

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

Gene Therapy in the Eye

Gene therapy for inherited retinal disease is showing much promise due to several factors unique to the eye. The eye is a small organ that is easy to get to, so implanting cells in them is much easier than elsewhere in the body. Importantly, the eye is what is immune-privileged, which means that cells implanted there are less likely to be rejected as they might be in other parts of the body.

According to Dr. Paul A. Sieving, Director of the National Eye Institute, National Institutes of Health, what makes the eye "a wonderful place to test therapy ideas," is that while it is obviously connected to the rest of the body by blood and nerve tissue, "the eye is a separate compartment. We only need to deliver a microscopic quantity of gene vector in order to try a treatment," unlike other gene therapy experiments, in which the gene and the virus that carries it, known as a vector, can circulate throughout the whole body system.

Another advantage is that in gene transfer trials involving the eye, outcomes will be crystal clear.



Paul A. Sieving, MD, PhD

"The visual system has very precise, quantifiable measures of function, and even tiny measures of success can be documented," he says.

https://nei.nih.gov/ https://www.aao.org/eye-health/

Importance of Exercise in Preserving Vision

It has long been common knowledge that even moderate regular physical exercise is beneficial for your heart and your well-being, but did you know that it can also help protect your eyes? According to the American Academy of Ophthalmology, two studies have shown that people who exercise regularly were less likely to develop serious, eye disease.

Glaucoma

In one study, British researchers, led by Dr. Paul J. Foster of the University College London (UCL) Institute of Ophthalmology, discovered that subjects who engaged in regular physical exercise over a 15-year period were less likely to develop glaucoma than people who were inactive. In the study group of 5,650 British men and women over the age of 48, Dr. Foster reported a 25 percent reduction in a key indicator of glaucoma risk. The study was published in *Investigative Ophthalmology & Visual Science (IOVS)*.

For people who already have glaucoma, even a brisk walk three times a week was found to lower intraocular pressure (IOP) and improve blood flow to the retina and optic nerve, but only as long as the exercise routine continued. "We cannot comment on the cause, but there is certainly an association between a sedentary lifestyle and factors that increase glaucoma risk," said Dr. Foster.

www.upi.com



Paul Foster, MD



Machelle Pardue, PhD



Jeffrey Boatright, PhD

Importance of Exercise in Preserving Vision

(continued from cover page)

Age-related macular degeneration (AMD)

Researchers at Emory University School of Medicine in Atlanta, GA, and the Atlanta Veterans Administration (VA) Medical Center in Decatur, GA, conducted studies that identify a relationship between level of physical activity and developing age-related macular degeneration (AMD) in mice. Brain-derived neurotrophic factor (BDNF) is a growth factor that contributes to the health and well-being of neurons, which

are found in the retina as well as other parts of the body. Dr. Machelle Pardue, the senior author of the study, and Dr. Jeffrey Boatright, coauthor, found that exercise raised levels of BDNF in the mouse retina, potentially improving retinal health.

These experiments strongly suggest that "exercise protects vision, at least in mice, by



increasing BDNF in the retina," said Dr. Boatright, an associate professor of ophthalmology at Emory. But whether exercise can prevent macular degeneration in human eyes is "impossible to know, based on the data we have now," said Dr. Pardue, a research scientist at the Atlanta VA. For now, those with a family history of retinal degeneration might want to discuss an exercise program with their doctor. This study was published in the *Journal of Neuroscience*.

www.nytimes.com

Diabetic Retinopathy

Many eye diseases are linked to other health problems such as diabetes or high blood pressure. Controlling the underlying disease leads to improved outcomes for your eyes. For example, in patients with diabetes, exercise can help in disease management and therefore reduce the risk of developing complications, including diabetic retinopathy.

The best news about exercise and your vision is that you earn the benefits with even a moderate regimen of physical activity, even 30 minutes a day, and the benefits continue as long as you maintain your more active lifestyle. Ask your doctor about the right exercise program for you.

www.aao.org/eye-health/



Researchers Discover Critical Trigger for Inflammation

A University of Virginia School of Medicine team of researchers has recently discovered an enzyme that plays a critical role in causing the inflammation that can ultimately lead to blindness. Dr. Jayakrishna Ambati, Professor & Vice Chair for Research of Ophthalmology, and Dr. Nagaraj Kerur, Assistant Professor, have identified that an enzyme called cGAS is the culprit. This enzyme plays an important role in the body's immune response to infections by detecting foreign DNA, but now this molecule has been newly identified to also play a key role in the dry form of age-related macular degeneration.

"It's really surprising that in macular degeneration, which, as far as we know, has nothing to do with viruses or bacteria, that cGAS is activated, and that this alarm system is turned on," Dr. Ambati said. "This is what leads to the killing of the cells in the retina, and, ultimately, vision loss."

"For the first time, we know in macular degeneration what is one of the very first events that triggers the system to get alarmed and start, to use an anthropomorphic term, hyperventilating. This overdrive of inflammation is what ultimately damages cells, and so, potentially, we have a way of interfering very early in the process," said Dr. Ambati.

The finding may lead to methods of halting the inflammation early on and potentially preserving sight. Researchers are already trying to create drugs that could inhibit the function of this enzyme. The UVA researchers expect that the development and extensive safety and efficacy testing of any drug to inhibit cGAS will take years.

The scientists also hope to develop a way to measure the levels of the enzyme in patients' eyes in order to determine when best to administer a treatment that blocks cGAS. "If they have high levels of this enzyme in their eye, they might be a wonderful candidate for this sort of treatment," Dr. Ambati said. "This is really precision medicine at the single-molecule level."

www.healthsystem.virginia.edu/



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Retina Research Foundation is dedicated to the eradication of retina disease through programs in research and education.



