RETINA RESEARCH FOUNDATION
NEWSLETTER

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Rapid Blood Sugar Decline May Lead To Vision Complications

Surely you have heard of the much discussed Ozempic effect? These days, stories of patient experiences with semaglutides (brand names: Ozempic and Wacovy injections and Rybelsus tablets) prescribed for type 2 diabetes mellitus and weight loss dominate the headlines and the airways. These medications have tremendous potential for improving health, with possibly protective effects on the heart, liver and kidneys in addition to helping people lose weight and reducing the risk of many ailments. However, less often discussed are the documented reports of rare instances of increased retina complications after starting these medications. In fact, the Ozempic patient information lists changes in vision as a possible serious side-effect of using the medication.

Why is this? Any treatment that rapidly lowers blood sugar levels may initially cause blurred vision, worsening of diabetic retinopathy and macular complications. Changes in sugar levels can cause a change in the shape of the eye's lens and cause blurred vision. The eye lenses of older adults becomes less flexible, so vision takes longer to stabilize when the body experiences changes in blood sugar levels. Other complications may include vitreous hemorrhage, macular edema, and the need for laser treatment or injection treatment for worsening diabetic retinopathy, and even temporary loss of vision, which usually can be treated. Fortunately, as the retina adjusts to lower sugar levels, these symptoms typically diminish within three to four months, and in the long run, the retina will be healthier as blood sugar is controlled.

The most important steps you can take if you are considering taking these medications are:

- See an ophthalmologist or a retina specialist to get an eye exam before beginning treatment. This is especially important if you know you have diabetes because of diabetes-related retina complications associated with this medical treatment.
- Make sure to let your ophthalmologist know of any other diabetes control medications you are using.
- Get your eyes checked regularly once you begin taking the medications. Your physician will track for any vision changes and recommend potential treatments if necessary.
- If you already have vision-threatening changes due to diabetes, routine monitoring of the retina during treatment will help to quickly identify any worsening and stave off any threat of permanent loss of vision from diabetic retinopathy.

Considering taking Ozempic or a similar medication?

Consult with your ophthalmologist before beginning treatment

Researchers continue to monitor the relationship between retina problems and blood sugar levels changes following use of semaglutides. A clinical study that is expected to end in February, 2027, known as the FOCUS trial, will provide more information about the long-term effects of using these medications on diabetic retinopathy and other diabetes-related complications.

Sources: AAO, NIH and Novo Nordisk

RRF 2024 Luncheon and Honorary Lectureship

RRF is pleased to announce that David M. Gamm, MD, PhD, will be the honorary speaker at the RRF spring luncheon to be held on May 15, 2024.

David M. Gamm, MD, PhD, is the Emmett A. Humble Distinguished Director of the McPherson Eye Research Institute, the Sandra Lemke Trout Chair in Eye Research, and a Professor of Ophthalmology and Visual Sciences at the University of Wisconsin-Madison. He is also a member of the Waisman Center Stem Cell Research Program, the UW Stem Cell and Regenerative Medicine Center, the American Society for Clinical Investigation, and the American Institute for Medical and Biological Engineering. In 2016, Dr. Gamm co-founded Opsis Therapeutics, where he currently serves as Chief Scientific Officer. The company's objective is to move stem cell therapies for degenerative retinal conditions into human clinical trials.

In his clinical practice, Dr. Gamm diagnoses and manages a wide range of pediatric eye and vision disorders. To improve patient care, Dr. Gamm also conducts potentially life-changing research. The driving concept behind Dr. Gamm's work is to one day be able to restore some measure of vision to patients whose sight has been diminished or lost due to damage to the cells of their retina(s). Specifically, his research focuses on advancing human pluripotent stem cell technology for the purpose of generating cells and tissues for use in retinal disease modeling and cell replacement therapies for blinding disorders such as retinitis pigmentosa and age–related macular degeneration.

When asked about his decision to concentrate his research efforts in this specific area, Dr. Gamm has said, "*When (University of Wisconsin scientist) James Thomson pioneered human embryonic stem cells in 1997, I saw the promise and possibility of taking his discovery in a direction that could be relevant and make a difference for retina patients for whom there are no treatments.*"

"*(Today) we and others are able to take a skin or blood sample and, through a series of steps, generate an unlimited supply of retinal cells from any individual. This never ceases to amaze me.*"

> *"As a pediatric eye surgeon, I diagnose and treat many kinds of inherited retinal disease. The most frustrating (cases) are the ones I cannot do anything about. To be part of taking this work (human pluripotent stem cell technology) forward in an effort to help patients and families is what gets me up in the morning."*

Sources: Harrington Discovery Institute, 2017-18 Annual Publication. Comments made following Dr. Gamm's selection as the 2016 Gund-Harrington Scholar. These scholars are selected for their outstanding research programs to slow, prevent or cure blindness; University of Wisconsin-Madison, Waisman Center post, Feb, 2023.

