RETINA RESEARCH FOUNDATION
NEWSLETTER

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The Human Gut's Link to Retinal Health

The human body is host to hundreds of trillions of microorganisms, together with their genome and surrounding environment referred to as the microbiome. This vast number of microbes, including bacterial, fungal and protozoal microorganisms, make up our microbiota that live in and on many parts of our body. These microorganisms live on our skin and in the human gastrointestinal tract – our gut, and even in the eye. A study conducted at the National Eye Institute (NEI) suggests that the eye possesses its own microbiome that protects against ophthalmic infections. "We've established the proof of concept of a central ocular microbiome," Anthony St. Leger, PhD, research fellow in NEI's Laboratory of Immunology, said. Citing abundant evidence that "good" gut bacteria have a key role in modulating immunity, he added, "Now we show that this relationship exists in the eye. That's important for how we think about treating ocular disease." (JAMA. 2017;318(8):689.)

A Gut-Retina Axis

The relationships between the body and the microorganisms are symbiotic and change as the body fluctuates between a steady, healthy state and disease. Scientific evidence has revealed a relationship between nutrition, the gut microbiota, chronic inflammation and a number of human inflammatory diseases, including those that cause chronic progressive retinal diseases, including age-related macular disorders (AMD), diabetic retinopathy (DR) and retinitis pigmentosa (RP).

There is strong interaction between the microbiome and the body's immune function, with many microbe metabolites activating the immune system. When healthy, the gut system is impermeable, not letting molecules cross wall linings, but when there are changes to the microbiome, the cell walls of the gut become permeable, allowing microbiota to leak into the body. Increased intestinal permeability contributes to chronic, low-grade systemic inflammation proven to lead to the development of numerous chronic diseases with inflammatory components. Over time, inflammation contributes to hastening aging at a cellular level. Basically, aging causes many body functions to decline, including a reduction in the diversity of the gut microbiome that compounds the body's inability to repair cell damage. For the retina, which is highly vulnerable to inflammation due to its poor renewal and repair capacity, even minor damage can have devastating consequences. These changes make the retina more susceptible to oxidative stress, hyperglycemia and increased intraocular pressure that can lead to glaucoma. Uveitis, AMD, Sjogren's syndrome associated with dry-eye, DR, RP, and glaucoma have been linked to gut microbiome abnormalities, although research is still in the early stages.

The microbiome is comprised of trillions of microscopic organisms that live in and on us and contribute to human health and disease, including retinal health.

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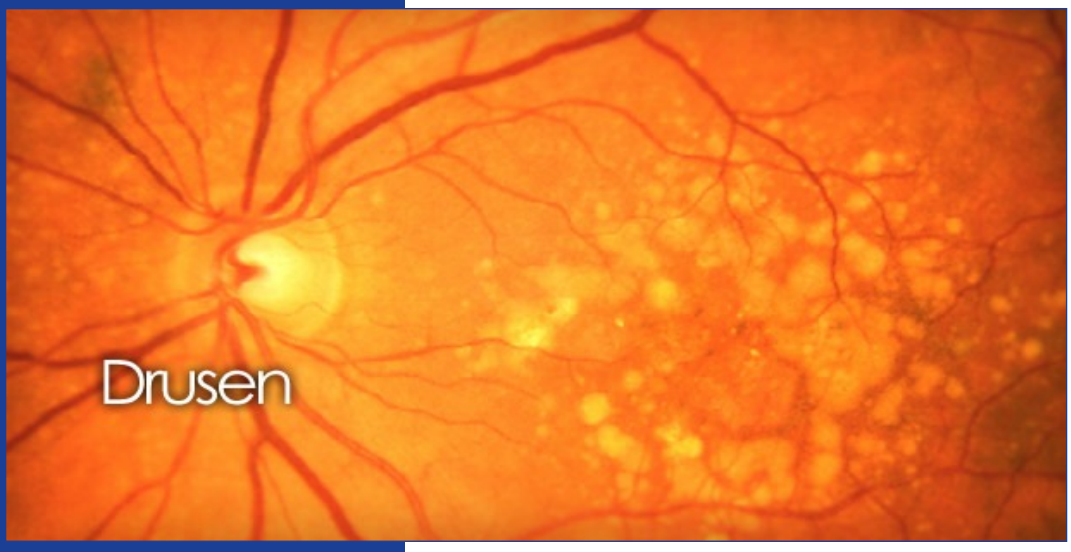
Can Changes in Diet Make a Difference?

