FALL 2018

IN FOCUS

A PUBLICATION FOR MEMBERS OF THE FOUNDATION FIGHTING BLINDNESS

‹ QUOTABLE ›

"Accept no one's definition of your life; define yourself."

Harvey Fierstein

WHAT'S INSIDE

Retinal Regeneration:
Releasing Your Inner Salamander

Thomas Reh, PhD, receiving his FFB 2018 Ed Gollob Board of Directors Award

For someone with a retinal disease such as retinitis pigmentosa or macular degeneration, their vision loss is caused by photoreceptor degeneration. Photoreceptors are the retinal cells that capture light and convert it into electrical signals, which are sent back to the brain where they are used to create the images we see.

Many research groups from around the world are investigating ways to create new photoreceptors from stem cells for transplantation into the retina for vision restoration. But this approach presents many challenges including risk of immune response to the new photoreceptors, as well as the difficulty in getting them to functionally integrate with the patient's existing retinal tissue. The delicate surgery often necessary for transplanting the new cells can be risky, as well.

However, Thomas Reh, PhD, an FFB-funded expert in retinal development and regeneration at the University of Washington, is working on an innovative approach with the potential to revolutionize how scientists go about restoring vision. He's trying to find a way to coax the retina to grow its own, new photoreceptors.

In fact, at the 2018 VISIONS Conference in San Diego, he received FFB's Ed Gollob Board of Directors Award for his research paper in the journal *Nature* on the emerging technique, which was inspired by his earlier work with amphibians.

"The paper is the culmination of research in my lab spanning more than 30 years. I first learned about the ability of salamanders to regenerate their retinas

Continued on page 3

>> *Help end blindness. Use the enclosed envelope to make a life-changing gift.*

Team Becca: An Inspired Family Takes on Usher Syndrome

By Lauren Moyer

Jake and Beth Lacourse are motivated every day to help their two-year-old daughter, Rebecca, overcome the challenges of Usher syndrome type 1B.

Two-year-old Rebecca Lacourse

Of course, there were difficulties when Rebecca was born deaf. But the diagnosis later on of Usher syndrome meant their daughter was also progressively losing her vision. Rebecca currently has bilateral cochlear implants, which provide more hearing for her, but she still has some trouble with balance and night vision.

Jake and Beth have been proactive in finding ways to help their daughter thrive as a toddler, and at the same time, they support research to find a cure for Usher syndrome.

Beth's cousin, who has Bardet-Biedl syndrome — another complex condition causing retinal degeneration, among other issues — reached out to Beth when Rebecca was first diagnosed to let her know about the Foundation Fighting Blindness. Since then, Beth started Team Becca to participate in the Boston VisionWalk. Beth also organized a fundraiser to celebrate Rebecca and help raise more funds for a cure. In just two years, their Team Becca fundraiser has had over 400 attendees and raised over $19,000 for the Foundation.

"We're most interested in supporting the research to find cures for Usher syndrome," says Beth. "That's why we participate in the VisionWalk and started our own fundraiser."

While Beth focuses on fundraising, Jake keeps busy through creative outlets to help his daughter. He recently invented a toy that would help Rebecca learn words using braille. This toy, called the BecDot, is a 3D printed rectangular box that introduces children to braille words using small, colorful toys and letters. Jake's BecDot invention has been featured in articles on *People*, *Today Show, TechCrunch*, and more.

"Rebecca inspires us and we just want to make her life easier," says Beth. "We want to feel like we are doing something to help her and are making an impact."

Beth and Jake want others being diagnosed with similar diseases to know that it's "not the end of the world."

"Rebecca is doing great," says Beth. "Of course there are struggles and there's ups and downs, but she's such a happy little girl. And she loves life and even when she falls down, she gets right back up. She's a very tough and determined girl."

You can follow Rebecca's journey on the Lacourse family's blog at https://memoriesforbecca.com/.

IN FOCUS

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when I was an undergraduate student at University of Illinois," said Dr. Reh. "There was a professor there, Dr. David Stocum, who studied limb regeneration in these amphibians. I was fascinated that these animals had this potential. When I started my own lab as an assistant professor in Calgary, I began to study regeneration in tadpoles."

Dr. Reh's paper in *Nature* highlighted his retinal regeneration advancements in mice. His team was able to derive neurons from retinal cells called Müller glia, which normally provide architectural support and a number of protective and waste-disposal functions. The new neurons connect with the existing circuits and the cells respond to light. However, the new neurons are not full-fledged photoreceptors, so there is much more work to be done in advancing the approach into a human study.