Andrea Arriola-López, MD

Gillingham Pan-American Fellowship Report

In the fall issue of RRF's newsletter, we reported that Dr. Andrea Elizabeth Arriola-López was completing her fellowship at Bascom Palmer Eye Institute in Miami, FL. Bascom Palmer is one of the top eye hospitals in the country, and she had many opportunities while there to advance her knowledge and expertise. Dr. Arriola has now returned to Guatemala City, Guatemala, to teach and treat patients. RRF is proud to sponsor this program in affiliation with the Pan-American Association of Ophthalmology.

The following is an excerpt from her report:

I attended the Bascom Palmer Eye Institute in Miami, Florida, USA, for six months under the direction of Thomas Albini, MD, and Eduardo Alfonso, MD, in the Uveitis Clinic; previously, I spent three years in Mexico City; one year as a research retina fellow and two years as a retina fellow.

While at Bascom, I was able to observe and participate in patient care, offer clinical judgement and helped outline treatment plans. I was able to attend the operating room, as an observer, every time Dr. Albini performed surgery and recorded all of them.



Left to right: AndreaNaranjo,MD,(international observer), Andrea Arriola, MD, and Nika Bagheri, MD, (second year Retina Fellow at BPEI)

I had the opportunity to contribute in activities under the guidance of Dr. Albini, making summaries, clinic cases and academic presentations, book chapters and helped on some research articles and editing surgical and procedures videos. I also participated in many academic activities, including grand rounds, lectures, and retina meetings shared with leaders in the field like Harry Flynn, MD, William Smiddy, MD, Jayanth Sridhar, MD, and Audina Berrocal, MD.

I acquired knowledge of approach, diagnosis and management of different uveitis entities, discussing cases during and after clinic by reviewing images, laboratory results and clinical findings, and also learned new skills to apply in the operating room.

(continued on page 5)



Gillingham Pan-American Fellowship Report

(continued from page 4)

This fellowship has been an extraordinary experience. The guidance of my mentor was magnificent and a decisive factor for me to grow as a person and as a physician and gave me the possibility to transmit the knowledge and continue my research endeavors in Guatemala.

Thank you again for your support, Andrea Elizabeth Arriola López, MD, MSc



Bascom Palmer Eye Institute



Guatemala City

Pictured on the right:

Sulaiman Alhumaid, MD, (former Uveitis fellow at BPEI), Andrea Arriola, MD, Thomas Albini, MD, (Associate Professor of Clinical Ophthalmology at Bascom Palmer Eye Institute, Retina and Uveitis Specialist at BPEI) and Nika Bagheri, MD, (second year Retina Fellow at BPEI) "The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them."

Sir William Bragg

British physicist and winner of 1915 Nobel Prize, 1862 - 1942







Early Detection Saves Vision

No matter what your age or stage of life, regular eye exams by your ophthalmologist are an important factor in identifying eye diseases early and therefore preserving vision. It is estimated that 61 million adults in the United States are at high risk for vision loss, but only half have visited an eye doctor in the past year.

Some common eye diseases have few symptoms in the beginning of the disease process and may go unnoticed for quite a while. A comprehensive dilated eye exam by an ophthalmologist will often identify eye diseases in the early stages when treatment to prevent vision loss is most effective. Early identification and treatment is important in preserving vision when diseases such as age-related macular degeneration, glaucoma, or diabetic retinopathy are discovered.

The number of blind and visually impaired people in the United States is predicted to double in the next few decades. Encouraging people to take better care of vision health with regularly scheduled eye examinations could reduce that number and significantly improve the quality of life for millions of Americans.

www.cdc.gov/features/healthyvision/

RRF Educational Programs

The mission of the Retina Research Foundation is to reduce retinal blindness worldwide by funding programs in research and education.

One of the educational programs that RRF supports, and has supported since 1993, is the Educational Trust Fund of the American Academy of



Ophthalmology (AAO). This fund makes it possible for AAO to produce and maintain educational resources for ophthalmologists, including online access to interactive cases and teaching videos. The program's goal is improving the general quality of care for patients by updating or streamlining treatment regimens. RRF is proud to be working in collaboration with AAO to improve educational opportunities for retina specialists.

6

New Instrument for Detailed Image of Entire Eye

A team of researchers has developed the first instrument that can provide a high-resolution image of the entire eye. This innovative technology could make eye examinations faster for patients by avoiding the need to undergo imaging with multiple instruments to look at different areas of the eye. Dr. Ireneusz Grulkowski at Nicolaus Copernicus University in Poland and Dr. Pablo Artal at the Universidad de Murcia in Spain collaborated to develop this new imaging system.



"Diseases such as glaucoma affect both the front and back portions of the eye," said Dr. Grulkowski. "An instrument that can examine the whole eye will improve the patient's experience because they won't have to go through imaging with different devices."

Ireneusz Grulkowski, PhD

In *Optica*, the journal of the Optical Society, these researchers show that their new optical coherence tomography (OCT) imaging system is able to image in great detail both the

front and the back of the eye, and also the interfaces of the eye's vitreous gel with the retina and lens. This new imaging capability could allow scientists to better understand how the vitreous gel that fills the eye interacts with the retina.

"We also want to use our instrument to measure opacities in the eye's crystal lens and the vitreous to better understand how various parts of the eye affect the deterioration of vision," said Dr. Grulkowski. "We believe that the ability to measure these opacities and other properties of the eye that couldn't be examined before will open up many new ophthalmology applications for OCT."

https://phys.org/news/



Pablo Artal, PhD



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