The gut microbiome can be influenced by several dietary components. This fact raises the possibility that in the future, manipulating the gut microbiota could impact retinal health. There is a growing body of research that supports the hypothesis of a gut-retinal axis, and the impact of dietary factors that lead to changed gut microbiota and inflammatory diseases of the eye. A study according to Rowan et al (2017) found dietary factors could represent a link between alternation of gut microbiota and AMD. A "high-glycemia diet" has been associated with some typical clinical signs of AMD, while the "lower-glycemia diet" was not, and was found to limit the accumulation of advanced glycation end products, polyunsaturated lipids often found in Drusen and related peroxidation end products.

A mouse model study showed that changes in the gut microbiome are linked to RP, observing retinal degenerative abnormalities like deterioration of retinal responsiveness to light stimuli and visual acuity. When an imbalance of gut microbiota was observed, levels of protective bacteria were lower and non-protective bacteria were higher in diseased mice compared to those without RP (Kutsyr et al. (2021)). It is becoming clear that the manipulation of the intestinal microbiota and the consequent maintenance of the physiological composition of the ocular microbiome both seem to represent valid alternatives for the prevention and or treatment of eye diseases.



The sign of an altered immune response in the retina is seen by deposits and later Drusen that gradually accumulate. Drusen likely do not cause AMD, but having Drusen increases a person's risk of developing AMD, and they may be a sign of AMD. Drusen are made up of lipids and proteins and can be seen by your ophthalmologist during a routine exam as yellow deposits under the retina.

Emerging as possible strategies for prevention and/or treatment are targeting the microbiota to restore or modulate its composition through the consumption of live bacteria (probiotics), non-digestible or limited digestible food constituents such as oligosaccharides (prebiotics), or both (synbiotics), or even fecal transplants. Although the clinical efficacy of probiotic therapy warrants further investigation, it does represent a promising field of research with potentially exciting results.

All this is to say that by incorporating probiotic and prebiotic foods into your diet, it will not hurt and just might help reduce inflammation, and at least not speed up the retina's aging process. Even more important are regular visits to your ophthalmologist who can monitor slight changes to the retina that might indicate future issues.

Source: Frontiers in Microbiology, 14 January 2022, Gut Microbiome in Retina Health: the Crucial Role of the Gut-Retina Axis, Scuderi, Troiani and Minnella

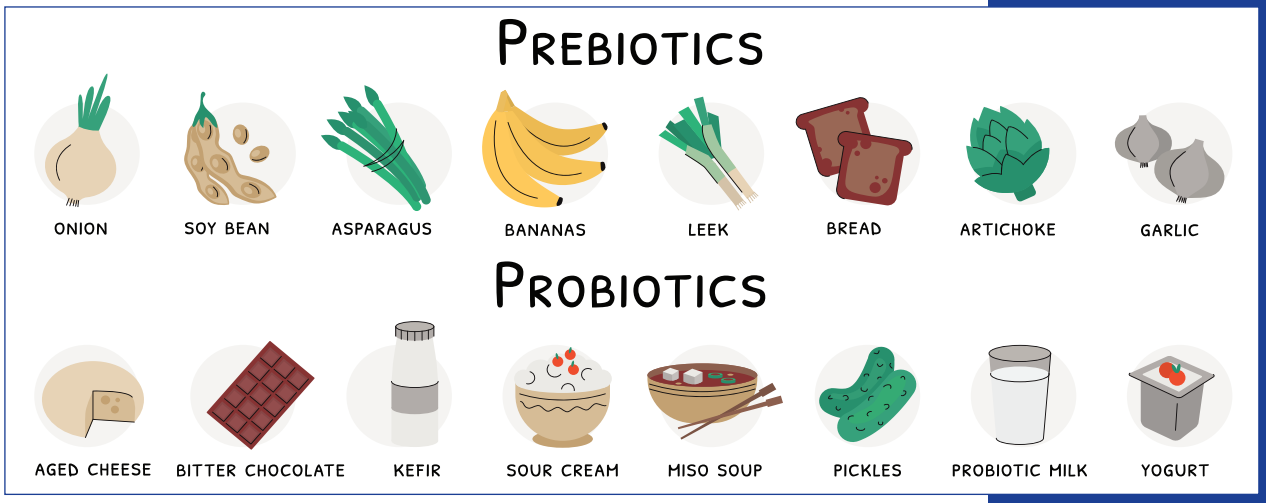
Foods Thought to Promote A Healthy, Balanced Gut

Two classes of foods, prebiotic and probiotic, are thought to positively impact the microbiota and help reduce inflammation.

