

RETINA RESEARCH FOUNDATION NEWSLETTER

Foresight for Sight

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Genes and Inherited Retinal Diseases (IRDs)

Inherited genes determine an individual's physical characteristics that we can see, such as eye color or eye shape. Genetic ophthalmologic researchers now have evidence that genes may play a role in visible vision problems that occur in otherwise healthy eyes in children and adults. The list of common vision problems includes strabismus (cross-eyes), amblyopia (lazy eye), and refraction errors such as myopia (nearsightedness), hyperopia (farsightedness), and astigmatism. But genetics are also responsible for unseen and more serious retinal diseases that can cause severe vision loss or even blindness. As a group, these diseases are referred to as Inherited Retinal Diseases (IRDs).

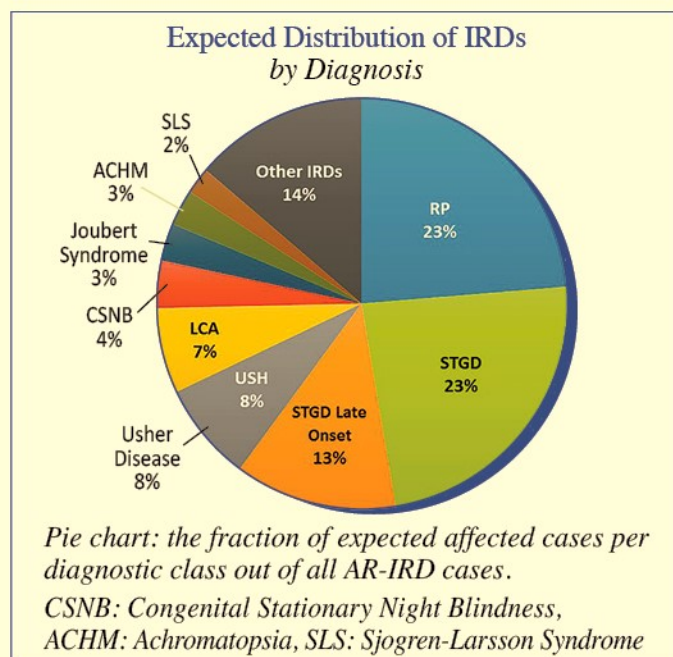
What are IRDs?

Inherited retinal diseases are a group of genetic disorders, where a change has occurred in one or more genes that contribute to proper retinal function. These conditions lead to vision loss, due to the progressive degeneration of the retina. IRDs are rare. They can affect individuals of all ages, can progress at different rates, and can be degenerative, meaning that the symptoms of the disease will get worse over time. Clinical symptoms vary across different IRD subtypes and some are more severe than others. **Retinitis Pigmentosa (RP)**, the most common form of IRD, retinal degeneration initially causes night blindness due to the loss of rod photoreceptor cells. In **Stargardt Disease (STGD)**, degeneration of a specific retinal region, the macula, causes a drastic change in central visual acuity. Other examples of IRDs are **Choroideremia**, **Cone-Rod Dystrophy**, and **Leber Congenital Amaurosis (LCA)**.

While it is currently unknown how many of our estimated 21,000 human genes are involved, more than 260 different genes have been identified as causing IRDs.

How rare are IRDs?

A recent computation of genotype data from six major world populations indicates that 2.7 billion people worldwide, 36% of the population, are healthy carriers of at least one gene mutation that can cause an autosomal recessive (AR) form of inherited retinal disease, a value that is probably the highest across any group of genetically caused conditions in humans. With this incidence, it would be expected that worldwide, 5.5 million people would be affected with an IRD, which is approximately one out of every 1,380 individuals.



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For more information on the genotype data computation study, visit: pnas.org/content/117/5/2710

Can IRDs be treated?

