RETINA RESEARCH FOUNDATION
NEWSLETTER
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Gene Therapies for Non-Hereditary Retinal Disease in Phase III Clinical Trials

Multiple gene therapies to treat non-hereditary retinal disease have reached Phase III clinical trials, the final phase necessary prior to submitting for drug regulatory approval. This is an encouraging development if you are one of the 1.5 million in the U.S. who receives treatment for the wet form of age-related macular degeneration, called neovascular age-related macular degeneration (nAMD). Simply put, the goal of these new gene therapies is to reduce the need for intravitreal injections by alternatively delivering sustained therapeutic levels of the agent proteins that treat nAMD within the eye.

Decades of retina research have revealed that, in some people, the cells of their retina secrete too much of a protein called vascular endothelial growth factor (VEGF) that causes the growth and leakage of the blood vessels in retina tissue. This process can be slowed or stopped by injecting drugs into the eye that bind and inhibit VEGF.

The introduction of intravitreal (IVT) anti-VEGF agents revolutionized the treatment of nAMD. Repeated IVT injections of anti-VEGF therapies effectively stabilize vision loss in the majority of patients with nAMD who adhere to treatment. The requirement for frequent injections and monitoring imposes a substantial burden on patients and caregivers, and can lead to poor adherence and suboptimal visual outcomes. By the third year of treatment, real-world discontinuation rates for anti-VEGF therapy have been reported as high as 42%. In addition, recent evidence suggests that the fluctuation of retinal fluid volume, from intermittent anti-VEGF therapy, may lead to poor long-term visual outcomes. Scientists and physicians are searching for alternatives to improve patient care and outcomes, and the gene therapies on the horizon are promising alternatives.

The first vision related gene therapy, also the first gene therapy to treat a disease, was approved by the FDA in 2017 to treat Leber congenital amaurosis (LCA), a rare, inherited condition causing vision loss from birth or early childhood. The disease is caused by genetic mutation(s), which hinders the production of a protein necessary for proper function of the retina's photoreceptor cells. The LCA gene therapy facilitates the production of the missing protein, and enables a return of function in the patient's existing photoreceptors.

Gene therapy, for non-hereditary conditions, using anti-VEGF therapy takes a different approach in that it enables the production of a synthetic protein that binds and inhibits the production of the VEGF protein that causes production of harmful, new, leaky blood vessels in the retina. RGX-314 anti-VEGF gene therapy has the potential to block VEGF for years following a surgical procedure in which a harmless virus, called adeno-associated virus (AAV), carrying the anti-VEGF gene, is injected under the retina. Another anti-VEGF gene therapy, ADVM-022, now called Ixo-vec can be injected into the vitreous in an office procedure, but it can cause eye inflammation. With promising safety and efficacy results in early clinical trials, both RGX-314 and ADVM-022 therapies are now in Phase III trials, which enroll larger numbers of patients and typically take one (1) to four (4) years.

Sources: Ophthalmology Times: May/June 2025; Author: Glen Yiu, MD, PhD; BrightFocus.org; Helio.com

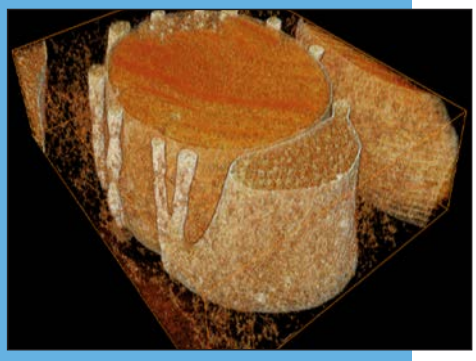
Newly Discovered Retinal Structure Exemplifies the Promise of Research

Oleg Alekseev, MD, PhD
Duke School of Medicine
Durham, NC

Scientists thought that they knew all there was to know about the anatomy of the human retina, based upon exhaustive electron microscopy studies conducted throughout the 1960s and 1970s. However, technology has continued to advance, and now allows scientists to see the miniscule structures within living cells in ever greater detail. Newly enhanced imaging, three dimensional electron tomography enables scientific mapping of an object with extraordinary resolution. In their desire for deeper understanding and knowledge about the causes of inherited retinal degenerative diseases, Dr. Oleg Alekseev and Dr. Vadim Arshavsky, at Duke School of Medicine, used this technology to further examine the small structures of the retina. What they found was unexpected and surprising, they found a previously unknown part of photoreceptor cells in the human retina. "We aimed to take a look at some very small structures," Alekseev said, "but we found something pretty major."