"The FFB is currently funding our research to derive actual photoreceptors from Müller glia," said Dr. Reh. "The next step would be to develop an appropriate gene therapy for humans to direct expression of the protein Ascl1, the catalyst for deriving photoreceptors from Müller glia."

Dr. Reh added that safety and efficacy studies in a large-animal model would be necessary before moving the approach into a clinical trial. "While more work needs to be done, Dr. Reh's regenerative therapy is potentially another achievable option for retinal regeneration that has advantages over transplantation," said Stephen Rose, PhD, FFB's chief scientific officer. "He's an innovator willing to look outside of the box. That is important in getting vision-restoring, retinal-disease treatments out to the people who need them."

Refillable Capsule Performs Well for Reducing Treatment Injections for Wet AMD

Genentech
A Member of the Roche Group

For many people with wet age-related macular degeneration (AMD), treatments like Lucentis® (ranibizumab) can save and even restore vision. They work by stopping the growth of leaky blood vessels that cause degeneration of photoreceptors and central vision loss.

However, these therapies require regular injections into the eye at an ophthalmologist's office. The regimen can be prescribed as often as monthly or at least several times a year.

Genentech's Port Delivery System (PDS) — a tiny, refillable capsule, slightly longer than a grain of rice — was developed to reduce the treatment burden by continuously delivering a special formulation of ranibizumab to the retina. The PDS, which is surgically implanted into the eye, may enable people with wet AMD to go several months before needing a refill.

For 59 PDS patients receiving the 100 mg/mL dose in a Phase II clinical trial, approximately 80 percent were able to go six months or longer until their first refill was required. The PDS is refilled using a customized needle in a minimally invasive office-based procedure.

Genentech is determining the most appropriate dose and treatment interval for its Phase III clinical trial for the PDS. Companies seek FDA approval for treatments if they perform well in Phase III.

"While current wet AMD therapies often work for patients, they require regular eye injections and visits to the eye doctor. Getting treatment can be burdensome, especially for elderly patients," says Stephen Rose, PhD, chief scientific officer, Foundation Fighting Blindness. "The Port Delivery System shows promise for reducing this inconvenience and helping ensure patients are getting the treatment they need to preserve their vision."

Recap: VISIONS2018 Conference Brings Together Visually Impaired Community

Nearly 500 attendees enjoyed the three-day conference showcasing advances in retinal research

FOUNDATION FIGHTING BLINDNESS

VISIONS2018

LEARN. SHARE. EXPERIENCE. HOPE.

Gene therapy session with (left to right) Shannon Boye, PhD, University of Florida; David Williams, PhD, UCLA; Tim Stout, MD, PhD, Baylor

Fai Mo, Volunteer of the Year, Western Region (left); Eddie Russnow, FFB Board Director

Benjamin Yerxa, PhD, FFB Chief Executive Officer, presents research update during opening luncheon

LCA session with (left to right) Shannon Boye, PhD, University of Florida; Ben Shaberman, FFB; Daniel Chung, DO, Spark Therapeutics

Canine and human representatives from Guide Dogs of America

Linda Worth, Colorado, receives 2018 Outstanding VisionWalk Award from Eddie Russnow, FFB Board Director

Representatives from Aira demonstrate their navigation technology

Emmett Cunningham, Jr., MD, PhD, Clarus Funds, delivers closing session presentation

Steve Alper, FFB Board Director, receives FFB's Builder of Sight Award

Thank you

to the following VISIONS2018 partners

Platinum Partner

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Gold Partners

Spark THERAPEUTICS

Shire

Silver Partner

MEIRAGTx

Bronze Partners

agtc

Second Sight

VITRISA THERAPEUTICS

David Brint, FFB Chairman (left); Steve Browne, FFB National Trustee (right)