Given the many different IRDs, your physician will complete a patient and family history, clinical eye exam and imaging, and possibly genetic testing to determine the correct diagnosis. Advancements are creating treatment options for patients, including clinical trials for therapies that may save vision, but options are limited and not available for all IRDs. Research to develop new therapies includes various

approaches such as efforts to stop the disease from advancing by preventing cell death and slowing the degeneration of light sensitive cells in the eye, to return some degree of sight to patients through targeted gene therapies, or to actively simulate sight through a device called a “retinal prosthetic” that uses technology to convert images into impulses that are sent wirelessly to the brain. Numerous RRF supported vision scientists are researching the causes of IRDs in search of cures, including gene therapy and neuroprotective agents that will ultimately lead to future treatments.

If you are diagnosed with an IRD, Advocate for Yourself. Take an active role in your disease treatment and stay aware of clinical research opportunities. There are tools, services, and resources that patients and their families can use to stay informed and find help.

- Ask your physician about genetic testing options. The results will provide the most detailed diagnosis and inform the recommendation of the best possible treatment for the specific IRD. Ask your physician about sources for free genetic testing. Genetic testing is often a requirement before a patient can participate in clinical trials.
- Participate in patient data registries such as **My Retina Tracker** found at: fightingblindness.org/my-retina-tracker-registry. The free registry helps to connect patients with clinical research.
- Join a support group for patients with an IRD, or connect to an online community.

For more information, visit: preventblindness.org/inherited-retinal-diseases/

RRF Scientist Researching IRDs: Dr. Wolfgang Baehr

Dr. Wolfgang Baehr's lab, based at the University of Utah Health Science Center, has a longstanding interest in using animal models to investigate inherited retinal diseases, particularly retinitis pigmentosa (RP), Leber congenital amaurosis (LCA), and cone-rod dystrophies (CRD). RP clinically causes night blindness and progresses to significant peripheral visual field reduction (tunnel vision). Central visual acuity and cone function are often preserved until late in the course of the disease, but patients with end-stage disease will have no light perception at all. LCA is an even more severe disease where both rod and cone photoreceptors degenerate early in life, and often children are born blind.

Continuing a project first funded by RRF in 2018, Dr. Baehr focuses on the mechanisms underlying the development of INPP5E null mutations in the retina. A null mutation in a gene usually encodes a specific enzyme that leads to the production of a nonfunctional enzyme or no enzyme at all. INPP5E is an enzyme functioning as a "phosphatidylinositol polyphosphate phosphatase" in photoreceptor inner segments. Mutations in INPP5E are associated with Joubert Syndrome, characterized by a number of symptoms including RP or LCA.

Dr. Baehr's research team wants to understand: **1)** the consequences of the INPP5E knockout when the gene is made inoperative, **2)** what happens to INPP5E interaction with membranes, **3)** how do phosphoinositide levels change in the inner segment, basal body and connecting cilium, and **4)** why do axonemes not extend and discs not form. Without a precise understanding of mechanistic details, prevention or cure of the resulting inherited retina disease is not possible.

For more information on Dr. Baehr's work, visit: retinaresearchfnd.org



Wolfgang Baehr, PhD
University of Utah Health
Science Center
Emmett A. Humble Research Project



*Crystal structure of human
INPP5E*

*Photo credit:
Bryan William Jones/Moran
Eye Center*



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

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Recognizing Lifetime Achievement in Retina

Charles L. Schepens MD/AAO Award to Dr. Julia Haller



Julia A. Haller, MD
Wills Eye Hospital

The 2020 RRF Charles L. Schepens, MD/AAO Award was given to Julia A. Haller, MD, Ophthalmologist-in-Chief at Wills Eye Hospital, Philadelphia, PA. Her award lecture, *Retina in the Pandemic: Hear Our Roar*, was delivered during the American Academy of Ophthalmology's (AAO) virtual annual meeting. Dr. Haller discussed how Wills Eye Hospital's doctors and clinics dealt with the challenges of providing patient care during the COVID-19 pandemic. A significant and lasting development arising from the health and safety concerns is the increased use of **telemedicine** as a way to maintain contact with patients when in-person visits are not possible. The successful use of the technology proved to be extremely effective and efficient in providing the expected high standards of care, while simultaneously maintaining contact with patients, so much so that telemedicine will be a permanent and expanded part of eye care services moving forward. Dr. Haller pointed out that retinal outpatient visits, new patient visits, intravitreal anti-VEGF injections, and imaging all declined at her institution in the early phase of the pandemic, but with use of telemedicine and resulting protocols for referrals, a steady increase in visits began again in April. This is important because research has shown

