

Author Ricki Lewis so graciously took notes from presentations at the CRB1 Research Symposium hosted by the Curing Retinal Blindness Foundation on Saturday, March 23, 2013 in Philadelphia, Pennsylvania, USA.

Below is a list of the presenters. Click on the presenter name to see notes on their presentation.

INTRODUCTION:

The Curing Retinal Blindness held its first annual research conference at Shriner's Pediatrics Hospital at Temple University School of Medicine on March 23, 2013. Mickey Selzer, MD, PhD, professor of neurology at Temple opened the meeting:

“Families of affected children yearn for a cure. Scientists are trained to revere the basic science, what we learn from disease. But scientists hunger to see their work translated into practical things that help people. We hope both the families trying to raise money and the scientists trained in ivory towers have a common goal of seeing a blueprint to developing a treatment in animals and translating it into a clinical trial.”

Kristin Smedley introduced Irene Maumenee, MD, Research Professor of Ophthalmology at the University of Illinois. “Dr. Maumenee was the first person we were referred to 13 years ago when Michael was diagnosed. In 2009 researchers found our gene, just when the *RPE65* gene therapy was hitting the news. Last summer, when we were ready to start moving forward, we saw her at the LCA conference and asked her to help us,” she said.

Irene Maumenee, MD Research Professor of Ophthalmology, [Pediatric & Adult Strabismus Service](#), Director, Ocular Genetics Laboratory, University of Illinois, Chicago

Dr. Maumenee is board certified in ophthalmology and medical genetics. She is the co-founder and president of the International Society for Genetic Eye Diseases. Her clinical and research interests are in the classification and management of hereditary ocular diseases, population genetics, and molecular genetics. She has been recognized by the AAO with their Senior Honor Award. She joined the faculty in 2008.

Stephen Tsang, M.D. Ph.D. Associate Professor of Pathology & Cell Biology and Ophthalmology, Columbia University, New York

Dr. Stephen Tsang's research efforts are to find new treatments for photoreceptor degeneration in retinitis pigmentosa (RP), age-related macular degeneration (AMD) and related retinal dystrophies, the most common forms of degenerative disease in the central nervous system and have profound impact on quality of life. “Our research paves the way toward "retinoplasty," reconstruction of interfaces between photoreceptors and their environment after the onset of retinal degeneration. Our approach involves the culture of human retinal stem cells from the ciliary body in eye-bank globes, and using those cultured cells to determine the combination of transcription factors involved in regulating their proliferation and differentiation into light-sensing photoreceptor neurons. These

experiments will identify the effectors regulating human retinal stem cell differentiation and proliferation, as well as testing the ability of in vitro generated stem cells to repopulate the diseased retina. Future applications may include patient-specific stem cells obtained from fine-needle aspiration of their ciliary bodies in the operating room. Based on our findings, we foresee the ability to manipulate the patients' own stem cells to cure their specific disease. This approach will solve the problem of limited supply of allograft rejection by using a patient's own cells.”

Patty Nishina, PhD, Professor, The Jackson Laboratory

Mouse models of vision research have been instrumental in identifying primary mutations within genes that lead to ocular disorders and in identifying pathways important in retinal function through modifier screens, protein, and expression profiling. Our program is dedicated to identifying genes which when mutated lead to ocular diseases, to identify mechanisms underlying the function of those genes as well as the resulting pathological changes. The models are derived both from spontaneous mutations as well as chemical mutagenesis screens. Our lab focuses primarily on genes affecting the neural retina and supporting structures such as the retinal pigmented epithelium, glial cells and vascular network.

Anand Swaroop, PhD, Chief, Neurobiology-Neurodegeneration and Repair Laboratory, National Eye Institute, Bethesda, Maryland

Dr. Swaroop is investigating how stem cells develop into nerve cells (particularly photoreceptors) in the retina, how these neurons connect to each other, and how they become dysfunctional or die during aging or in disease conditions. His goal is to use this understanding of biological pathways of differentiation, homeostasis, aging, and disease pathogenesis, to develop new treatments for blinding retinal conditions. Dr. Swaroop has authored over 200 peer-reviewed research papers that have appeared in journals such as the *Proceedings of the National Academy of Sciences*, *Nature Genetics*, and the *New England Journal of Medicine*. He has also served as a reviewer of scientific publications for major journals, including *Science* and *Cell*.