Retinal-Disease Therap

Inherited Retinal Disease

(select

Gene Therapies	Progress
Achromatopsia (CNGB3) – AGTC	Phase 1/2
Achromatopsia (CNGB3) – MeiraGTx	Phase 1/2
Achromatopsia (CNGA3) – AGTC	Phase 1/2
Achromatopsia (CNGA3) – Tubingen Hosp	Phase 1/2
Choroideremia (REP1) – Nightstar	Phase 3
Choroideremia (REP1) – Spark	Phase 1/2
Choroideremia (REP1) – Tubingen Hosp	Phase 2
LCA and RP (RPE65) – MeiraGTx	Phase 1/2
LCA and RP (RPE65) – Spark	FDA Approved
RP (PDE6B) – Horama	Phase 1/2
RP, Usher, others (optogenetic) – Allergan	Phase 1/2
RP, Usher, others (optogenetic) – GenSight	Phase 1/2
RP (RLBP1) –Novartis	Phase 1/2 Pen.
Retinoschisis (RS1) – AGTC	Phase 1/2
Retinoschisis (RS1) – NEI	Phase 1/2
Stargardt disease (ABCA4) – Sanofi	Phase 1/2
Usher syndrome 1B (MYO7A) – Sanofi	Phase 1/2
X-linked RP (RPGR) – AGTC	Phase 1/2
X-linked RP (RPGR) – MeiraGTx	Phase 1/2
X-linked RP (RPGR) – Nightstar	Phase 1/2

y Clinical-Trial Pipeline

es and Dry AMD: 33 trials

trials)

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Cell-Based Therapies	Progress
AMD-dry (RPE) – Astellas	Phase 1/2
AMD-dry (RPE) – Cell Cure	Phase 1/2
AMD-dry (RPE on scaffold) – Regen Patch	Phase 1/2
RP, Usher (retinal progenitors) – jCyte	Phase 2b
RP, Usher (retinal progenitors) – ReNeuron	Phase 2
Stargardt (RPE) – Astellas	Phase 1/2

Molecules, Proteins, AONs	Progress
AMD-dry (C3 inhibitor) – Apellis	Phase 3
AMD-dry (C5 inhibitor) – Ophthotech	Phase 2
Bardet-Biedl (metformin) – Tubingen Hosp	Phase 2 Pen.
LCA (CEP290, AON) – ProQR	Phase 1/2
Stargardt disease (emixustat) – Acucela	Phase 2
Stargardt disease (deuterated vit A) – Alkeus	Phase 2
Stargardt disease (C5 inhibitor) – Ophthotech	Phase 2

Visit **www.ClinicalTrials.gov** for more details and trial contact information.
This document is for informational purposes only. Information is subject to change, and its accuracy cannot be guaranteed. Created June 2018.

www.FightBlindness.org

FFB Funding More than $2 Million in New Research

By Ben Shaberman

The Foundation Fighting Blindness has announced funding for seven new research projects to advance the development of treatments and cures for retinal degenerative diseases. Each project will receive a total of $300,000 over a three-year period.

The grants were selected through FFB's annual call for research proposals from individual investigators. Seventy scientists submitted requests for funding. Applications were reviewed by FFB's Scientific Advisory Board, which is comprised of the world's leading retinal experts.

"Many of the funded research projects are cross-cutting, meaning they have the potential to benefit a broad range of people, independent of the mutated genes causing their retinal diseases," says Stephen Rose, PhD, FFB's chief scientific officer. "Also, some projects address a critical gap in our understanding and modeling of disease, and have potential to move the field forward in a significant way."

Here are summaries of the seven new projects:

Gene Therapy to Preserve Vision by Protecting Cones
Daniel Lipinski, PhD, Medical College of Wisconsin

Dr. Lipinski is developing a gene therapy to prevent the degradation of proteins that leads to the death of cones, the photoreceptors that provide central vision, vision in lighted conditions, and the ability to read and drive. Such a treatment has the potential to help people with retinitis pigmentosa, Leber congenital amaurosis, and Usher syndrome by working independent of the patient's gene mutation.

Designing Optimal Viral Gene-Delivery Systems for Retinal Diseases
Leah Byrne, PhD, University of Pittsburgh

Scientists engineer viruses to deliver therapeutic genes to the retina. The optimal design of a given gene therapy delivery system depends on the type of retinal cell that needs to be treated. Designing a delivery system includes choosing the right promoter (i.e., the gas pedal for the gene) and the right capsid (i.e., the container for the gene). Dr. Byrne will create a toolbox

of efficient and specific viral capsids and promoters for every retinal cell type, and make it available to the research community, thereby enhancing and expediting gene-therapy development for retinal diseases.

An Optogenetic Therapy with Improved Light Sensitivity
John Flannery, PhD, University of California, Berkeley

Optogenetic therapies bestow light-sensitivity (visual function) to surviving retinal cells after photoreceptors are lost to advanced retinal diseases such as retinitis pigmentosa, Usher syndrome, and age-related macular degeneration. However, many current optogenetic therapies in development have limited light sensitivity and will only work in very bright settings. Dr. Flannery's team is developing optogenetic approaches that will work in a broader spectrum of lighting conditions and potentially provide better perception of details than other optogenetic alternatives in clinical trials.

