RETINA RESEARCH FOUNDATION
NEWSLETTER
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Retina Research Foundation Newsletter is published three times per year: Spring, Summer and Fall.

Foresight 20/20: The Right Course

The Retina Research Foundation motto is *Foresight for Sight*. You could say RRF and supported scientists pursue **Foresight 20/20**. Unlike 20/20 hindsight, where by looking back at events, the right course of action becomes clearly seen, **Foresight 20/20** is planning for what we think will happen before it happens.

In the context of retinal research, scientists build upon existing research to expand our collective understanding of the retina, beyond what is currently known, looking toward solutions that will ultimately benefit humanity by preventing retinal vision loss or blindness. Not all research efforts will result in the intended success, nonetheless, they will contribute meaningfully to the collective understanding.

As we approach a new decade, let's consider the RRF 2020 research pilot-grant recipients who will move our collective knowledge forward by addressing a range of research, including gene therapy and nanotechnology, among others.

The 2020 cohort of retina researchers funded by RRF pilot study grants expanded to 16 pilot studies, including 12 renewals and four new or first-time funding recipients. Seven studies are located within Texas research facilities, including Baylor College of Medicine, University of Texas Medical Branch at Galveston and Texas A&M Health Science Center. Other researchers' labs are within universities in Florida, Indiana, Iowa, Massachusetts, Tennessee, Utah, West Virginia, and Wisconsin. These studies were selected by the RRF Grants Committee from a robust group of renewal and new funding requests, the largest in recent years.

Research Areas of Focus

More than 260 retinal disease genes have been characterized, and basic research leading to potential gene therapy options for inherited retinal disorders is highly dynamic. Gene therapy is a technique for replacing disease-causing defective genes with normally working ones. Foundational to gene therapy is an understanding of the genes that govern proper functioning of the retina, the mechanisms of action, and the necessary molecules or proteins.

RRF pilot studies contribute to the understanding of genetic implications for retina function, aging, and dysfunction, often with a focus on a particular disease. A number of projects focus on specific proteins or enzymes and their role in vision or retinal inflammation responses. Others focus on the mechanisms and nutritional requirements for proper functioning of the retina, including implications of the gut microbiome on neovascularization of the retina.

Pilot grantees also study the use of technology on a molecular scale, nanotechnology, for diagnosis, prevention, or treatment to eradicate retinal disease. Using engineered nanodevices and structures, scientists can study and repair human biological systems on the molecular level. Gene delivery using viral vectors and nanoparticles used in drug delivery are two current research applications for nanotechnology. The most common delivery mechanism is a carrier molecule called a vector, and the most common vector is a genetically altered

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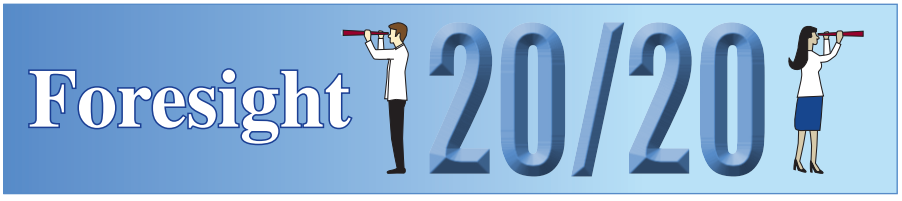

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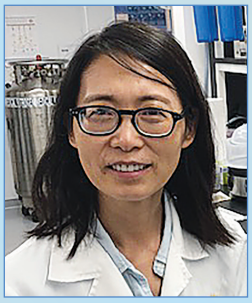
virus, which carries the genetic material into the target cell.

Retina researchers are making advancements in finding the optimal virus to carry the gene harmlessly, and in surgical techniques to inject the vector into the eye.

The goal of improved clinical treatments for retinal diseases is an aspect of RRF's foresight aimed to reduce retinal vision loss or blindness. Each scientist's idea represents a step closer to new treatment regimens, and is tested through a carefully designed pilot study. Pilot-study findings often lead to new and larger studies and future clinical trials that ultimately put new treatments into widespread use in patient care. Much progress has been made, and with **Foresight 20/20**, RRF is focused on funding the next breakthrough developments in retina research.

Visit **retinaresearchfnd.org** to learn more about this year's pilot-study researchers and their projects.

New 2020 Pilot Study Researchers



Hong Yu, PhD
Bascom Palmer Eye Institute, University of Miami

James Monaghan, PhD
Northeastern University

Luke A. Wiley, PhD
Institute for Vision Research Center, Carver College of Medicine

Miliam Brantley, MD, PhD
Vanderbilt University Medical Center

The Puzzling Question of Retina Photoreceptor Replacement

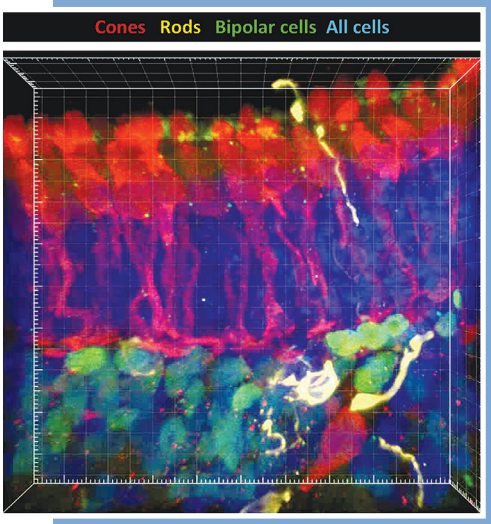
February Scientific Speaker: Dr. David M. Gamm