The newly discovered structure is described as a large, mechanically reinforced protrusion attached to each rod photoreceptor and has been named the accessory inner segment (aIS).

"The function (of the aIS) isn't known yet," Dr. Alekseev said, "but we presume it serves as a physical support to hold the photoreceptor." Photoreceptors are long and narrow. The researchers think that the aIS, which appears to be a uniquely human structure, holds everything together, providing stability and preventing the photoreceptors from collapsing and flopping. "We need to explore this structure further," Dr. Alekseev said. "It's very likely that some diseases are caused by defects in the aIS, and now we have the opportunity to explore those diseases, improve our ability to diagnose patients, and start thinking about treatments." Now that aIS has been discovered, the next step is to understand the molecular composition of its unique parts and unveil the promise of what new information can be learned about human diseases in the eye.



A cross section of where the accessory inner segment (aIS) on the right attaches to the rod photoreceptor. Image courtsey of Duke School of Medicine.

Over 300 known genes make photoreceptors functional. A mutation in any one of those genes can cause a photoreceptor to work improperly and can lead to irreversible blindness. Genetic testing helps solve only around 70% of cases, but this discovery opens the door to studying additional previously overlooked genes that may be involved in forming and maintaining the aIS.

Dr. Alekseev's clinical and research interests are in inherited retinal degenerations, including conditions like retinitis pigmentosa, Stargardt disease, macular pattern dystrophies, and syndromic retinal degenerations. His current research is centered on developing gene-agnostic approaches, focused on the disease-causing intracellular pathways, to extend the longevity of ailing photoreceptors in degenerative retinal conditions, and thereby preserve the vision of affected patients. The approaches he investigates include both gene-therapy and small-molecule-based therapeutic modalities. In addition to his other sources of grant funding, Dr. Alekseev is supported by RRF for a pilot study project that aims to develop a gene therapy for mutations in the prominin-1 gene, which are well known to cause severe and irreversible vision loss from the inherited retinal degenerative conditions he sees in his patients.

Source: Duke University School of Medicine

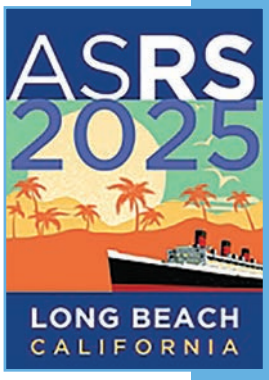
Pioneering Researcher Bridges Scientific Innovation With Clinical and Surgical Practice

Dr. Rajendra S. Apte, a distinguished professor at Washington University School of Medicine (WashU), is the 2025 recipient of **RRF's Pyron Award**. The RRF Pyron Award is presented by the American Society of Retina Specialists (ASRS), and recognizes an outstanding vision scientist whose work contributes to knowledge about vitreoretinal disease. This award is made possible by an estate gift to RRF from Gertrude D. Pyron, an eminent geologist from San Antonio, Texas. Dr. Apte gave the award lecture entitled, *Illuminating the Unknown: Advancing Retinal Science to Restore Vision*, at the ASRS Annual Meeting, held on August 1st in Long Beach, CA. In addition, he received an unrestricted $45,000 research grant to support his ongoing research interests.

Rajendra S. Apte, MD, PhD
Washington University
School of Medicine
St. Louis, MO

As a retinal surgeon and scientist, Dr. Apte's pioneering research bridges scientific innovation with clinical and surgical practice. His groundbreaking discoveries in retinal diseases, particularly those related to aging and inflammation, have increased our understanding of conditions like age-related macular degeneration, diabetic retinopathy, and glaucoma. Specifically, he discovered that a dysfunction in the immune system hinders clearing of lipids in the eye, which creates an environment of inflammation, eventually leading to more advanced stages of disease where retina neurons die. This research into neurodegeneration, drusen (including lipid deposits) biogenesis and angiogenesis has translated into new therapeutic possibilities prior to vision loss.

