A PROPOSAL FOR THE
HEAR SEE HOPE FOUNDATION

VISUALIZING A CURE

SEPTEMBER 2017

ACCELERATE
THE CAMPAIGN *for* UW MEDICINE

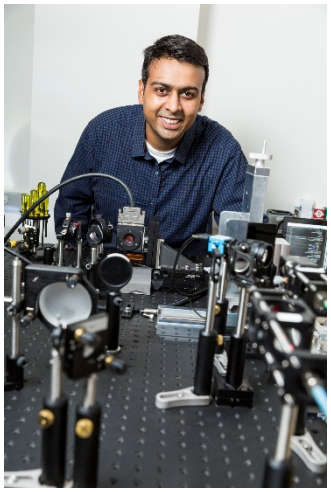
VISUALIZING A CURE:

UNDERSTANDING CONE DEGENERATION IN USHER SYNDROME AND RETINITIS PIGMENTOSA

Within the retina, photoreceptors make up one of the most important and most vulnerable cell classes afflicted by retinal degenerative diseases, like those present in Usher syndrome patients. Drs. Jennifer Chao and Ramukar Sabesan, clinical and research faculty at the UW Medicine Eye Institute and Vision Sciences Center, are collaborating on a new approach to visualize what happens to the photoreceptors damaged by retinal degeneration using high-resolution advanced adaptive optics imaging – a next generation technology developed in our labs. This research is critical to advancing our understanding of these diseases and whether potential therapies aimed at preserving and restoring central vision to patients will be successful.

RESEARCH SUMMARY

- The goal of this research project is to better understand the mechanism of how central vision is affected in patients with Usher Syndrome and Retinitis Pigmentosa (RP) using our high-resolution adaptive optics imaging system.
- Drs. Chao and Sabesan hypothesize that in patients with Usher Syndrome and RP, the cone photoreceptors (those responsible for our central vision) have impaired function early in the disease process — before there is loss of central vision — due to starvation of the cells.
- At the UW Medicine Vision Sciences Center, we have designed and built an adaptive optics imaging system that can detect, measure, and map the structure and function of cone photoreceptors at an individual cell level in a living human eye.
- With this new technology, we are now able to detect whether non-functional cone photoreceptors are present, and if they are capable of being stimulated.
- Ultimately, this study will help us to determine whether potential therapies aimed at preserving and restoring central vision in patients with Usher Syndrome and RP will be successful.



A NEW APPROACH FOR USHER SYNDROME

Recent approaches to treating diseases such as Usher Syndrome or RP include the use of stem cell transplants of photoreceptors, gene therapy, and chemical reanimation. However, a fundamental issue in understanding these diseases and translating potential therapies to patients is the ability to visualize their effectiveness at restoring function at the individual cell level. Until recently, the ability to study individual photoreceptor cell function in patients has been a challenge in the field because of the eye's unique optics and because the retina is constantly moving.

The UW Medicine Eye Institute and Vision Sciences Center is one of only a few institutions in the United States to have designed and built an adaptive optics imaging system capable of imaging the human retina at a singular cellular level. Furthermore, our adaptive optics equipment has the ability to fix an image on the retina, allowing scientists to study cells that are not functioning properly and explore opportunities to stimulate those cells and measure the effects of any treatment with extreme precision. [See sample images in Figure 1]

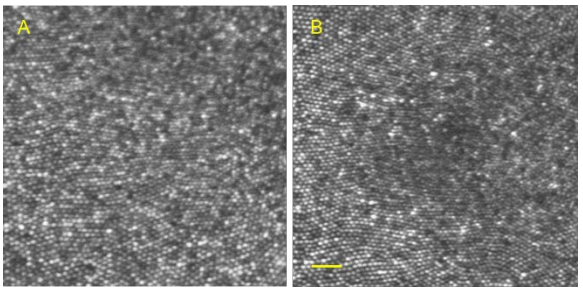


Figure 1: Human foveal cone mosaic imaged with adaptive optics imaging system in the Sabesan lab. A) and B) are reflectance images with illumination centered at 543nm and 840nm respectively. Each spot denotes a cone photoreceptor and is about 2-4 microns in diameter. The scale bar is 20 microns.

Drs. Chao and Sabesan theorize that in patients with Usher Syndrome and RP, the central cones show signs of disruption in their structure and function before it is clinically noticeable. Several recent studies have shown that the loss of central cone function may be caused by the "starvation" of the cells following the loss of their rod photoreceptor counterparts. Using animal models with RP, researchers have shown that they can reverse some of the damage seen in cones and even restore their functionality with an injection of glucose into the subretinal space (4) (5) (6).

Using our adaptive optics imaging equipment, we propose to map the progression of cone photoreceptor dysfunction in patients with Usher syndrome and RP in order to gain a more complete picture of disease etiology, progression, and possibilities for clinical intervention. In addition, we also seek to demonstrate that cone photoreceptors are only dormant in Usher and RP patients and not completely lost. This finding in patients would confirm what has been observed in animal models and open up new avenues of research for the therapeutic reanimation of cones. The presence of dormant cones would that mean either preserving or restoring central vision in patients with late stage Usher Syndrome or RP is possible.

This new collaboration between the Chao and Sabesan Labs is an opportunity to test the feasibility of conducting these imaging studies in patients with a broad array of retinal diseases, such as will be possible in our new Retina Center at UW Medicine opening in 2018. This proposal is fundamentally distinct from the current efforts of both labs and is a natural next step in our pursuit to translate new therapies developed in the lab to new cures that can be administered clinically. With the results of this research, we intend to apply for federal NIH funding and other private grants in order to support continuing research in this new and promising area of study.

BUDGET

We have received initial funding support for this project from a Latham Vision Research Innovation Award, which was granted by the UW Medicine Department of Ophthalmology in August 2017.

With additional pilot funding of $25,000 or more from the Hear See Hope Foundation, we will be able to fund a portion of a salary for a research assistant for one year to aid in patient enrollment, image acquisition, analysis and interpretation of the data, and manuscript preparation. Additionally, these funds will be used towards the purchase of two new detectors that will allow us to acquire images of cone photoreceptors inner segments in Usher and RP patients.

We estimate that the full study will take three years to complete, with a total cost of $225,000. We envision this project as the beginning of a new field of research that will be ongoing at the UW Eye Institute and Retina Center. This funding will support the salary for a full-time research assistant ($60,000, including benefits) for three years, as well as provide partial salary for a clinical trials coordinator. It will also completely equip our current adaptive optics imaging equipment with the hardware needed to acquire images of cone inner segments or dormant cones ($30,000).

THANK YOU!

We are grateful for the past support of the Hear See Hope Foundation and we look forward to discussing this new proposal with you. Please feel free to contact Abbey Norris, director for philanthropy, at 206.221.8274 or abbeyn@uw.edu with any questions.

Thank you for your consideration of this request.

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Box 358045, Seattle, WA 98195-8045
206.543.5686 / writemed@uw.edu