Inhibiting Immune Response to Transplanted RPE Cells
Trevor McGill, PhD, Oregon Health & Science University

One concern with retinal cell transplantation is a harmful immune response to the newly introduced cells. Retina microglia are first-responder immune system cells that help the retina to recognize and fight foreign substances. While this is a normal biological defense mechanism, this response can adversely affect the transplantation of healthy cells into the retina. Dr. McGill is investigating drugs that can inhibit microglia

when retinal pigment epithelial cells (RPE) are transplanted to treat retinal conditions such as age-related macular degeneration and Stargardt disease.

VLC-PUFA Therapeutics for Dry AMD and Dominant Stargardt Disease

Paul Bernstein, MD, PhD, University of Utah

Very long-chain polyunsaturated fatty acids (VLC-PUFAs) are non-dietary fats that are uniquely found in the retina and just a few other tissues in the human body. They are believed to be essential for the maintenance of photoreceptors. Mutations in the gene ELOVL4 lead to depletion of VLC-PUFAs and autosomal dominant Stargardt disease. Dr. Bernstein is working with lipid chemistry specialists at the University of Utah to develop potential VLC-PUFAs treatments to be tested in the lab. Earlier studies suggest that VLC-PUFAs may also be beneficial to people with dry age-related macular degeneration.

Identifying Genetic Modifiers that Affect Severity of Stargardt Disease

Frans Cremers, PhD, Radboud University Medical Center, Netherlands

Autosomal recessive Stargardt disease is most often caused by mutations in the gene ABCA4. However, the severity of vision loss varies widely in patients, even between siblings with the same mutations in the same family. Researchers believe there are other genetic modifiers that impact disease severity. Dr. Cremers and his team are genetically analyzing Stargardt disease in families and sibling pairs to identify potential modifier genes, which may also be targets for vision-preserving therapies.

Large Animal Model Development for Usher Syndrome 1B

Martha Neuringer, PhD, Oregon Health & Science University

Animal models for Usher syndrome have been of limited use, because they don't exhibit vision loss (only exhibit hearing loss). Dr. Neuringer and her colleagues are using the gene-editing technique CRISPR/Cas9 to develop a large animal model of Usher type 1B, which is caused by mutations in the gene MYO7A. She believes that these animals will exhibit vision loss and will therefore be useful for testing potential Usher 1B therapies.

Global Survey Details Achromatopsia Patient Journey

People with Achromatopsia describe long journey to diagnosis & their experiences living with their condition

Achromatopsia is a rare inherited retinal disease most commonly caused by mutations in the CNGB3 and CNGA3 genes and is associated with severely reduced visual acuity and extreme photosensitivity, resulting in daytime blindness. Profound sensitivity to light during the day results in significant impairment in visual function, and many patients cope by wearing darkly tinted glasses to lessen the effect of light sensitivity.

Results of a new global survey conducted by the patient advocacy organization Achroma Corp. provided previously unavailable insights into the experience of people with achromatopsia.