With over 185 peer-reviewed publications in journals such as *New England Journal of Medicine, Nature, and Cell*, Dr. Apte has significantly advanced retinal medicine. His leadership in clinical trials and role as co-founder of and key advisor to multiple life science companies highlights his commitment to translating research into precision medicine-based therapeutics. His contributions to our understanding of NAD+ and lipid metabolism and how it impacts disease pathophysiology have extended beyond the eye into diverse clinical stage programs targeting Alzheimer's disease, acute kidney injury, cardiovascular and musculoskeletal diseases.



Gertrude D. Pyron

Dr. Apte has said, "You have to think long-term 5 to 10 years down the road – because any difference you make to your profession, to the public health or to science, is not going to be achieved overnight." He embodies this mindset as a mentor at WashU and to trainees and young faculty around the country, shaping the careers of many clinicians and scientists. His body of work is the perfect illustration of what a bench to bedside approach should look like.

Sources: ASRS; RRF; WashU Medicine

RRF's ARVO Travel Grant Award Program

RRF's mission is two-fold, to fund programs in retina research and education. The ARVO Travel Grant Award Program perfectly represents the synergistic result of these goals working together to inspire young researchers interested in vision science. Supported by an estate gift from Joseph M. and Eula C. Lawrence, the ARVO RRF Travel Grants provide a unique opportunity for young researchers to attend the annual meeting of ARVO – the Association for Research in Vision and Ophthalmology – to present their research and visit with their peers at the largest scientific meeting of eye and vision researchers in the world. In 2025, nearly 11,600 scientists from more than 75 countries attended, including basic and clinical researchers, clinicians, surgeons, educators and students in ophthalmology and vision science. For this year's meeting, 28 young researchers received RRF Lawrence travel grants, increasing the total number of recipients of these grants to 910 since 1993. A travel grant award can offer these promising scientists and clinicians a first glimpse into the fascinating, challenging, and complex field of vision research.

Let's consider the impact of this year's program on one recipient, Julia Greenwood, an MD candidate (2027) at Northwestern's Feinberg School of Medicine, Chicago, IL. As a medical student interested in ophthalmologic research, Ms. Greenwood, circled in the picture, attended her first conference ever with assistance from her RRF travel grant. Her research project on predictors of diabetic retinopathy complications, which she presented during the meeting, was also featured in the 2025 Abstracts Issue of IOVS, the journal of ARVO.

Ms. Greenwood's experience is exactly what RRF aims to provide for all awardees – to support and encourage aspiring physician scientists, early in their careers, in their continued pursuit of training and experiences that will lead to improved patient care for retinal diseases. You can learn more about RRF's educational efforts, including RRF's travel grant and fellowship programs by visiting retinaresearchfnd.org.

Ms. Greenwood's Post-Meeting Thoughts

First Time Attending ARVO?
Yes.

How did attending the meeting benefit you?
Attending the ARVO meeting was an amazing experience! It provided a valuable opportunity to present my research to a diverse audience -- including professionals in biotech, the pharmaceutical industry, PhDs, medical students, and ophthalmologists working in retina. It was insightful to receive thoughtful questions and suggestions for my project, which gave me some new perspectives and ideas moving forward. I also appreciated the chance to network and learn about a wide range of projects, both within my area of interest and in areas of ophthalmic research I was unfamiliar with. Exploring the technologies and products showcased at the exhibit booths was fun and interesting. It was inspiring to see how many people are passionate about their work and how much progress has been made in the field.