Many types of cells in the body regenerate, for example, bone or superficial skin cells, but highly specialized cells, like those found in the retina, do not regenerate. As an individual ages, these non-regenerating cells also age. In the case of the retina, cell loss may cause diseases such as age-related macular degeneration (AMD), and are a significant cause of blindness. It is estimated that up to 11 million people in the United States have some form of AMD, and in the next 30 years, this number is expected to double to nearly 22 million as the U.S. population ages. AMD, along with many other retinal diseases and injuries, specifically affects cells in the outer retina layers, which is comprised of photoreceptors and retinal pigmented epithelium, or RPE cells. The goal for scientists researching currently untreatable diseases and injuries caused by photoreceptor death is figuring out how to replace these critical pieces in the complex retina puzzle.

Dr. David Gamm presenting: Missing Pieces, the Complex Puzzle of Photoreceptor Regeneration

During his February visit with the RRF Board of Directors, David M. Gamm, MD, PhD, RRF Emmett A. Humble Distinguished Director of the McPherson Eye Research Institute at the University of Wisconsin, discussed his laboratory's efforts to answer this question. His research aims to generate authentic human photoreceptors from a type of stem cell called human induced stem cells (iPSCs), applying techniques that are suitable for use in patients with retinal degenerative diseases.

Human iPSCs have the ability to differentiate into all cell types in the body and hold potential to be a source of 1) biological material for modeling retinal development and disease in the laboratory dish, and 2) "spare parts" for devising cell-based treatments for debilitating retinal degenerative diseases like AMD.



Capowski et al. Development 2019

To facilitate the latter challenge, Dr. Gamm's laboratory is researching strategies to deliver donor photoreceptors and/or RPE cells beneath the retina in an organized and controlled manner using microengineered scaffolds. To generate the donor cells, they have developed the first 3D retinal organoid culture method that utilizes human embryonic stem cells and iPS cells, which has since yielded key insights into the steps needed to build a functioning human retina.

In addition, Dr. Gamm's laboratory studies have probed and established the authenticity of these lab-created human photoreceptor cells (rods and cones), RPE cells, and retinal tissues.

Dr. Gamm discussed many of the challenges encountered in installing these "new" photoreceptors in severely damaged host retinas. His research has led to numerous breakthroughs, and he and his team have filed multiple patents as their research moves closer to human clinical trials.

Dr. Alice McPherson and Dr. David Gamm

Facts About Age-related Macular Degeneration

- The disease blurs the sharp, central vision needed for everyday activities, such as seeing faces, reading, needlework, and driving.
- Age is a primary risk factor for age-related macular degeneration. The risk of getting advanced age-related macular degeneration increases from two percent at age 50-59, to nearly 30% at age 75 or older.
- Macular degeneration is the leading cause of vision loss in Americans over age 60.
- There are two forms of macular degeneration – dry and wet. The most common form, accounting for 90% of diagnosed cases, is the dry form where the light sensitive cells of the macula slowly break down and the macula thins.

Age-related Macular Degeneration's impact on vision

- There is no treatment or cure for advanced dry macular degeneration, but treatments which stop or delay the progression to advanced stages are possible.
- Wet macular degeneration, in which leaky blood vessels grow under the retina, accounts for only 10% of diagnosed cases, but 90% of legal blindness. It is managable by regular physician care. Wet macular degeneration is always preceded by the dry form of the disease.

Maintaining a healthy lifestyle may reduce the risk of developing macular degeneration. Consuming a nutritious diet full of green leafy vegetables, yellow and orange fruit, fish and whole grains; exercising regularly, wearing sunglasses or hats when outdoors, not smoking, controlling any medical conditions, and having regular eye exams all reduce a person's risk.

Sources: NIH, NEI

Rare Form of Congenital Blindness Receives Pioneering Genetic Treatment

Inherited retinal disease specialists at Baylor College of Medicine successfully treated three young siblings born with a rare form of hereditary blindness, using the first FDA-approved gene therapy to ever exist for a genetic disease.

The novel therapy treats patients with RPE65-associated Leber Congenital Amaurosis (LCA), an eye disorder that begins in infancy and typically worsens over time, and is caused by mutations in both copies of the RPE65 gene. The mutation alters a key vision-enabling protein. The therapy, also known as gene replacement therapy, reverses the effects of this condition by replacing the mutated gene with a healthy copy.