Prebiotic Foods: Prebiotic foods feed the microbiota. Many foods contain prebiotic fiber, but typically do not contain enough for a therapeutic dose. A list of the most common foods with a higher percentage of fiber to feed your gut microbiota, which are easy to find and tolerate includes:

- Garlic
- Bananas and plantains
- Chicory root, often a coffee additive
- Honey
- Asparagus
- Artichokes and jerusalem artichokes
- Leeks and onions
- Whole grains
- Legumes
- Unpasteurized apple cider vinegar
- Dandelion greens and root
- Cooked and cooled potatoes and rice
- Some mushrooms, shiitake, maitake, and reishi
- Marine Algae – spirulina, chlorella, nostoc
- Brewer's yeast.

Be aware, when you introduce prebiotic foods into your diet, you could experience some discomfort. It is best to consult with a physician prior to making any major dietary changes.



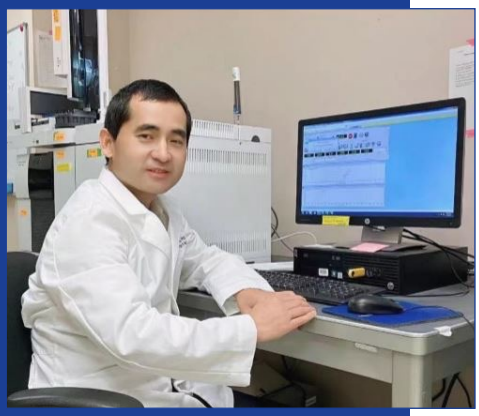
Probiotic Foods: Probiotic foods contain live bacteria and add to the gut's microbiota. There are several different classes and types of probiotics, some of the most common include: *Bifidobacterium, Lactobacillus and Saccharomyces boulardii*, which is a type of yeast.

Food manufacturers may also call probiotics "live or active cultures." Many fermented products contain probiotics. Examples of probiotic foods include:

- Aged cheeses, such as cheddar, gouda, or mozzarella
- Kefir, a probiotic milk drink
- Traditional buttermilk *(must not be cultured)*
- Dairy and non-dairy yogurt
- Fresh, sour dill pickles
- Kombucha, a fermented tea
- Miso
- Sauerkraut
- Water or brine-cured olives.

Source: medicalnewstoday.com

RRF Researcher Studies Nutritional Strategies for Future AMD Treatment



Dr. Jianhai Du, West Virginia University School of Medicine, Morgantown, WV, RRF funded researcher since 2019.

Jianhai Du, PhD, Associate Professor in the Departments of Ophthalmology and Visual Sciences, and Department of Biochemistry, West Virginia University School of Medicine, is interested in the role of nutritional building blocks in the health of the retina. More specifically he researches the relationship between retinal degeneration and the amino acid, proline. Proline catabolism, the breaking down of this complex molecule into more simple components, releases energy and produces metabolic fuel for the retina. The human body does make proline, integral to stimulating the body's production of collagen and other mechanisms, but it is also consumed when eating protein-rich foods such as fish, egg whites, dairy and meat.

The retina is one of the highest energy-consuming organs, exceeding the energy needs of even the brain. The retina receives its nourishment from the retinal pigment epithelium (RPE), a layer of cells between the light-sensitive photoreceptors of the retina and a layer of blood vessels, called the choroid, lying below. The RPE's intermediary role is to nourish the retina and maintain its health by transporting molecules in and out, getting rid of dead cells, secreting hormones, modulating immune factors, and more. Research suggests that the RPE's crucial role in supporting the retina has the effect of magnifying the degeneration process, and is, in fact, the eye tissue where macular degeneration begins.

With RRF's support, Dr. Du has established that mice, fed a diet without proline, show decreased visual function, strongly suggesting that proline is important to maintaining retinal metabolism and function. Dr. Du also has found that an RPE-specific proline transporter (SLC6A20A) is important for retinal energy metabolism and visual function, and that the RPE uses dietary proline to produce crucial amino acids to nourish the neural retina. In a mouse model where a critical molecule (PRODH) needed for proline catabolism is deleted, Dr. Du is measuring levels of retinal metabolism, visual function and retinal degeneration. Subsequently, he will test gene therapy to reintroduce the PRODH to the eye's retinal tissues to determine whether proline catabolism has a role in protecting the retina from degeneration. Dr. Du's goal with this research project is to develop a nutritional-based treatment for age-related macular degeneration based upon his knowledge of the effects of proline deficits in retinal tissues, and possibly using gene therapy to address those deficits.