**Seo-Hee Cho, PhD, Assistant Professor, Anatomy and Cell Biology
Assistant Professor, Shriners Hospitals Pediatric Research Center, Temple University, Philadelphia**

Dr Cho's research goal is to understand the molecular and cellular mechanisms underlying normal development and degenerative retinal diseases, and to establish the intervening strategies. Topics we currently study include: (I) Functional analysis of apical polarity gene *Pals1* during retinal and lens development, (II) Pathophysiological study of degenerative retinal diseases, LCA (Leber Congenital Amaurosis) and RP (Retinitis Pigmentosa), to understand disease-causing mechanisms. We are particularly interested in polarity defects in retinal progenitor cells, which cause early-onset, photoreceptor degeneration in LCA type 8, (III) Cell-transplantation and gene-based therapies to restore vision loss in LCA8-like mouse models in animal settings, (IV) Investigating the function of tumor suppressor-oncogene signal transduction pathways, TSC2-mTOR and Hippo-Yap, in eye development. Fundamental questions that we are trying to answer through these studies include, but are not limited to: (1) How is organ size determined?

How are cellular contact inhibition signals translated and coordinated to cell proliferation activity in the nucleus? (2) How is cell size determined? How are differential cell sizes achieved and maintained? (3) What are the functions of the apical polarity complex during CNS development? (4) Can visual impairment in degenerative retinal diseases be rescued by gene- or cell-based therapies? Currently, we are using a combination of molecular and cellular methods, high-throughput (microarray), imaging (including confocal and multi-photon) and mouse genetics approaches (including conditional knock-out technology).

Curt Scribner, MD, MBA, Senior Vice President of Medical and Regulatory Affairs, RRD International, California

Dr. Scribner is Senior Vice President of Medical and Regulatory Affairs at RRD International, LLC. Dr. Scribner is a board certified physician in internal medicine and has direct experience running large clinical programs. He joined RRD from Intarcia Therapeutics, where he was the Vice President of Regulatory and Quality Affairs and Chief Regulatory Officer. Previously, Dr. Scribner was Chief Regulatory Consultant for Quintiles Consulting, where he developed and wrote numerous NDA, BLA, IND, IDE, 510(k), PMA, and MAA applications. Prior to Quintiles Consulting, Dr. Scribner spent 10 years at FDA, where he held a variety of positions and was involved in reviewing products regulated by the Center for Biologics. Dr. Scribner holds an MD from the University of Colorado College of Medicine, an MBA from the University of Maryland College of Business and Management, and a BA in biology from Grinnell College.

Leonide Saad, PhD, President and Chief Executive Officer, Alkeus Pharmaceuticals Inc., Boston

Dr. Saad founded Alkeus Pharmaceuticals with the goal of developing sight-saving, transformative medicines for the most serious and untreatable causes of blindness. Prior to Alkeus, he was partner in a boutique life sciences management and consulting firm in New York City, providing business and strategic guidance to biotechnology and pharmaceutical companies. He was previously at Proteus Venture Partners, an early stage, California based venture fund focused on stem cells and regenerative medicine.

Dr. Saad holds a PhD focused on tissue engineering from MIT, a certificate of Financial Technology from MIT Sloan School of Management, a MS in Mechanical Engineering from MIT, a BS and MS in Applied Mathematics from University of Paris VI, and is a graduate from Ecole Polytechnique, Paris, with a concentration in organic chemistry and physics.

Daniel Chung, DO, MA, senior research investigator, FM Kirby Center for Molecular Ophthalmology of the Scheie Eye Institute at the University of Pennsylvania School of Medicine, Clinical Investigator in the CHOP/Penn RPE65 LCA Gene Therapy Clinical Trial Team.

