

Therapeutic Strategies for Large Protein Coding Genes in Usher Syndrome Virtual Meeting Thursday-Friday May 13-14, 2021

Day 1: Thursday May 13, 2021

Session 1: Genetic Interventions for Protocadherin 15 Related Disorders (Usher 1F)

8:15 Elliot Chaikof introduces Alex Hewitt

Alex Hewitt, MD, PhD is a Professor of Ophthalmology at the Menzies Institute for Medical Research at the University of Tasmania in Australia. He received his MD from the University of Tasmania, his PhD from the Flinders University of South Australia and completed a residency in ophthalmology at the Royal Victorian Eye and Ear Hospital in Melbourne after which he was a Novartis Research Fellow at the Lions Eye Institute in Perth Australia. Prof. Hewitt's research interests lie in the genetics of a wide range of ocular disorders, including glaucoma and retinitis pigmentosa, as well as in the application of stem cell-based models of eye disease and the development of genetic therapies.

8:45 Alex Hewitt introduces Livia Carvalho

Livia Carvalho, PhD leads the Retinal and Genomic Therapies Research Group at the Lions Eye Institute in Perth Australia. After completing a BSc in Biological Sciences from the University of Brasilia, she pursued further studies in the UK, completing a Masters in Neuroscience and a PhD in Genetics at the University College London Institute of Ophthalmology. Following additional postdoctoral studies in the areas of inherited degenerative eye diseases and ocular gene therapy at UCL and Harvard, she joined the Lions Eye Institute. Prof. Carvalho's research program focuses on the development of therapies for inherited vision loss, including Usher Syndrome, using AAV technologies, as well as investigating basic cellular and molecular mechanisms responsible for vision loss.

9:15 Alex Hewitt introduces Zubair Ahmed

Zubair Ahmed, PhD is Professor Otorhinolaryngology-Head & Neck Surgery at the University of Maryland. Prof. Ahmed was a postdoctoral fellow with Tom Friedman in the Laboratory of Molecular Genetics at the NIDCD, as a member of team that first identified the R245X mutation in PCDH15 as a frequent cause of Usher 1F Syndrome. Prof. Ahmed's research program seeks to understand how the retinal and inner ear sensory epithelia develop and function to improve our understanding of these organs at the molecular level. His studies in both Usher syndrome and oculocutaneous albinism aim to decipher the pathophysiology of these disorders in animal models for the purpose of developing new strategies to prevent and treat these neurosensory disorders.

Session 2: Optimizing Effectiveness and Safety of Therapeutic Interventions

10:00 Kris Saha introduces Connie Cepko

Connie Cepko, PhD is Bullard Professor of Genetics and Neuroscience at Harvard Medical School and a Howard Hughes Investigator. She was a doctoral student with Phil Sharp at MIT and pursued postdoctoral studies with Richard Mulligan at the Whitehead Institute. Prof. Cepko helped develop retroviral vectors for transduction into the nervous system for lineage analysis and studies of in vivo gene function. Her laboratory has focused on the topic of cell fate determination in the retina through the analysis of the behavior of progenitor and stem cells. More recently, she has been studying mechanisms of photoreceptor death in retinitis pigmentosa and macular degeneration with efforts to develop gene therapy using AAV vectors to provide greater cone survival.

10:30 Elliot Chaikof introduces Kris Saha

Kris Saha is Associate Professor of Biomedical Engineering at the University of Wisconsin-Madison and holds the Kathryn and Latimer Murfee Chair in the McPherson Eye Research Institute. Kris also currently serves as the Chair of the NIH Somatic Cell Genome Editing Consortium and an active member of the NSF Center for Cell Manufacturing Technologies at the University of Wisconsin. He completed his PhD at Berkeley and a postdoctoral fellowship with Rudolf Jaenisch at the Whitehead Institute. His research is directed at gene editing and cell engineering of human cells found in the retina, CNS, liver, and blood. Prof. Saha is a member of the National Academies' Forum on Regenerative Medicine.