Dr. Du, far right, and his laboratory team.

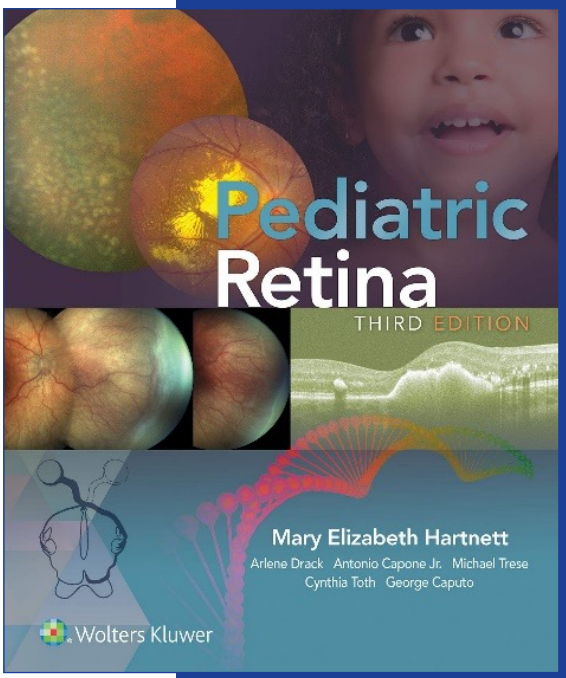
Hartnett Receives 27th Annual Gertrude D. Pyron Award

The RRF Gertrude D. Pyron Award recognizes outstanding vision scientists whose work contributes to knowledge about vitreoretinal disease. The award offers a research grant and honorarium, and is presented each year at the ASRS Annual Meeting at which time the recipient delivers a lecture. Chosen by the ASRS Awards Committee, the 27th annual award recipient is Mary Elizabeth Hartnett, MD.

Dr. Mary Elizabeth Hartnett Calvin S. and JeNeal N. Hatch Presidential Endowed Chair in Ophthalmology and Visual Sciences, Distinguished Professor, University of Utah.

Dr. Hartnett is an adjunct professor at the University of Utah in the departments of Neurobiology and Pediatrics. She is also the founder and director of Pediatric Retina at the John A. Moran Eye Center and principal investigator of the Retinal Angiogenesis Laboratory.

Dr. Hartnett's NIH-funded laboratory of vascular biology and angiogenesis has studied mechanisms causing pathology in age-related macular degeneration (AMD) and retinopathy of prematurity (ROP). Her work in AMD has been to understand the mechanisms involved in activation and invasion of choroidal endothelial cells in front of the RPE in order to maintain vasculature that is physiologic and not damaging beneath the RPE. Her lab's work in ROP provided the proof of concept to regulate an angiogenic signaling pathway by inhibiting VEGF to facilitate more normal intraretinal vascularization toward the ora serrata as well as to inhibit abnormal extraretinal neovascularization. She has applied her work to protocol development of collaborative clinical trials.



Dr. Hartnett's prolific publication record includes 227 articles in peer-reviewed journals and over 40 book chapters. She created the first-ever academic textbook on the subject, Pediatric Retina, an invaluable resource for residents and ophthalmologists worldwide, which offers a comprehensive overview of all aspects of diagnosis and treatment of major medical and surgical diseases in this challenging field.

Dr. Hartnett has received numerous awards, including in 2019, the Paul Kayser / RRF Global Award, presented at the Biennial Pan-American Association of Ophthalmology Congress, and in 2017, the RRF Mills and Margaret Cox Macula Society Research Project Grant, administered by The Macula Society.

Retina Research Foundation Luncheon

The RRF community of leaders, scientists, supporters and friends gathered on May 11th for the 2022 RRF Luncheon and Honorary Lecture. It was an opportunity to celebrate RRF's achievements in vision preservation since its founding in 1969, and to educate attendees about new advances in science and academics. To date, RRF has contributed nearly $40 million to basic research projects focused on eradicating blindness due to retinal disease and/or degeneration.