Dr. Chung endeavors to find gene-based therapies for blindness secondary to inherited retinal degenerative diseases in children and adults, and to characterize their disease clinically. He received a BS in Biology and a MA in Family Counseling in from Eastern Nazarene College, went on to the New York College of Osteopathic Medicine from 90-

94. He was selected as an Intramural Research Training Award Fellow at the National Eye Institute/National Institutes of Health in Bethesda, Maryland, for work in ocular gene therapy. He went on to internship and residency in ophthalmology in Akron, Ohio, and completed a clinical fellowship in pediatric ophthalmology and a research fellowship in ocular genetics at the Cleveland Clinic Foundation. He has been an invited lecturer, both nationally and internationally, and holds grants from several foundations and the National Institutes of Health.

Dr. Chung has been invited to share his expertise in sub-retinal delivery of gene therapy vectors at numerous institutions in the US and Europe. Dr. Chung has membership in the American Osteopathic Association, American Academy of Ophthalmology, the Association for Research in Vision and Ophthalmology, the American Society of Gene and Cell Therapy, the American Society of Human Genetics and The International Society of Genetic Eye Diseases. He also serves on the editorial board of the Journal of Clinical and Experimental Ophthalmology

PATIENT REGISTRY DISCUSSION

Dr. Scribner discussed patient registries, which FDA will require. He's working on one for Friedrich's ataxia. A patient registry requires informed consent and assent from kids under 7. An IRB (academic or independent) is required for manipulating tissues. What do we want to do with the data?

Dr. Nishina described a patient registry that's worked well for the Alstrom syndrome community. "Every 3-4 years, basic scientists and clinicians have a clinic where they bring in patients and do studies," she said. Dr. Maumenee's been maintaining such registries for years.

Meeting ended with Mike Smedley facilitating a discussion of goals moving forward.

A NOTE ABOUT OUR NOTE TAKER, RICKI LEWS:

Ricki Lewis, PhD, author of *The Forever Fix: Gene Therapy and the Boy Who Saved It*

is an accomplished genetic counselor and science writer, educator and public speaker with 25 years of experience in the field. She has built a multifaceted career around writing, teaching and communicating about the exciting world of the life sciences, especially genetics and biotechnology, to a wide variety of audiences.

Lewis earned a PhD in genetics from Indiana University in 1980, where she worked with homeotic mutations in *Drosophila melanogaster* (i.e., flies that had legs growing out of their heads due to mixed up stem-like cells). She has been a genetic counselor at an OB/GYN practice since 1984, and has taught various biology courses at SUNY Albany, Empire State College, and Miami University.

Lewis has published thousands of articles in a range of different places – from magazines and medical journals, to encyclopedias, annual reports for biotech and pharmaceutical companies, technical reports, women's health pamphlets, book reviews, a bioethics blog, and a screenplay. Her articles have appeared in *Discover*, *Nature*, *Science*, *The Scientist*, *Genetic Engineering News*, *The FDA Consumer*, *Applied Neurology*, *Medscape Today*,

and various consumer and business magazines. She is also the author of *The Forever Fix: Gene Therapy and the Boy Who Saved It* (St. Martin's Press 2012), the first book to tell the complete and ongoing story of gene therapy for the general public.

Lewis is author or co-author of four life science university-level textbooks published by McGraw-Hill Higher Education, and an essay collection published by Blackwell Science. Her college textbook, *Human Genetics: Concepts and Applications*, is in its tenth edition and widely used throughout the U.S. by non-science majors.

Lewis' goal in writing and speaking is to engage and educate people who fear science in a way that enables them to make sense of what is happening in their world so that they can make informed decisions. Lewis claims that she uses her journalism experience to keep her science writing “interesting and very up-to-date, even futuristic.” Ricki writes about and connects many topics in genetics on her blog, Genetic Linkage, at www.rickilewis.com.