that even short term interruptions in treatment can have lasting vision consequences. Dr. Haller indicated research clinical trials were initially affected, but are "back on track." She closed by saying, "retina has risen to the challenges to every aspect of our mission during the pandemic with leadership and courage."

Retina Research Foundation &
Schepens International Society
are proud to congratulate



Julia A. Haller, MD

13th Recipient of the
Charles L. Schepens, MD
AAO Award



Retina Research Foundation



To view highlights of Dr. Haller's lecture, visit: aao.org/interview/highlights-from-2020-schepens-lecture

Telemedicine, an effective technology solution for providing quality eye care.

Paul Kayser International Award in Retina Research to Samuel M. Wu, PhD

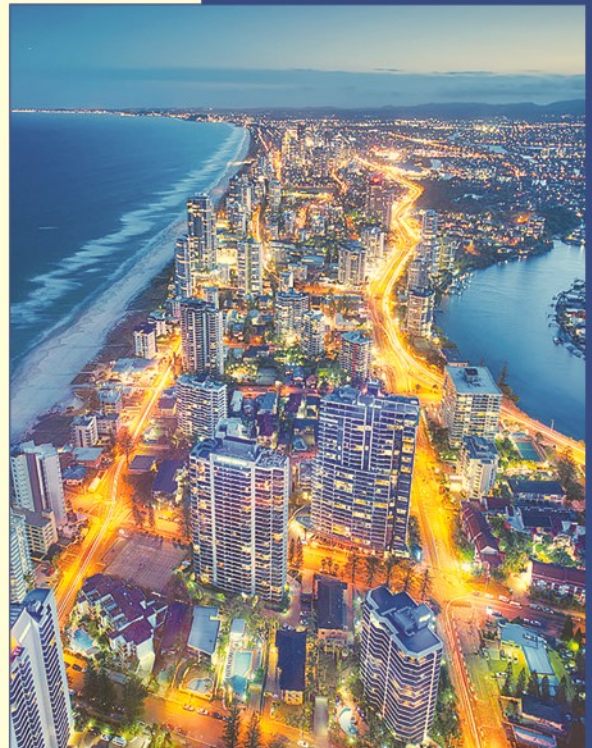
Samuel Miao-Sin Wu, PhD, Professor of Ophthalmology, Neuroscience, and Molecular Physiology and Biophysics at Baylor College of Medicine, Houston, Texas, was selected by an ISER-appointed committee as the 2020 recipient of the Paul Kayser International Award by the International Society of Eye Research (ISER), an award given in collaboration with RRF since 1986.

Dr. Wu's presentation lecture, "*A2 Amacrine Cell mediated Signaling Pathways in Healthy and Diseased Mammalian Retinas*," was given during a virtual webinar in December, 2020. Usually this award is given at ISER's Biennial Meeting, so Dr. Wu will have the opportunity to travel to the 2022 ISER meeting that will be held on the Queensland Gold Coast, Australia where he will be recognized for his 2020 RRF Paul Kayser International Award.

Dr. Wu, also an RRF pilot study researcher, explores the detailed molecular and synaptic mechanisms underlying retinal function and eye diseases. His laboratory pioneers investigations on rod and cone photoreceptor interactions and parallel information pathways in the retina. Dr. Wu has made discoveries on how individual ion channels, receptors, synapses and gene products carry out retinal function in normal animals and cause dysfunction in mouse models for IRDs such as retinitis pigmentosa, Bardet Biedl Syndrome, and glaucoma. For nearly four decades, RRF has significantly contributed to Dr. Wu's research and laboratory, which is considered one of the most highly advanced in the world. To learn more about his research, visit retinaresearchfnd.org.