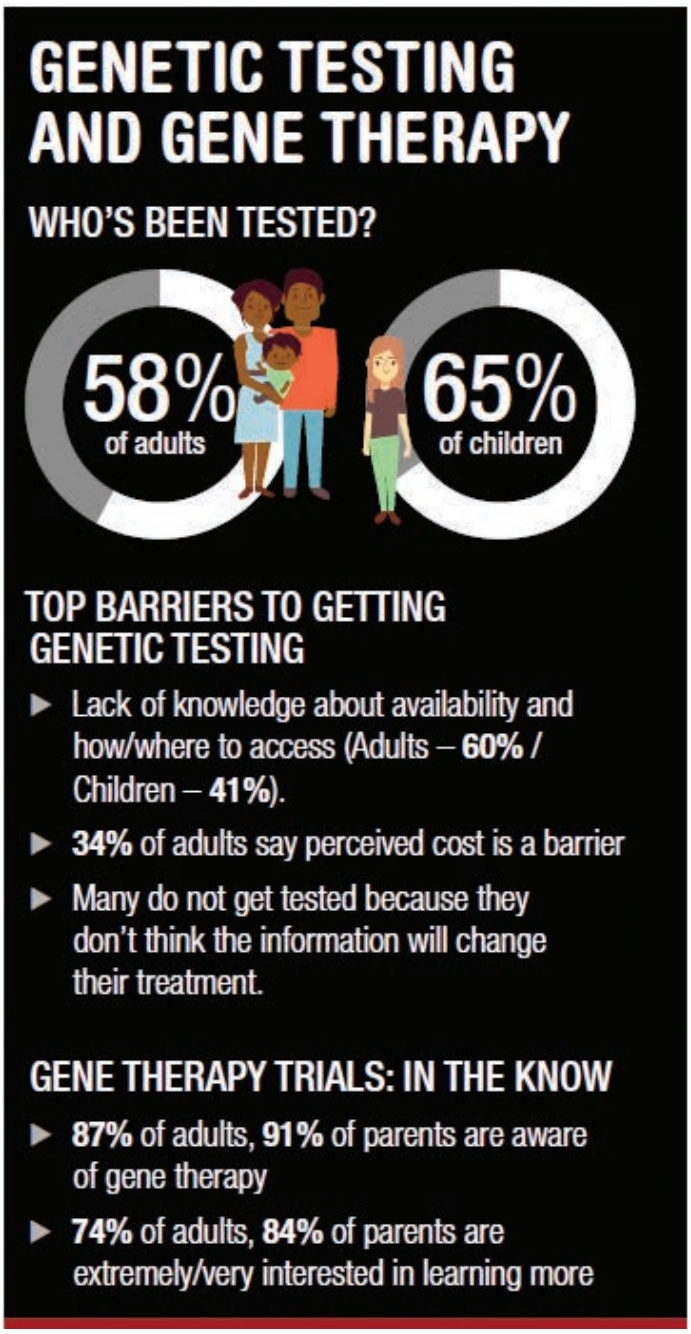
The *Understanding the Achromatopsia Patient Experience* online survey was conducted on behalf of Achroma Corp. and in partnership with the gene therapy company Applied Genetic Technologies Corporation (AGTC). It received 226 responses from individuals who have been diagnosed – or have a child who has been diagnosed – with achromatopsia.

The survey results indicate that only 58 percent of adults and 65 percent of children with achromatopsia have received genetic testing to confirm the correct diagnosis and the underlying gene responsible. Additional information about the survey can be found at www.achromacorp.org/PatientJourney.html.

Currently, members of the Foundation Fighting Blindness registry who reside in the United States and have a clinical diagnosis of an orphan inherited retinal dystrophy studied by the Foundation can participate in a FREE genetic testing and ocular genetic counseling study with the assistance of their eye doctor. This research study is available through the Foundation Fighting Blindness registry "My Retina Tracker℠" (www.myretinatracker.org).

By knowing their specific gene mutation, achromatopsia patients, as well as others living with inherited retinal diseases, may have the opportunity to participate in applicable clinical trials. These clinical trials are investigating potential treatments for the condition while also advancing the scientific understanding of their disease.

AGTC is recruiting for two separate Phase 1/2 clinical trials for individuals with achromatopsia caused by mutations in either the CNGB3 or the CNGA3 gene. For information about the AGTC gene therapy clinical trial program, please visit www.agtc.com.



Results from Understanding the Achromatopsia Patient Experience Survey

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VisionWalk

A CURE IS IN SIGHT

The Foundation Fighting Blindness VisionWalk program includes approximately 40 walk events annually in cities throughout the U.S. Each walk is fun and family friendly and offers an opportunity for communities to come together in support of the Foundation's mission to fund research leading to cures for blindness caused by retinal degenerative diseases. Register at **www.VisionWalk.org**

Indianapolis	9/8/2018
Cincinnati/N. KY	9/22/2018
Montgomery County, MD	9/23/2018
Twin Cities (Minneapolis - Saint Paul)	9/23/2018
Pittsburgh	9/29/2018
Philadelphia	10/6/2018
St. Louis	10/6/2018
Washington (Seattle)	10/6/2018
Colorado	10/13/2018
Charlotte	10/20/2018
Houston	10/20/2018
Westchester-Fairfield, NY	10/21/2018
Triad, NC	10/27/2018
Los Angeles	10/27/2018
Boston	10/27/2018

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IN FOCUS

This and previous issues of ***In Focus*** are **available online**, where you can get the latest retinal-research information as well as updates on the Foundation's activities on your PC and mobile devices.

Accessible, electronic versions of the newsletter are also available.

For an online and accessible version of In Focus, go to:

www.Blindness.org/InFocus

AT A GLANCE

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PLANNED GIVING

Please consider, as part of your lasting legacy, remembering the Foundation Fighting Blindness in your will, trust, or other estate planning. For more information, visit our planned giving website at

www.MyPlanToFightBlindness.org