RRF will hold its biennial luncheon at noon on May 15, 2024.

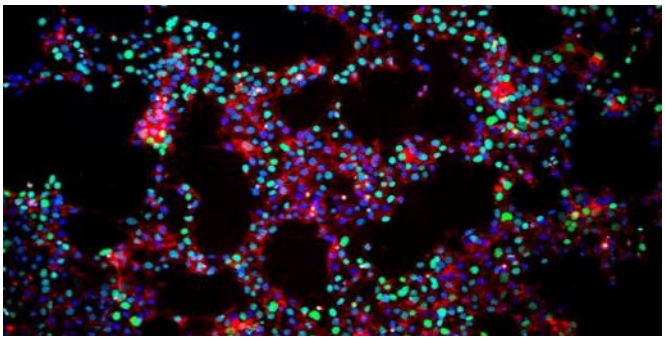
If you are interested in attending to learn more about Dr. Gamm's groundbreaking research and RRF's vision research programs, please contact the RRF office at rrf@retinaresearchfnd.org or 713/797-1925.

Human Induced Pluripotent Stem Cells (hiPSC): A Brief History and Explanation

The Nobel Prize in Physiology and Medicine

The Nobel Prize for Physiology and Medicine was awarded to the Japanese stem cell researcher, Shin'ya Yamanaka, and his British colleague, Sir John Gurdon, in 2012 for their discovery of reprograming mature cells into human induced pluripotent stem cells.

Based on a method developed by Sir Gurdon, Dr. Yamanaka succeeded in rejuvenating (reprogramming) mature cells of an adult organism by using transcription factors, to return the cells to a developmental stage similar to an early embryonic state. These cells were then almost as versatile as embryonic stem cells and could form many different tissue types, such as nerve or blood cells. Like embryonic stem cells, these reprogrammed cells are also pluripotent.



Induced pluripotent stem cells that have been reprogrammed from normal adult human tissue but have not yet been differentiated. *Image courtesy of Gladstone Institutes*

Simply, the term *"pluripotent"* in biology means capable of developing into fully-differentiated cell types. Two types of pluripotent cells available for research are: embryonic stem cells (ES) that have the unlimited capacity to divide, self-renew and differentiate into cells of early primary germ cell layers, and human induced pluripotent stem cells (hiPSC), that are derived from adult somatic cells, any of the body's cells except the reproductive (germ) cells, that have been genetically reprogrammed to an embryonic stem (ES) cell-like state through the forced expression of genes and factors important for maintaining the defining properties of ES cells.

Today, cell lines exist that provide a good basis for use in scientific research. Importantly, clarification as to whether hiPSCs actually fully correspond to ES cells in their abilities is a question still being studied, and extensive research continues to ensure there are not unintended consequences of their use. One advantage of hiPSCs over ES cells is that no embryos have to be used to produce them. Importantly, the reprogrammed cells are compatible with the immune system of the cell donor and are therefore particularly promising for therapeutic modeling and use.

Sources: UCSF; Stem Cell Network

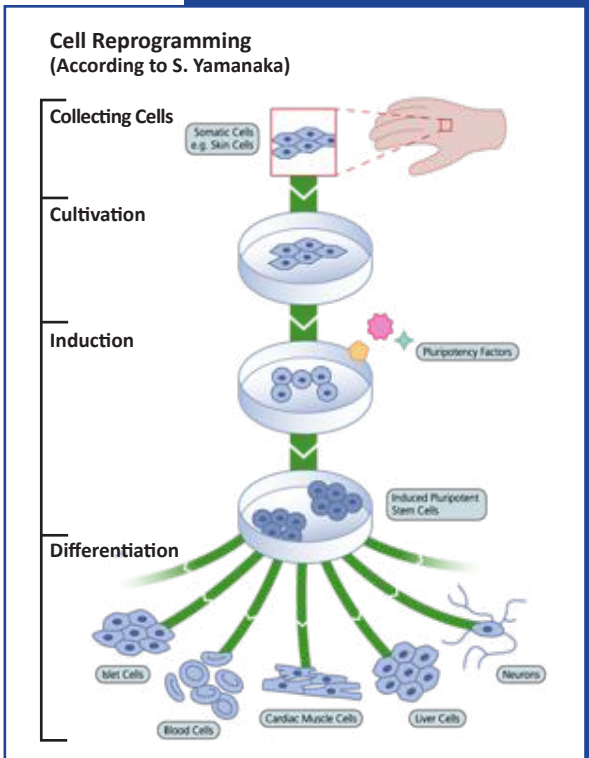


Fig.: Derivation of induced pluripotent stem cells.