11:00 Kris Saha introduces Budd Tucker

Budd Tucker, PhD is the Howard Ruby Chair for Regenerative Ophthalmology and Professor of Ophthalmology and Visual Sciences at the University of Iowa. Prof. Tucker received his Ph.D. in neuroscience and subsequently pursued postdoctoral training with Michael J. Young at the Schepens Eye Institute at Harvard Medical School. At the University of Iowa, Prof. Tucker is the director of both the DeZii Translational Vision Research cGMP Facility and the Ruby Retinal Engineering Laboratory, where he is focused on development of gene augmentation and autologous cell replacement strategies for the treatment of heritable retinal degenerative blindness.

11:30 Kris Saha introduces Alberto Auricchio

Alberto Auricchio, MD is Professor of Medical Genetics at the University in Naples, and Coordinator of the Molecular Therapy Program at Telethon Institute of Genetics and Medicine (TIGEM), which includes 18 research groups dedicated to understanding the molecular mechanisms of rare genetic diseases. Prof. Auricchio's research is focused on gene therapy of retinal and metabolic diseases using AAV vectors. His group contributed to the Phase I/II clinical trial of Luxturna, the first approved gene therapy drug for an ocular disease and to the development of gene therapy for mucopolysaccharidosis VI. In 2019 Prof. Auricchio received the International Prize for Scientific Research honoring the memory of pharmaceutical entrepreneur Arrigo Recordati, in recognition of his work in Orphan diseases.

Session 3: Animal Models of Protocadherin 15 Related Disorders (Usher 1F)

1:00 David Corey introduces Vince Tropepe

Vince Tropepe, PhD is Professor in the Department of Cell & Systems Biology, as well as in the Department of Ophthalmology at the University of Toronto and a member of the Ontario Institute for Regenerative Medicine. He also serves as Vice-Dean of Research in the Faculty of Arts & Science. Prof. Tropepe completed his Ph.D. in Developmental Biology at the University of Toronto studying neural stem cells in the developing and adult mouse brain and retina and, subsequently pursued a postdoctoral fellowship at the Whitehead Institute. His research interests are focused on the molecular and cellular mechanisms of neurogenesis and neurogenic plasticity during development and in the context of retinal disease and regeneration.

1:30 David Corey introduces Monte Westerfield

Monte Westerfield, PhD is Professor of Biology and a member of the Institute of Neuroscience, University of Oregon and Director of the Zebrafish International Resource Center and ZFIN, the zebrafish model organism database. Prof. Westerfield completed doctoral studies in Physiology and Pharmacology at Duke and was a Fulbright Scholar at the Max Planck Institute in Munich, Germany and Neurobiology at Harvard Medical School. He has served as Director of the Institute of Neuroscience at the University of Oregon and on advisory councils to the NIDCD. He has been the recipient of Sloan, Fogarty and Guggenheim Fellowships, the Talbot Award, and the Von Humboldt Prize, and is a Fellow of the AAAS. Prof. Westerfield studies the molecular genetics of Usher syndrome.

2:00 Elliot Chaikof introduces David Corey

David P. Corey, PhD is the Bertarelli Professor of Translational Medical Science in the Department of Neurobiology at Harvard Medical School. Prof. Corey received a Ph.D. in neurobiology from Cal Tech, followed by a postdoctoral fellowship at Yale, and continued his career at Harvard Medical School, the Massachusetts General Hospital, and as a Howard Hughes investigator. Prof. Corey has defined the mechanisms of hair-cell mechanotransduction that have led to fundamental advances in our understanding of auditory system function at the cellular and molecular level using methods ranging from single-cell electrophysiology to single-molecule force spectroscopy to cryo-EM. He has developed methods for gene therapy in the inner ear and, more recently for inherited eye diseases. Prof. Corey is a member of the American Academy of Arts & Sciences.

