

## **Foundation Fighting Blindness Investing Nearly \$6.5 Million in New Grants**

By Ben Shaberman, Senior Director, Scientific Outreach & Community Engagement

Thanks to our successful fiscal year of fundraising which ended on June 30, 2019, the Foundation has committed \$6.5 million for 14 new research projects for inherited retinal diseases. The newly funded research efforts include development of a CRISPR/Cas9 therapy for retinitis pigmentosa, a retinal imaging technique using artificial intelligence, and several therapies that have strong potential to treat a wide range of inherited retinal diseases.

“We are delighted to expand our grants portfolio with several highly impressive projects that address several key research priorities and critical needs. Furthermore, the projects are being led by the world’s top retinal scientists,” says Brian Mansfield, PhD, executive vice president of research/interim chief scientific officer at the Foundation. “These grants wouldn’t have been possible without the generosity of our donors over the last year – their support through major gifts, walks, dinners, mail, and personal initiatives. The hard work and commitment of our donors is incredible and continues to successfully drive our mission.”

The Foundation currently funds a total of 80 research grants.

Summaries of new grants for Fiscal 2020 (beginning July 1, 2020):

### **Next Generation Optogenetics for Vision Restoration**

**Deniz Dalkara, PhD**

Institut de la Vision (France)

\$2.5 million over 5 years

Optogenetic therapies hold promise for restoring vision in people with advanced retinal disease regardless of their underlying mutation. Dr. Dalkara and her team are developing an optogenetic therapy that can be administered to different retinal cell types depending on the condition (stage of disease) of the patient’s retinal structure. Furthermore, the approach has the potential to bestow a higher degree of sensitivity (i.e., better vision) than current optogenetic approaches in clinical trials and translational studies.

## **Development of small molecule modulator for preserving vision in people with retinitis pigmentosa**

**Stephen Martin, PhD**

University of Texas at Austin

\$900,000 over 3 years

Dr. Martin and his colleagues are developing a small-molecule modulator known as TMEM97/σ2R that can be administered into the vitreous in a slow-release formulation to delay the progression of photoreceptor loss and to preserve vision in people with retinitis pigmentosa. The emerging therapy is designed to work independent of the underlying gene mutation causing the disease. The goal is to develop a drug that can be moved into toxicology studies in preparation for a clinical trial.

## **Gene editing to treat retinitis pigmentosa (RHO mutations)**

**Alberto Auricchio, MD**

University “Federico II” (Italy)

\$300,000 over 3 years

Mutations in the gene rhodopsin (RHO) are a frequent cause of autosomal dominant retinitis pigmentosa. Dr. Auricchio is developing a gene-editing therapy – homology-independent targeted integration (HITI) which uses CRISPR/Cas9 – to cut and replace both the normal and mutated copies of RHO. Though he will be testing the treatment in mice with a specific mutation, the therapy is being designed to work for all mutations in RHO.

## **Modulating microRNAs to prevent retinal cell death**

**Sandro Banfi, MD**

Telethon Institute of Genetics and Medicine TIGEM

\$300,000 over 3 years

Tiny pieces of RNA known as microRNAs are considered therapeutic targets, because they play a role in many cellular processes including programmed cell death. Previous research conducted by Dr. Banfi provided evidence that inhibition of certain microRNAs can prevent or slow degeneration of retinal cells. Dr. Banfi is evaluating inhibition of microRNAs 181 a/b as a therapeutic approach (prevention of cell death) in several mouse models of inherited retinal disease. The approach may be beneficial to people with a broad range of retinal degenerative conditions.

## **Enhancing metabolism in photoreceptors to treat retinal degenerations**

**W. Clay Smith, PhD**

University of Florida

\$300,000 over 3 years

Glycolysis is the process that breaks down glucose to provide fuel for cells in the body. Dr. Smith's goal is to boost glycolysis in photoreceptors to slow degeneration. He is working to accomplish this by delivering a modified arrestin1 protein to photoreceptors in various animal models. This approach is designed to work independent of the disease-causing gene mutation, so it has the potential to help people with a broad range of inherited retinal diseases.

## **Unraveling gene defects underlying inherited retinal diseases**

**Isabelle Audo, MD, PhD**

Institut de la Vision (France)

\$300,000 over 3 years

While mutations in more than 270 genes have been linked to inherited retinal diseases, about one third of patients won't have their disease-causing gene mutation identified when they receive genetic testing. Dr. Audo and her team are using whole genome sequencing and subsequent tests in patient cells to identify their novel gene mutations. Results of the study will be published and shared with the research community. The results of the study will help doctors diagnose more patients and identify more candidates for clinical trials.