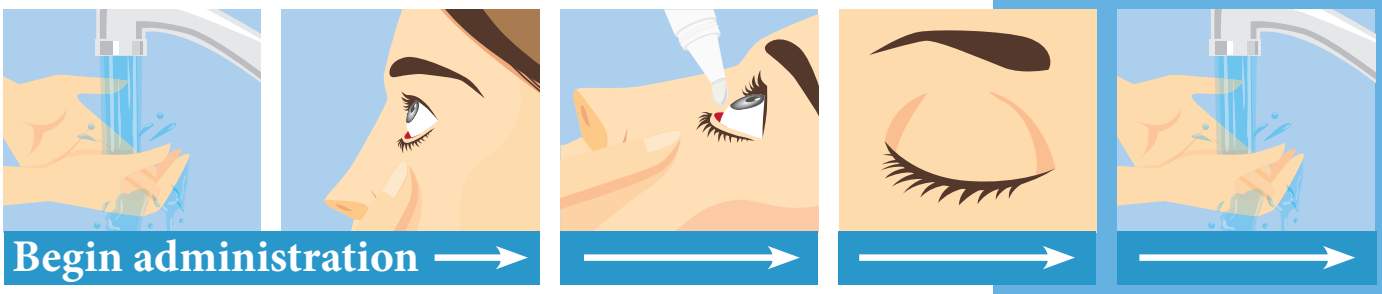
Did this meeting open up any new opportunities for you?
The meeting gave me new perspectives for my current project and new ideas for future projects. I was able to network with other researchers within and outside my institution, which was helpful.

Words of thanks:
I want to express my sincerest thank you to the Retina Research Foundation/Joseph M. and Eula C. Lawrence Travel Grant for making it possible for me to attend ARVO. This was the first conference I've ever attended, and the experience was invaluable for my growth as a researcher and future clinician.

How To Correctly Put in Eye Drops

There is a best way to ensure your eye drops make it into your eye and work as intended. With many different types of eye drops and reasons why you might use them, proper administration of eye drops can be essential to protecting your eyes and preserving your vision. Eye drops may be recommended to relieve redness or itching, or to treat a variety of eye conditions like allergies, dry eyes, infections, glaucoma, or following an eye procedure or cataract surgery, and ideally, you should only use eye drops as suggested or prescribed by an ophthalmologist or other healthcare professional. It is also beneficial to consult with your provider should you learn of a product recall. If you experience any issue or unexpected side effects while using eye drops, perhaps discharge from the eye, discomfort, pain, or vision changes, stop using them and immediately speak with your doctor.

Proper Eye Drop Administration Steps:



Since it is important to make sure the drops correctly get into your eye, follow the sequence of steps outlined below to administer the drops:

1. Read and follow your doctor's instructions,
2. Wash your hands with soap and water,
3. With one hand, pull your lower eyelid down and away from your eyeball, making a pocket for the drops,
4. Tilt your head back and look up,
5. With the other hand, hold the eye drop bottle upside down with the tip just above the pocket. To avoid contamination of the sterile drops, be sure not to touch the tip of the applicator with your fingers or to touch the tip to your eye,
6. Squeeze the prescribed number of eye drops into the pocket,
7. Close your eye, do not blink, and press your finger lightly on your tear duct (small hole in the inner corner of your eye) for at least a minute to keep the eye drops from draining into your nose,
8. If you need to administer different drops for different eye conditions, wait at least five (5) minutes between administrations,
9. Finish off by again washing your hands.

Sources: AAO, NEI

Don't Pass Up the Watermelon This Summer, Your Eyes Will Benefit

During summer, there are many seasonal food options that will benefit your eyes, and what could be more synonymous with summer than watermelon? In addition to supporting hydration, it is a good source of antioxidant vitamins and nutrients that promote health and may even prevent certain health conditions, including those of your eyes. Staying hydrated is important for proper body function, and helps with body temperature regulation, normal organ function, and nutrient delivery to cells, among other things. Remember your eye tissue requires enormous amounts of energy to work properly and resist inflammation. The small arteries and blood vessels within the retina nourish the tissue, and benefit from some of the same nutrients that are needed for a healthy heart. Check out below the vitamins and nutrients needed for healthy eyes and then, try out an eye-healthy recipe using watermelon. Pairing watermelon with other foods that are good for your eyes can be a great addition to your next BBQ cookout or picnic!