Eye Floaters: What Are They? Are They Treatable, and When Do They Really Matter?

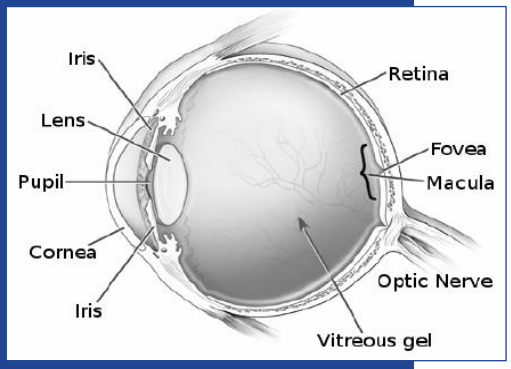
Shawn Kavoussi, MD

RRF Scientific Advisor and Advisory Trustee: Shawn Kavoussi, MD

Dr. Kavoussi is a board certified retina surgeon and the founder of the Texas Retina Center located in the Texas Medical Center.
For more information, visit drkavoussi.com

Eye Floaters
Source: drkavoussi.com

Certainly we all have noticed small squiggly lines or dots, collectively termed "floaters," moving across our field of vision; particularly when looking at the sky or a bright computer screen.



Source: National Eye Institute

Floaters can resemble strands of hair, cobwebs, circles and/or dots. Though they may appear as if located in front of our eyes, they in fact originate inside of our eyes; and represent a normal structure known as the vitreous.

The vitreous is a clear, gel-like sack that fills the eye's largest cavity behind the iris and pupil. While mostly comprised of water, small amounts of collagen and hyaluronic acid help give the vitreous its shape and make the floaters visible in certain lighting situations, which is normal even at a young age.

In the absence of trauma, floaters can remain relatively stable for several decades. But as the years pass and the eye ages into the third, fourth, fifth and sixth decades, the vitreous contracts and liquefies, gradually lifting itself from the retinal surface at the back wall of the eye, which can render the floaters gradually more visible.

The time the floaters really matter is when a sudden, spontaneous change or increase in floaters or black specks in one eye can be seen, representing a separation of the rear portion of the gelatinous sack from the retinal surface. The new floaters may be accompanied by intermittent flashing lights in the same eye, representing ongoing traction of the vitreous gel against the retina in certain small areas.

Why is this a critical time? Because detached retinas, which can lead to irreversible vision loss, are caused by torn retinas; and studies show that approximately 10% of the general population develops a torn retina at or around the time of this vitreous gel separation.

The sudden onset of new flashes or floaters in one eye is a critical time to see a retinal specialist for a dilated eye exam.

If detected early enough, a torn retina can be treated with a quick in-office laser procedure without further consequence. However, if left untreated, a torn retina progresses to a detached retina, which can result in vision loss and requires urgent surgical repair.

Torn and detached retinas aside, certain patients develop larger-than-average floaters that can become bothersome as they interfere with reading, driving and computer work. The brain can adapt to even large floaters after several months, but both laser and surgical floater removal options are available to treat unmanageable floater symptoms for the right candidates as a last resort.

In summary, most floaters are harmless and represent normal cavities within the gel-like structure of the eye. But any sudden change or increase in floaters in one eye, especially if accompanied by flashing lights, warrants an urgent retinal exam so that any vision-threatening conditions can be identified and promptly treated.

Protecting Your Eyes From Sun Damage Extends Beyond Viewing the Total Eclipse

Millions of Americans are expected to watch the total solar eclipse this month, and even with wearing eclipse glasses, some will become worried about inadvertent damage to their eyes. Fortunately, the vast majority of eclipse viewers will be fine, and even if someone experiences eye strain, the effects will most likely be temporary. The symptom to be concerned about is blurred vision, which may be noticed in hours up to a day following the event.