## **Elucidating the disease pathway of cone dystrophy with supernormal rod response (CDSRR)**

**Sheila Baker, PhD**

University of Iowa

\$300,000 over 3 years

CDSRR is diagnosed in children and young adults based on a very unusual pattern of electrical activity in the retina. The retinal disease is caused by mutations in the gene KCNV2. Dr. Baker is using CRISPR/Cas9 to create a mouse model of CDSRR so that she and the research community can better understand how the disease occurs and identify targets for treatments.

## **Identifying optimal CRB1 protein for treating Leber congenital amaurosis (LCA) and retinitis pigmentosa (RP)**

**Jeremy Kay, PhD**

Duke University

\$300,000 over 3 years

Mutations in the gene CRB1 cause LCA and RP. The CRB1 gene can express different forms (isoforms) of protein. Dr. Kay believes he has identified a CRB1 isoform that will work well in a gene therapy for people. He is evaluating the rescue efficacy and expression pattern of this isoform. His efforts will help CRB1 gene therapy developers design the optimal gene therapy for people with CRB1 mutations.

## **Evaluating subsets of RPE cells affected by age-related macular degeneration**

**James Handa, MD**

Johns Hopkins University

\$300,000 over 3 years

Age-related macular degeneration (AMD) is a complex condition causing degeneration of retinal pigment epithelial (RPE) cells, which provide a support system for photoreceptors. When RPE cells don't work properly or die off, photoreceptors degenerate. Dr. Handa believes subsets of RPE cells are pathologic in AMD and play a lead role in driving the disease. His goal is to better understand and identify the changes in diseased RPE cell subsets and investigate potential targets for treating them.

## **Identifying adaptive optic measures for assessing structural and functional changes in inherited retinal diseases**

**Jessica Morgan, PhD**

University of Pennsylvania

\$300,000 over 3 years

Adaptive optics scanning laser ophthalmoscopy (AOSLO) is a powerful technology for imaging individual cones in patients with inherited retinal diseases. Dr. Morgan and her team are using state-of-the-art, noninvasive multi-channel AOSLO retinal imaging combined with adaptive optics functional testing to precisely characterize disease progression in patients with inherited retinal degenerations including retinitis pigmentosa, Stargardt disease, and Leber congenital amaurosis. The knowledge gleaned from her research can help doctors better measure retinal disease progression and effects of therapies in clinical trials.

## **Combining structural imaging and functional testing to evaluate retinal health and disease progression**

**Ramkur Sabesan, PhD**

University of Washington

\$300,000 over 3 years

The optoretinogram (ORG) is an emerging technique for measuring the activity of individual photoreceptors. Adaptive optics enables researchers to measure the structure of individual photoreceptors. Dr. Sabesan is using these techniques to correlate retinal structure and function in patients with retinitis pigmentosa and those without retinal disease. His findings will help the research community better evaluate retinal disease progression and the efficacy of emerging therapies in clinical trials.

## **Deep machine learning to identify functional and structural changes in photoreceptors**

**Yi-Zhong Wang, PhD**

Retina Foundation of the Southwest

\$300,000 over 3 years

Dr. Wang is using optical coherence tomography (OCT) enhanced with deep machine learning, a form of artificial intelligence, as a highly sensitive approach for measuring functional and structural changes in outer segments, the light-sensitive protrusions in photoreceptors. The project includes “training” the neural network to evaluate features of outer segments. The research team will be evaluating the technique in RUSH2A (USH2A natural history study) participants for correlating outer segment structure with visual field sensitivity. The project may ultimately help researchers identify an endpoint for treatments in clinical trials.

## **Predicting disease progress in people with Stargardt disease using a deep learning algorithm**

**Peter Zhao, MD**

University of Michigan

\$65,000 over 1 year

Diana Davis Spencer Clinical Fellowship

Dr. Zhao is developing a deep learning algorithm, a form of artificial intelligence, to analyze fundus (back of the eye) autofluorescence images of patients with Stargardt disease. Developing a deep learning algorithm will facilitate identification of patients whose disease is more likely to progress in the near future. Patients at risk of disease progression make good candidates for clinical trials of treatments that are designed to slow or halt vision loss.



**Investigating retinal structure and function in people with X-linked retinitis pigmentosa caused by RPGR mutations**

**Marco Nassisi, MD**

Institut de la Vision (France)

\$65,000 for 1 year

Diana Davis Spencer Clinical Fellowship

Dr. Nassisi is conducting a retrospective analysis of collected data, including functional and structural parameters to model disease progression, in people with X-linked retinitis pigmentosa caused by RPGR mutations. His goal is to better understand how different mutations in the gene affect vision loss. Ultimately, he wants to determine endpoints that can be used in clinical trials of gene therapies and other emerging treatments.