into effective neuroprotection and regeneration treatments for CNS axonopathies. Specifically, we exploit the anatomical and technical advantages of the mouse retinal ganglion cells (RGCs)/optic nerve system to study optic neuropathies, especially glaucoma, the leading cause of irreversible blindness. RGC is the only neuronal type to relay visual information from the retina to the brain through the optic nerve, which is formed by projection axons sent exclusively from RGCs and conveniently separated from RGC somata in the inner retina. This distinct anatomical compartmentalization provides a relatively simple but robust in vivo model for cutting-edge subcellular manipulation/tracing/imaging, straightforward interpretation of RGC soma and axon degeneration, and definitive assessment of neural repair treatments. I have chosen to work on three fronts that need breakthroughs to achieve our long-term goal: 1) Develop clinically relevant animal glaucoma models that faithfully replicate human diseases, which will enable us to better understand glaucomatous neurodegeneration and discover translatable neural repair strategies; 2) Develop imaging-based in vivo RGC/optic nerve neuronal function/activity, morphology and metabolism assays to longitudinally analyze the progression of degeneration and responses to neuroprotection and regeneration treatments; 3) Identify potent neuroprotection and regeneration targets by innovative genetic screening and develop specific and effective gene and small molecule therapies. We have made significant progress on all three fronts that I will share with the audience.

Oct. 10, 2024: Stan Louie, PharmD

Seminar Title: The Use of Lipidomics in Ocular and Neurodegenerative Disease
Time: 3 p.m. via Zoom and in-person (hybrid)

Speaker Bio: Stan Louie is Professor of Pharmacy at Alfred Mann School of Pharmacy and Pharmaceutical Sciences, University of Southern California. He is the Director of the Clinical Experimental Therapeutics (CXPT) graduate program, and the Deputy Director of the Ginsburg Institute of Biomedical Therapeutics. Currently, his research focus is understanding the molecular mechanism(s) associated with inflammation and molecular mechanisms promoting tissue resolution, focusing on the RAS and bioactive lipid pathways.

Seminar Summary: His lecture will illustrate how to use functional targeted lipidomics to dissect the molecular mechanism(s) of ocular diseases and their translation to neurodegenerative diseases as well. In particular, he will highlight how to use these

datasets to unveil hidden molecular pathogenesis and the development of effective strategies that are able to treat progressive ocular diseases.

Nov. 21, 2024: King-Wai Yau, Ph.D.

Seminar Title: Dark Noise from Visual Pigments
Time: 3 p.m. via Zoom and in-person (hybrid)

Speaker Bio: Dr. King-Wai Yau was born in South China and grew up in Hong Kong. After high school and a year of medical school at the University of Hong Kong, he came to the US in 1968, receiving a B.A. in physics from Princeton University in 1971 and a PhD in neurobiology from Harvard University in 1975. After postdoctoral work with Denis Baylor at Stanford and with Sir Alan Hodgkin at Cambridge, UK, he became Assistant Professor of Physiology and Biophysics at the University of Texas Medical Branch at Galveston in 1980. He relocated to Johns Hopkins University School of Medicine in 1986 as a Howard Hughes Medical Institute Investigator and Professor of Neuroscience. He has been there since.

Dr. Yau is a Member of the National Academy of Sciences and the National Academy of Medicine, and a Fellow of the American Academy of Arts and Sciences, as well as a Member of Academia Sinica, Taiwan. He has won numerous prestigious awards in vision research, including the ARVO Friedenwald Award, the António Champalimaud Vision Award, the Beckman-Argyros Award, the Helen Keller Prize, the RRF Paul Kayser International Award, the CNIB Chanchlani Global Vision Research Award, the Balazs Prize, the Alcon Award in Vision Research (twice), the Ruth and Milton Steinbach Award, the Magnes Prize, the MERIT Award, and the Rank Prize in Optoelectronics.

Seminar Summary: The talk will be about Dr. Yau's very recent work on dark noise from rod/cone visual pigments in health and in disease.

Dec. 12, 2024: Seth Blackshaw, Ph.D.

Seminar Title: Building and Rebuilding the Retina One Cell at a Time
Time: 3 p.m. via Zoom and in-person

Speaker Bio: Dr. Seth Blackshaw received his B.A. and M.S. in biochemistry in 1991 and his Ph.D. in neuroscience from Johns Hopkins School of Medicine in 1997, working with Solomon Snyder. He performed postdoctoral research with Connie Cepko at Harvard Medical School, and was appointed Assistant Professor of Neuroscience at Johns Hopkins

School of Medicine in 2004, where he is now a full Professor. His research has focused on the regulation of cell fate specification and neuronal regeneration in the retina and hypothalamus, hypothalamic regulation of innate behaviors, and the development of new tools for functional proteomics. He has published over 200 peer-reviewed articles and has received numerous awards, including the Sloan Foundation Research Fellowship, the Esther A. and Joseph Klingenstein Fellowship in the Neurosciences, and the W. M. Keck Foundation Distinguished Young Scholar in Medical Research Award.

Seminar Summary: I will discuss our lab's use of single-cell multiomics to analyze vertebrate retinal neurogenesis, regeneration, and the gene regulatory networks that govern these processes. I will present insights we've gained into evolutionarily-conserved mechanisms controlling temporal patterning and cell fate specification in retinal progenitors, and show how these mechanisms have been adapted to drive the development of the cone-dominant retina of the 13-lined ground squirrel. I will close with a discussion of how we have applied similar approaches to identify molecular mechanisms controlling and restricting injury-induced reprogramming of Müller glia into neurogenic progenitors, and how we have used this to induce robust levels of glial-derived neurogenesis in mammalian retina.