RRF was pleased to welcome honorary speaker, Dr. Marc Boom, President and CEO, Houston Methodist, a hospital system that includes a world-renowned research institute. Dr. Boom led Houston Methodist in its efforts to educate the public about COVID-19 and the need for vaccines. The hospital system was the first in the country to mandate vaccines for employees and physicians. Over 2,500 organizations nation-wide followed, adopting vaccine mandates that impacted millions of healthcare professionals and staff, and ensuring the provision of patient care throughout the pandemic. Dr. Boom discussed Houston Methodist's academic research program, stressing the system's commitment to attracting premier physicians and researchers to Houston, to promoting innovation through leading-edge clinical trials and to adapting the latest clinical and technical advances to provide our community with the safest and highest quality care possible.

Dr. Alice McPherson
Founder and President,
Retina Research Foundation

Marc L. Boom, MD, MBA
2022 RRF Honorary Lecturer

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Bishop Scott Jones and
Mary Lou Reece

Rich Walton
RRF Board Director and
Dr. Alice McPherson
RRF Board President

Dr. Zheng Jiing and
Dr. Jason Chen, RRF Chair,
Baylor College of Medicine

RRF Welcomes New Members To Board of Managing Directors

The RRF Board of Managing Directors is pleased to share the announcement of new members, Joseph W. Royce and Lewis H. Gissel, III who joined the Board as of April, 2022.

Joseph W. Royce

Mr. Royce practices law in Houston as Senior Counsel with Gray Reed & McGraw LLP. His legal career spans over 50 years in the fields of estate planning, administration of estates and trusts, and the operation of private foundations. He currently serves as Trustee, Ralph H. and Ruth J. McCullough Foundation; Trustee, Phi Delta Theta Foundation; Trustee, William A. and Madeline Welder Smith Foundation; and Member of Advisory Council, Briscoe Center for American History, University of Texas.

After receiving his BA in History from Southwestern University and graduating from the University of Texas Law School, Mr. Royce clerked for Judge John V. Singleton, Jr. in Houston. While working there, he met and later married Jacque Royce. Together, they raised two children, who have eight children. Jacque and Joe were 40-year members of Chapelwood United Methodist Church until Jacque, a longtime member of the RRF Board of Managing Directors, passed away in 2021. Mr. Royce's association with RRF goes back 30 or more years, to the time when Dr. Alice McPherson first saved his wife's sight following a detached retina. She became a Managing Director of RRF in 2006 and devoted a great deal of time and effort to her role. Mr. Royce is excited to be joining the RRF Board of Managing Directors and to carry on this relationship.

Lewis H. Gissel, III

Mr. Gissel currently serves as Executive Vice President for Texas Regional Bank and is responsible for all commercial banking activities for the Houston Region. His banking and finance experience spans nearly three decades in Houston and includes a focus on non-profit, healthcare, franchise and commercial and industrial industries. His interest in retina research stems from personal retinal issues, which led him to becoming a third generation patient of Dr. Alice McPherson, and from his long-standing familiarity with the work of the Foundation through his father, deceased RRF Board Member, L. Henry Gissel, Jr.

Mr. Gissel is a member of The Forest Club, St. Martin's Church, and The Houston Livestock Show & Rodeo. He has served as Past President of The Forest Club and Spring Branch Memorial Sports Association and presently is serving as Co-Chair 2017 Spring Branch Independent School District Bond Oversight Committee.

Mr. Gissel holds a BBA in Marketing from the University of Mississippi. He and his wife, Amy, have two children, who like their parents are Spring Branch ISD graduates. As a family, they enjoy taste testing the best BBQ from around the state, traveling to tropical beach destinations and of late, playing competitive pickle ball.

Jacque and Joe Royce
RRF Luncheon, 2015

Amy and Lewis Gissel, reigning
Forest Club Pickle Ball Champions

RETINA RESEARCH FOUNDATION
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Roger Dale Rorie
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Richard Murray

IN HONOR OF

Patricia K. Boyd
Gus and Agatha Brann
Gus Comiskey, Jr.
Howard and Ada Kiatta

Bob Brown and Family
Sugar Land Lions Club Charity

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John and Charlotte Henderson Estate
Marcella Dale Mangiaracina Estate

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YOUR GIFT TO RRF CAN SAVE SIGHT. Your support is vital to what we do. The success of our efforts to stimulate innovative research to better understand the retinal diseases that damage and destroy vision depends on donations from our community. RRF accepts secure donations at retinaresearchfnd.org, or you can mail your donation to the RRF office. If you are an Amazon shopper, you can also support RRF by making your online purchases through amazonsmile. It's easy to give this way. Use the link on RRF's website or go to smile.amazon.com to register and select RRF as your charity of choice. Once selected, all your future purchases will result in an automatic donation to RRF of 0.5%, at no additional cost to you. Thank you!

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