Session 4: Perspectives on Therapeutic Options for Retinitis Pigmentosa and Usher Syndrome

2:45 Elliot Chaikof introduces Jacque Duncan

Jacque Duncan, MD is Professor of Ophthalmology and Director of the Retinal Degenerations Clinic and Retinal Electrophysiology Laboratory at UCSF. Dr. Duncan serves as Chair of the FFB Scientific Advisory Board Chair and Executive Committee Chair for the FFB Clinical Consortium. She leads the Consortium RUSH2A natural history study of the rate of progression in USH2A-related retinal degeneration. Prof. Duncan received her MD and completed a residency in ophthalmology at UCSF, followed by a medical retina fellowship at the University of Pennsylvania, before returning to UCSF. Dr. Duncan has participated in numerous clinical trials focused on retinitis pigmentosa and macular degeneration, as well as trials of the Argus 2 retinal prosthesis and as a member of the Data Safety Monitoring Committee for numerous trials of gene therapies for retinal degeneration. Her studies have led to improved strategies to quantify cone photoreceptor integrity and novel outcome measures for monitoring disease progression.

3:15 Elliot Chaikof introduces Gwenn Geleoc

Gwenn Géléoc, PhD is Professor at Harvard Medical School and Co-Director of the Holt/Géléoc Lab at Boston Children's Hospital. She obtained a PhD in Sensory Neurobiology from the University of Sciences in Montpellier, followed by postdoctoral fellowships at the University College London and at Harvard Medical School with Professor David Corey. Prof. Geleoc studies the development of inner ear hair cells to unravel the role of deafness genes associated with hair cell function and more precisely mechano-electrical transduction and voltage dependent channels shaping the hair cell receptor potential. She is developing new therapies, including gene replacement therapy, for the treatment of deafness and balance, with a particular focus on Usher syndrome.

Session 5: Tools for Genome Repair

3:45 Elliot Chaikof introduces David Liu

David R. Liu, PhD is the Richard Merkin Professor and Director of the Merkin Institute of Transformative Technologies at the Broad Institute, the Thomas Dudley Cabot Professor at Harvard University, and a Howard Hughes Medical Institute investigator. Prof. Liu completed his doctoral studies at Berkeley before joining the faculty in the Department of Chemistry and Chemical Biology at Harvard. Dr. Liu's research integrates chemistry and evolution to illuminate biology and enable next-generation therapeutics. Base editing, prime editing, PACE, and DNA-templated synthesis are four examples of technologies pioneered in his laboratory. He is a member of the National Academy of Medicine and the National Academy of Sciences and the scientific co-founder of Editas Medicine and Beam Therapeutics, among others.

4:15 Elliot Chaikof introduces Erik Sontheimer

Erik Sontheimer, Ph.D., is Professor of RNA Therapeutics and Molecular Medicine at the University of Massachusetts and holds the Pillar Chair in Biomedical Research. Prof. Sontheimer earned his Ph.D. from Yale, followed by postdoctoral studies at the University of Chicago. His long-term research focus has been on the roles of RNA molecules in regulating genome function, including CRISPR RNA-guided immune systems in bacteria and their applications in genome engineering. Among other advances, in 2008 his group demonstrated that CRISPR systems target DNA molecules directly, and was the first to recognize and articulate CRISPR's potential for genome engineering laying the groundwork for the CRISPR revolution in gene therapy. Dr. Sontheimer is a co-founder of Intellia Therapeutics and served as the inaugural Chair of the NIH Somatic Cell Genome Editing Consortium.

Day 2: Friday May 14, 2021

Session 6: Clinical Trials for Usher Syndrome (ASL interpreted)

8:30 Elliot Chaikof introduces Katarina Stingl

Katarina Stingl, MD is the Head of the Clinical Unit for Retinal Degenerations and Rare Eye Diseases and Head of the Research Lab for Retinal Functional Diagnostics at the University of Tübingen in Germany. Prof. Stingl received her MD and completed her clinical training at the University of Tübingen. She is the lead clinical investigator for **RUSH1F**, the multicenter Usher 1F natural history study. Prof. Stingl's clinical and scientific focus is in the area of retinal functional diagnostics and electrophysiology of vision, hereditary retinal degenerations, orphan eye diseases, and neuroprosthetics. She is a member of the European Reference Network for Rare Eye Diseases.