Vitamins	**Antioxidants are nutrients that remove potentially damaging oxidizing agents from the body and play a critical role in eye health. Antioxidants slow down the process of oxidation, a cause of cell aging and death.**	**Foods**
Vitamin A	Produces the pigments in the retina of the eyes, and is a vital nutrient for the eyes' photoreceptors that determine vision quality in low-light conditions. Vitamin A is only present in animal products, but the body can convert some plant nutrients into Vitamin A.	Egg yolks, Dairy, Liver, Spinach, Dark leafy greens, Carrots, Pecans, Watermelon
Vitamin C	Highly concentrated in the aqueous humor fluid in front of your eye lenses, it is thought to be a key antioxidant for preventing age-related cataracts. Your body cannot produce this nutrient on its own, but it can be easily found in several fruits and vegetables.	Broccoli, Kale, Peppers, Oranges, Watermelon
Vitamin E	Protects critical fatty acids from oxidation.	Almonds, Sunflower seeds, Avocados, Pecans and other nuts
Carotenoids lutein and zeaxanthin	These compounds are present in the light-sensitive tissue of the retina at the rear of your eyes.	Chard, Spinach, Kale, Raspberries, Peaches, Watermelon
Flavonoids	**L**inked to improved function in retinal ganglion cells, the neurons that link the retina to the sections of the brain that process visual input. Flavonoids in hot, caffeinated tea may reduce the risk of developing primary open angle glaucoma (POAG). Consuming a variety of sources of flavonoids is best.	Dark chocolate, Red wine, Berries, Citrus, Tea
Fatty Acids	**Fatty acids are created by our body when we digest fats, and support a range of functions in our eyes. Two fatty acids in particular, omega-3 and gamma-linolenic acid (GLA), are notable for their relevance and preventive value for many eye conditions.**	**Foods**
Omega-3	Important for maintaining eye health. Omega-3 contributes to the cell membranes structures in the eyes and supports visual function. Also, omega-3s have anti-inflammatory properties, which can help alleviate symptoms of dry eye syndrome and reduce the risk of developing age-related macular degeneration and glaucoma.	Salmon, Mackerel, Sardines, Flaxseeds, Chia seeds, Walnuts, Pecans and other nuts

Kale, Feta and Watermelon Salad

COOK TIME Prep Time 5 mins; Total Time 5 mins
SERVINGS 4 people
CHEF Dannii Martin

Ingredients

- 100 g curly kale chopped (1.5 cups, about a bunch or ½ a pre-prepped bag)
- 2 tablespoon olive oil
- 2 tablespoon apple cider vinegar
- 0.5 lemon (juice only)
- 2 garlic clove crushed
- 1 pinch sea salt and ground black pepper
- 280 g watermelon diced (2 cups, about 6 slices or a quarter of a watermelon)
- 60 g feta cheese
- 10 pecans crumbled
- fresh mint (optional)

Watermelon salad
Image credit:
Hungry Healthy Happy/
Chef Dannii Martin

Instructions

1. Roughly chop kale, wash well and put into a large bowl.
2. Add olive oil, apple cider vinegar, lemon juice, garlic clove, sea salt and ground black pepper to the kale and mix well.
3. Add watermelon, feta and mint and gently mix.
4. Serve topped with pecans.

Notes

- Grilling watermelon really brings out the flavor, changes the texture and makes a great addition to this salad. Cut the watermelon into big chunks/slices so it doesn't fall through the grill.
- Don't like kale? Substitute spinach to keep this dish "eye healthy."
- Want more greens in your salad? Add chunks of cucumber or celery for added texture.
- Want some sweetness? Swap out the apple cider vinegar for balsamic vinegar, or add a drizzle of pomegranate.
- Don't let the watermelon rinds go to waste. Pickle them by bringing to a boil: 1C apple cider vinegar, 1T vanilla extract, 1 ½C water, 2T salt, 1C sugar, 1T pickling spice or ½ t whole allspice berries, ½ t peppercorns. Boil 3 minutes until sugar dissolves, and carefully pour over rinds in 2 to 4 pint glass jars. Refrigerate for 24 hours before eating. Will keep 1 month unopened, and up to 3 weeks after opened.

Sources: Johns Hopkins Medicine, Healthline, Hungryhealthyhappy.com, Simplyrecipes.com.

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NEWSLETTER

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CONSIDER MAKING A DONATION TODAY!

RRF is a public charity and our efforts to cure retinal disease are enhanced by support from our community. RRF accepts secure donations at retinaresearchfnd.org. To go directly to the RRF online giving page, focus your phone's camera (Android or iPhone with iOS 11 or later) or your iPad, on the QR code displayed here and open the link. Of course, you can always mail your donation to the RRF office.

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For more information on ways to give, call: 713-797-1925. Thank you for helping us fund innovative research to discover cures for the retinal diseases that damage and destroy vision!

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