During the 2017 total solar eclipse it is estimated that 150 million Americans viewed the event. There were around 100 documented cases of eye damage across all of America and Canada, according to Ralph Chou, an expert on eclipse eye safety with the University of Waterloo in Canada. The reason it is hard to do real damage is simple; looking at the sun at any time is difficult because it is so bright that it is uncomfortable. The human eye has evolved to avoid staring directly at the sun, we blink, tears form, and we look away.

It is more likely that you may damage your eyes from repeated exposure to the sun while you are outdoors or driving – at any time of year. Just as eclipse glasses protect your eyes when viewing a solar eclipse, routinely wearing sunglasses with ultraviolet (UV) protection will protect your eyes year-round, as will wearing a hat.

Ophthalmologists treat a number of conditions that can result from longer-term exposure to the sun and can be discovered during a routine eye exam or when symptoms become bothersome:

Cataracts: Cataracts produce cloudy or blurry vision and reduce night vision. Over 50% of Americans older than 80 have cataracts or have had them removed. Sun exposure without adequate eye protection can trigger or speed cataract development.

Macular degeneration: While more research needs to be done, it's possible that sun damage is linked to macular degeneration. This eye disease causes loss of vision in the center of your eye, making your vision blurry and the likelihood of developing it increases with age and repeated sun exposure over time.

Photokeratitis: This painful eye condition can be compared to a sunburn that affects parts of your eye, usually the cornea and most often is experienced in both eyes. The cornea is the clear protective outer layer of your eye. If you have photokeratitis, in addition to pain, you may notice blurred vision, have a feeling that something is in your eye, or get a headache. Rarely there might be a temporary loss of vision.

Cancer: You can get skin cancer on any part of your body, including the skin near your eyes, on your eyelids or in rare cases, in the eye itself, called ocular melanoma. This form of cancer is most serious and can be deadly if it spreads inside your body.

Growths on the eye: Sun damage can cause growths on your eye. A pterygium is a fleshy overgrowth of the conjunctiva, the thin clear membrane on the surface of the eye. In most cases, a pterygium grows from the inner corner of the eye, nearest the nose. A pterygium requires treatment because it can scar the cornea. Another growth, pinguecula, can be on the inside or outside of the eyelid on the conjunctiva. This growth can cause dry eyes, redness, and inflammation.

Sources: NPR, NIH

Newly Funded 2024 RRF Pilot Study Research Grants

Researchers receiving RRF pilot study research grants conduct experimental, basic science projects designed to investigate previously unstudied or understudied lines of inquiry into the causes of retinal diseases. The emphasis of the program is to obtain new understanding and to advance scientific knowledge with the hope that these studies lead to future ongoing projects and ultimately, to new therapies for treating vision loss from retinal diseases.

From a very competitive grant application pool, five new researchers are receiving funding in 2024:

Ching-Kang Jason Chen, PhD, University of Texas Health Science Center at San Antonio, Department of Molecular Medicine;

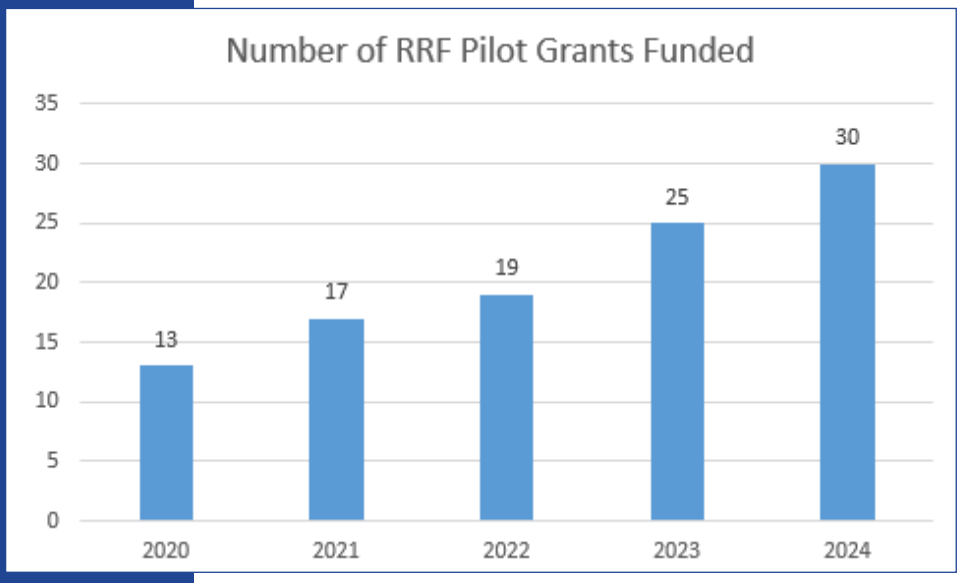
Eleftherios Paschalis Ilios, PhD, Massachusetts Eye and Ear Infirmary, Department of Ophthalmology;

Jakub K. Famulski, PhD, University of Kentucky, Department of Biology;

Georgia Zarkada, PhD, University of Connecticut, Department of Physiology and Neurobiology.