9:00 Elliot Chaikof introduces Francesca Simonelli

Francesca Simonelli, MD is Professor of Ophthalmology at the University of Campania in Naples. She received her MD degree from the University of Naples, where she also completed a residency in ophthalmology. Prof. Simonelli is President of the Italian Society of Ophthalmologic Genetics, a member of the Telethon Institute of Genetics and Medicine, of the National Fighting Blindness Committee of the Italian Ministry of Health. Prof. Simonelli currently is the lead clinical investigator for the Usher 1B natural history study.

Session 7: Cadherin 23 Related Disorders (Usher 1D)

9:30 Elliot Chaikof introduces Andrea Maddalena

Andrea Maddalena, PhD studied biotechnology at the University of Padova, completed a Masters at the University of Geneva and a PhD at the University of Göttingen on AAV-based gene therapy for Parkinson's disease. Dr. Maddalena served as a member of the Telethon Institute of Genetics and Medicine (TIGEM) in Naples, Italy, where he pursued the development of AAV-based gene therapy for retinal disease, specifically Usher syndrome and currently working with Prof. Sonja Kleinlogel, as a member of the Translational Optogenetics Group in the Department of Physiology at the University of Bern. Dr. Maddalena is applying CRISPR/Cas technology to introduce genes encoding light-sensitive proteins in order to transform retinal neurons into photoreceptor-like cells.

Session 8: Usherin Related Disorders (Usher 2A)

10:15 Erwin Van Wyk introduces Qin Liu

Qin Liu, MD, PhD is an Assistant Professor of Ophthalmology at Harvard Medical School and a member of the Ocular Genomic Institute at the Massachusetts Eye and Ear. Prof. Liu trained as an ophthalmologist and received her PhD in Molecular Ophthalmology from Peking Union Medical College. She subsequently pursued postdoctoral training at the Kirby Center for Molecular Ophthalmology at the University of Pennsylvania studying the molecular mechanisms of inherited retinopathies using a combination of genetically modified animal models and molecular biological approaches. Prof. Liu's current research program is focused on developing therapeutics for inherited retinal diseases, particularly those caused by mutations in large genes, using CRISPR/Cas9-based gene editing technologies.

10:45 Elliot Chaikof introduces Erwin Van Wyk

Erwin Van Wijk, PhD is an Assistant Professor in the Donders Institute for Brain, Cognition, and Behavior at Radboud University in Nijmegen, the Netherlands, where he directs the Usher Syndrome Therapeutics Research Unit. Following the completion of his doctoral studies focused on the USH2A-associated protein network and a postdoctoral fellowship at Johns Hopkins, Prof. Van Wijk joined faculty at Radboud University with a focus on defining the pathogenic mechanisms underlying Usher syndrome and associated inherited disorders using the combination of proteomics and zebrafish models. Prof. van Wijk is developing genetic therapies for USH2A-associated retinal degeneration, including antisense therapies to correct aberrant splicing and frame skipping. His work led to the development of QR-421a, a first-in-class RNA therapy for Usher Syndrome 2A, licensed to ProQR Therapeutics, with promising results in the Phase I/II Stellar trial.

11:15 Erwin Van Wyk introduces David Birch

David Birch, PhD is Scientific Director of the Rose-Silverthorne Retinal Degenerations Laboratory at the Retina Foundation of the Southwest in Dallas Texas. Dr. Birch received his PhD at the University of California, Santa Barbara and trained with Eliot Berson at the Berman-Gund Laboratory at Harvard Medical School before joining the Retina Foundation of the Southwest. He has had continuous funding from the National Eye Institute to pursue research into the causes and effects of inherited retinal degeneration and macular degeneration. Through translational and clinical studies, Dr. Birch's work has been at the forefront of efforts to improve functional outcome measures including the establishment of the Southwest Eye Registry, a unique genetic database of over 4000 patients with inherited retinal diseases.

1:00 - 2:30 PM Session 9: Myosin7A Related Disorders (Usher 1B)

1:00 Elliot Chaikof introduces David Williams

David Williams, PhD is Professor of Ophthalmology and Neurobiology at the Stein Eye Institute at UCLA. He received his Ph.D. in Neurobiology at the Australian National University and pursued postdoctoral studies in retinal cell biology at the University of California, Santa Barbara. Prof. Williams investigates photoreceptor cells and the associated retinal pigmented epithelium in health and in disease. His research team has been involved in defining the cellular basis of retinal degeneration in Usher syndrome, choroideremia, and macular degeneration, including preclinical gene therapy studies for Usher syndrome 1B.