Dr. Timothy Stout
Chair of Ophthamology
Baylor College of Medicine

"A normal copy of the human RPE65 gene is placed into a virus that is designed to infect the right cells in order to make the RPE65 protein," said Timothy Stout, MD, PhD, retina surgeon and chair of ophthalmology and director of the Cullen Eye Institute at Baylor College of Medicine. "We inject the virus underneath the retina in these patients, the virus is then able to infect the diseased cells and to permit the expression of the missing protein. We have been able to show that this arrests the progression of the disease. The technology is remarkable because we can use a harmless, engineered virus to correct a blinding defect."

This latest advancement signals the potential of gene therapy to successfully treat additional retinal genetic diseases for which there are no other treatments. "There are millions of people who have problems with the other 300 genes that function as moving parts of the retina," said Dr. Stout, who was the principal investigator in a clinical trial for RPE65 gene therapy. "We should treat genetic diseases for which we have no other treatments with gene replacement therapy. It might not cure this disease, but it seems to work well in reverting or stopping the progression."

Left to right:
Dr. Timothy Stout, Dr. Roomasa Channa, Dr. Christina Weng, and Dr. Tahira Scholle, ophthalmologists at Baylor College of Medicine

Image: Daniel Kramer

RPE65-associated LCA patients who have been treated with this novel gene therapy have seen improvements in light sensitivity, visual field - how wide of an area people can see, and sight in dark conditions.

Baylor College of Medicine is one of 10 institutions in the U.S. where retinal surgeons have the expertise and specialized skills to treat patients with RPE65 deficiencies with this latest gene therapy advancement.

Source: CHI St. Luke's Health

Welcome New RRF Board Director Patricia K. Boyd

Patricia K. Boyd

Patricia K. Boyd joined the RRF Board of Directors in March, 2020, after serving as an RRF Advisory Trustee since 2013.

Mrs. Boyd is a fifth-generation Texan, born and raised in Tyler, Texas. In 1957 she married Don R. Boyd, another Tylerite and fellow University of Texas at Austin graduate. Together, they moved to Corpus Christi in 1959, where she was a full-time mother and community volunteer. After her husband's death in 2000, Mrs. Boyd moved to Houston in 2004. Mrs. Boyd has three children and seven grandchildren including one granddaughter who has Stargardt Disease. She is a lifelong Methodist, now a member of St. Luke's United Methodist Church in Houston. For 50 years, Mrs. Boyd has enjoyed a family ranch in Goliad County, Texas – a working and hunting ranch, plus a wonderful family spot. Her other interests are travel, reading, mahjong, theater, golf, and music.

Mrs. Boyd's affiliations and memberships include: The University of Texas – President's Associates, Chancellor's Council, Littlefield Society, and the Hill Society. Mrs. Boyd has deep interest in healthcare as reflected by her service to M.D. Anderson President's Circle, Houston Methodist's Society for Leading Medicine, and the Retina Research Foundation. Additional civic interests include: The Houston Symphony, Ima Hogg Ceramic Circle, The Blue Bird Circle, and Zeta Tau Alpha.

Vision Changes Over Time

The good news reported at the beginning of 2020 is that for the first time in four years the average life expectancy in the U.S. rose to 78.9 years. Additional good news is that vision research breakthroughs due to gene therapies, stem cell research and technological advances are on the visible horizon — good news because, as we live longer, our vision does change.

If you have no underlying health issues, here is what you can expect to happen to your 20/20 vision as time goes by:

In Your 40s

Fortunately, vision doesn't begin to change until we reach age 40. After 40, presbyopia, or trouble with near vision focus, becomes common. The eye lens is not as flexible as it once was, decreasing the ability to see small things, up close. Reading glasses can help you continue

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to do the things that require close vision. Also, the risk of having dry eye or computer vision syndrome increases at this age.

Seeing things "close up" begins to be challenging for many in their 40's.

In Your 50s

Risks increase for cataracts, glaucoma, and macular degeneration. Often these diseases show no symptoms until the damage is already done. Dry eye increases, especially in women.

In Your 60s

The potential for age-related diseases significantly rise once you reach 60. In addition, the ability to see in low lighting decreases, and most people develop protein globs in the interior of their eyes that create shadows on the retina, called floaters. Floaters and spots are particularly noticeable when looking at a blank background such as a computer screen or the clear sky. If floaters, spots, or flashing in your vision develop suddenly, that is cause for alarm and needs instant attention. Yearly physicals are important to check for other health problems that can lead to eye problems such as diabetes.

Vision acuity in low light decreases with age.

In Your 70s and Older

Research shows that four out of five seniors either have cataracts or have already had corrective surgery. Surgery to replace the clouded lens is the only treatment, and is 99% successful. At this age, color vision further declines and some peripheral vision is lost, possibly up to a 30-degree reduction, a real issue for driving.

Changes in vision are an inevitable part of living a long life. Some age-related eye changes are almost universal and not related to disease, but unfortunately, there are age-related eye diseases that occur more frequently as the years pass. Staying healthy by maintaining an active lifestyle and eating a diet full of fruits and vegetables will support you in fending off potentially more serious vision problems. Most importantly, around age 50, regular visits to your ophthalmologist are essential to keeping your vision clear and free from conditions that may cause serious damage.

Night time vision distortion due to cataracts.

Source:
CDC.gov, data briefs – number 355, January 2020

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