Thanh Hoang, PhD, University of Michigan, Department of Ophthalmology;

Throughout the last five years, RRF has more than doubled the number of annual award grants. Visit retinaresearchfnd.org to learn more about the 30 pilot study research projects currently funded by RRF.



Cholesterol May Have Your Ophthalmologist Seeing Yellow Spots

The first thing you might think about upon hearing the word "Cholesterol" is heart disease, but cholesterol, a type of fat or lipid, is essential for the healthy functioning of many processes in the body, and is a significant component of all mammalian cell membranes, including those found in the retina. The onset of age-related health conditions, metabolic disorders or diabetes can lead to a buildup of cholesterol in the retina similar to other parts of the body like the heart and vascular system, the brain and spinal cord; however, disruptions in these complex lipid processes in the retina are also associated with several congenital and age-related disorders.

Particularly as we age, it is important to have annual eye exams even when your vision seems normal. During your exam, your physician may see lipid and protein deposits – yellow spots, under the retina, called Drusen. While having a few smaller Drusen deposits are usually harmless and sometimes naturally disappear, in larger quantities, Drusen may be an early sign of retina disease. The Drusen deposits can be soft or hard and sometimes, they crystalize making them very reflective and visible in images of the eye. It is important to note that having these deposits signals that the cholesterol homeostasis, the cellular balance of cholesterol within the retina, is disrupted.

There's no treatment available for Drusen, and its specific role in the development of age-related macular degeneration (AMD), a progressive eye condition that can impair central vision, is still not fully understood.

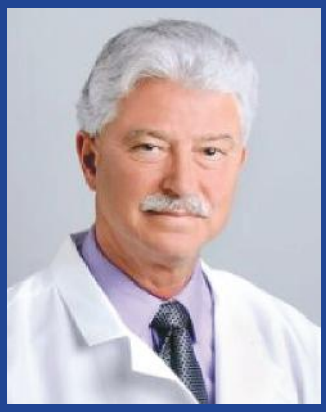
Extensive Drusen, as shown in this retina photo, increases the risk of AMD.

An expert on this topic, Dr. Steven Fliesler affiliated with SUNY, University of Buffalo, New York, and colleagues conducted a comprehensive review of the published research, from the past five decades, looking at the role cholesterol plays in retina health, with a focus on animal studies or animal derived cell in vitro studies.

Dr. Fliesler's review indicates that the fundamental processes involved in establishing and maintaining retina cholesterol homeostasis appear to be fairly well understood, particularly under normal physiological conditions. It is an essential component in the healthy functioning of retina cells.

Dr. Fliesler's review also identified knowledge gaps, and with new tools and techniques now available, future research will be able to address and answer remaining questions about abnormal conditions and move closer to development of new therapies. Areas needing further research include: understanding why some retina cells (photoreceptors) are more sensitive to changes in cholesterol than others, and specifically why are photoreceptor cells, whose loss of function leads to development of diseases such as AMD, more susceptible to damage or even death from buildup of certain types of cholesterol than other cells in the retina?

To protect your vision and especially if you have cholesterol related health concerns, visit your ophthalmologist regularly, and maintain healthy lifestyle habits such as exercising regularly and eating a diet full of fruits, vegetables, whole grains and healthy protein-rich foods like fish and seafood, legumes and nuts.



Steven J. Fliesler, PhD
Distinguished Professor, State University of New York (SUNY) and Vice-Chair/Director of Research Department of Ophthalmology, Jacobs School of Medicine and Biomedical Sciences, SUNY-University at Buffalo.

Dr. Fliesler is a recipient of the **RRF Paul Kayser International Award in Retina Research** given in collaboration with the International Society for Eye Research (ISER). First presented in 1986, this international award recognizes lifetime achievement by a vision scientist who has made a significant contribution to the understanding of vitreoretinal diseases or disorders. Dr. Fliesler received his award and presented a lecture at the biennial ISER meeting held in Queensland, Australia, in February, 2023. The award includes a $45,000 research grant in support of his ongoing work.

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