1:30 David Williams introduces Mark Pennesi

Mark Pennesi, MD, PhD, is an Associate Professor of Ophthalmology and Chief of the Paul H. Casey Division of Ophthalmic Genetics at Oregon Health & Science University, where he also holds the Kenneth Swan Endowed Professorship. Dr. Pennesi pursued an MD-PhD at Baylor College of Medicine, which was followed by a residency in Ophthalmology at UCSF. Dr. Pennesi is developing novel therapeutic regimens for inherited retinal diseases and is the PI or Co-PI on numerous clinical trials including gene augmentation therapy for Type 1B Usher syndrome and X-linked retinitis pigmentosa, as well as antisense therapies for USH2A-related retinopathy, among many others trials. He is also the PI on the Allergan-Editas Brilliance trial where in March 2020, the first patient was treated with in vivo CRISPR gene editing; in this instance for Leber congenital amaurosis 10, a CEP290-related retinopathy.

2:00 David Williams introduces Wade Chien

Wade Chien, MD is an Associate Professor in the Department of Otolaryngology-Head and Neck Surgery at Johns Hopkins. Prof. Chien received his MD from the University of Southern California, completed a residency in otolaryngology at Harvard, and a neurotology fellowship at the Johns Hopkins. In 2011, Prof. Chien joined the NIDCD as an investigator in the inner ear gene therapy program. His laboratory, as part of the NIDCD Otolaryngology Surgeon-Scientist Program, is focused on developing gene therapy as a treatment option for hereditary hearing loss, including the application of genome editing and AAV based technologies.

Session 10: Development of Precision Drugs

2:30 Elliot Chaikof introduces Kate Zhang

Kate Zhang, PhD is Vice President for Biological Development at Editas Medicine. Dr. Zhang joined Editas in 2018 and is responsible for leading translational science and early- and late-stage biological development. Prior to joining Editas Medicine, Dr. Zhang spent more than 20 years at Genzyme/Sanofi, leading multiple teams in Protein and Cell Therapeutic Development to support approval and commercialization of multiple biologics, including Cerezyme, Fabrazyme, Myozyme for Gaucher, Fabry and Pompe diseases, respectively. She subsequently served as head of global translational science responsible for rare diseases. Dr. Zhang graduated from Tsinghua University and received a PhD in Biochemistry at Queen's University, followed by postdoctoral studies at the NIH.

3:00 Elliot Chaikof introduces Naveed Shams

Naveed Shams, MD, PhD is the Chief Scientific Officer at ProQR Therapeutics in Leiden, the Netherlands. Prior to joining ProQR, Dr. Shams was Chief Scientific Officer at Santen, a global ophthalmology company with over 20 years of experience in global drug development, including Novartis and Genentech/Roche. He has played a significant role in developing important ophthalmology products, including Zaditor®, Rescula®, and Lucentis®. Dr. Shams received his MD degree from Dow Medical College in Pakistan and his PhD from the University of South Carolina. Dr. Shams served as a member of the faculty at Schepens Eye Research Institute and the Department of Ophthalmology at Harvard.

3:30 Elliot Chaikof introduces Matthew Goddeeris

Matthew Goddeeris, PhD is Head of Rare Disease Research at Eloxx Pharmaceuticals exploring the application of read-through molecules to identify compounds for the treatment of genetic diseases. Eloxx is currently conducting two Phase 2 clinical trials of its lead molecule, ELX-02, in individuals with nonsense-mediated cystic fibrosis. Dr. Goddeeris earned his PhD from Duke University in Cell and Developmental Biology and pursued postdoctoral studies with Kevin Campbell at University of Iowa investigating muscular dystrophy. He has led small molecule drug discovery programs directed at improving mitochondrial function in rare muscle and metabolic disorders, initially at Mitobridge and subsequently at Astellas.