*Samuel Miao-Sin Wu, PhD
Cullen Eye Institute
Baylor College of Medicine*



*Australian Gold Coast
photo credit: Luke Zeme*



*Dr. Richard Hurwitz
Texas Children’s Hospital,
Baylor College of Medicine*

RRF Scientist Researching Childhood Cancers and IRDs: Dr. Richard Hurwitz

RRF affiliated researcher, Dr. Richard Hurwitz, Texas Children’s Hospital, Baylor College of Medicine, Houston, Texas, is looking for ways to treat children with advanced retinoblastoma. He has completed the first clinical trial using “suicide gene therapy,” a method of forcing tumor cells to produce a protein that converts a drug to a locally toxic agent to treat the disease. Dr. Hurwitz is also interested in developing gene therapy options for inherited retinal degenerative disorders such as Stargardt Disease. His gene therapy delivery strategy uses a harmless virus to deliver the correct genetic material to selected cells in the eye. For more information on Dr. Hurwitz’s work visit: retinaresearchfnd.org

2021 New RRF Pilot Study Researchers



Erika D. Eggers, PhD
University of Arizona

“Investigation and modulation of inner retinal dysfunction in diabetes”



Vladimir Kefalov, PhD

Washington University in St. Louis

“Understanding how the G90D and G90V rhodopsin mutations cause blindness”



Andrius Kazlauskas, PhD
University of Illinois at Chicago

“Hyperglycemia-induced mitochondrial adaptation”



Seongjin Seo, PhD
University of Iowa

“Development of mutation-independent gene therapy approaches for CEP290-LCA”

Is Something Wrong With My Child's or Grandchild's Vision?

You might not realize your child or grandchild is suffering from a vision problem because children often are not aware that they have one. They cannot articulate that they are losing sight and they easily adapt to gradual vision loss. The most important way you can protect their vision is by maintaining regular visits to your pediatrician or family doctor during which your child will receive a simple vision test. If needed, your physician will make a referral to an ophthalmologist.



But as a parent or grandparent, are there clues that can indicate a vision problem? Yes, persistent squinting is one, and another can be found in family photos! If you notice a white or yellow light shining in your child's or grandchild's eye in a photo, it



*A visible "glow" or white pupil in the child's eye
Photo credit: Childhood Eye Cancer Trust*

might be an indication of a problem. Physicians call this "white pupil," sometimes it is called "the glow." These glows can be symptoms of more than 20 different eye diseases and conditions such as retinopathy of prematurity found in premature infants, a growth or retinoblastoma - a rare tumor in the eye, an inherited retinal disease (IRD) such as familial exudative

vitreoretinopathy (FEVR) or Norrie disease, or a cataract, retinal detachment or dysplasia. When family gatherings can again take place, pay special attention to those treasured family photos, and if you see a white pupil or "the glow" appearing repeatedly in a young child's photos, both eyes should be checked promptly.

A GIFT TO RRF CAN SAVE SIGHT

Retina Research Foundation, a public foundation, supports research directed toward treating, preventing or curing all retinal diseases that damage and destroy vision. Your support is vital to the success of our efforts. RRF accepts secure donations at retinaresearchfnd.org. You can also support RRF by making your online purchases through [amazon smile](https://www.amazon.com/smile). Use the link on RRF's website or go to smile.amazon.com to register. Select RRF as your charity of choice. Once selected, all future purchases will result in an automatic donation to RRF of 0.5% of your purchases, at no cost to you. Thank you!

ALL GIFTS AND BEQUESTS ARE TAX DEDUCTIBLE.

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Jarlene Phelps

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Suzanne S. Miller
Mr. and Mrs. Frank Farese

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