CORAL GABLES, FLORIDA // SEPTEMBER 8–9, 2016

HOPE FOR VISION SCIENCE SYMPOSIUM

A one day conference dedicated to research into treatments and cures for retinal degenerative diseases

HOPE for VISION
www.hopeforvision.org

HOPE FOR VISION SCIENCE SYMPOSIUM

"Dwell in possibilities."
– emily dickinson

It is an honor to most cordially welcome you to the Hope for Vision Science Symposium. There will be a series of Symposia presented on cutting edge research and technology that aims to treat, cure, or restore vision loss due to retinal degenerative diseases.

You are amongst the most eminent scientists in the diverse and exciting areas of retinal degenerative research. Accept our heartfelt gratitude and support as you endeavor in the areas ranging from stem cell studies, gene therapy, microchips and implants to restore or preserve vision, neuroprotective factors, as well as novel drug therapies.

The meeting place is generously donated by the Institute for Cuban and Cuban-American Studies [ICCAS] located on the beautiful campus of the University of Miami in Coral Gables, Florida. Hope for Vision is a 501c3 non-profit organization dedicated to raising funds to advance ground-breaking scientific and medical research for the treatments and cures of blinding genetic retinal diseases.

Hope for Vision distributes the funds raised for sight saving research at leading institutions whose scientists are working tirelessly for cures and treatments of blinding retinal diseases. We aim to foster communication between those at the forefront of research on retinal degenerative diseases ,and preservation and restoration of vision.

We extend an opportunity for you to present your latest research findings, meet with colleagues, and discuss your work in a welcoming environment. The presentations will be followed by a period of open discussion at the end of the day. Enclosed are the abstracts that will be presented today. We appreciate your participation greatly. It is our hope that this Scientific Research Symposium will foster mutual relationships, and a foundation for cooperation among researchers across countries and disciplines.

On behalf of Hope for Vision and all those challenged by vision loss and blindness, we would like to once again welcome you to this important Science Symposium. We hope that it will be a productive worthwhile meaningful enriching experience for you. YOU ARE OUR HEROES. We hope you can feel how our hearts see you…

With gratitude and love,

betti lidsky
HOPE FOR VISION

SCIENTIFIC SYMPOSIUM 2016 AGENDA

HOPE for VISION
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9:00 AM
WELCOME BY DR. ALEX COHEN
Chairman, Hope for Vision Board of Visionary Scientists

9:30 AM
DR. KIN-SANG ANSON CHO
Postnatal onset of retinal degeneration by loss of embryonic *Ezh2* repression of Six1

9:45 AM
DR. DAVID BIRCH
New outcome measures for clinical trials in retinal degenerative disease

10:00 AM
DR. MICHELLE HASTINGS
Antisense oligonucleotides for the treatment of Usher syndrome

10:15 AM
DR. DEBORA FARBER
Human embryonic stem cell-derived extracellular vesicles (hESEVs) and their potential use for retinal regeneration

10:30 AM
DR. BYRON LAM
Choroideremia Gene Therapy

10:45 AM
DR. ELLIOTT SOHN
Biocompatibility of a novel biopolymer scaffold for retinal cell transplantation in the subretinal space of pigs

11:00 AM
Break

11:15 AM
DR. ALFRED LEWIN
Gene Delivery of Secreted Cell Penetrating Peptides to Prevent Retinal Degeneration in a Mouse Model of Oxidative Stress in the Retinal Pigment Epithelium

11:30 AM
ZHUO-HUA PAN
Optogenetic Gene Therapy for Vision Restoration

11:45 AM
DR. JOHN FLANNERY
Optogenetic vision restoration

12:00 PM
DR. RONG WEN
Treatment strategies for DHDDS-associated RP: Can small compounds work?

12:15 PM
DR. STEPHEN TSANG
Too little vs. too late in treating retinitis pigmentosa

1:00 PM
Lunch Break

2:00 PM
DR. PETR BARANOV
Glial cell derived neurotrophic factor for photoreceptor rescue: direct and indirect neuroprotection strategies

2:15 PM
DR. SAMUEL JACOBSON
Complexity of the retinal degeneration in RP caused by *rhodopsin* gene mutations

2:30 PM
DR. ALUN BARNARD
Developing new treatments for blindness in the MacLaren Research team

2:45 PM
DR. ALEX COHEN
Moderated Open Discussion

5:00 PM
Meeting Closed

ABSTRACTS

POSTNATAL ONSET OF RETINAL DEGENERATION BY LOSS OF EMBRYONIC *EZH2* REPRESSION OF SIX1

Kin-Sang Anson Cho, PhD

Some adultonset disorders may be linked to dysregulated embryonic development, yet the mechanisms underlying this association remain poorly understood. Congenital retinal degenerative diseases are blinding disorders characterized by postnatal degeneration of photoreceptors, and affect nearly 2 million individuals worldwide, but ~50% do not have a known mutation, implicating contributions of epigenetic factors. We found that embryonic deletion of the histone methyltransferase (HMT) *Ezh2* from all retinal progenitors resulted in progressive photoreceptor degeneration throughout postnatal life, via derepression of fetal expression of *Six1* and its targets. Forced expression of *Six1* in the postnatal retina was sufficient to induce photoreceptor degeneration. *Ezh2*, although enriched in the embryonic retina, was not present in the mature retina; these data reveal an *Ezh2*-mediated feedforward pathway that is required for maintaining photoreceptor homeostasis in the adult and suggest novel targets for retinal degeneration therapy.

NEW OUTCOME MEASURES FOR CLINICAL TRIALS IN RETINAL DEGENERATIVE DISEASE

David G. Birch, PhD

New ways to quickly determine whether an intervention is effective are crucial for the rapidly increasing number of potential therapies available for clinical trials. Clinical outcome measures have typically involved measuring cone-mediated vision, such as visual acuity and light-adapted visual fields. Our recent work has focused on two alternative strategies. One involves a structural measure, ellipsoid zone (EZ) width or area, derived from optical coherence tomography. EZ measures may substantially reduce the length of clinical trials due to the low repeat variability. The other involves measures of rod sensitivity, which is typically reduced early in the disease process. Measures of EZ area and rod visual field may provide complementary outcome measures for treatment trials, especially where the primary disease is in the rod photoreceptors.

ANTISENSE OLIGONUCLEOTIDES FOR THE TREATMENT OF USHER SYNDROME

Michelle L. Hastings, PhD

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Usher syndrome (USH) is the leading genetic cause of combined hearing loss and blindness. Type 1 Usher (USH1) is the most severe form of the disease and is characterized by profound hearing impairment and vestibular dysfunction from birth, and progressive retinal degeneration. USH1 is caused by mutations in the USH1C gene in ~6-8% of cases. Mice with the human *USH1C* c.216G>A splicing mutation (Ush1c^{216AA}) have profound hearing loss, progressive deterioration of visual function and retinal degeneration. We designed an antisense oligonucleotide (ASO) drug, ASO-Ush, which base-pairs to the 216A mutation and blocks the deleterious pre-mRNA splicing caused by the mutation. ASO-Ush partially restores *Ush1c* gene expression in Ush1c^{216AA} mice following a single dose shortly after birth. Ush1c^{216AA} mice treated with ASO-Ush had normal vestibular behavior and dramatically improved hearing for up to six months of age (Lentz et al., 2013). Ush1c^{216AA} mice treated with a single intravitreal (IVI) injection of ASO-Ush exhibited a modest improvement in visual function and retinal structures that correlated with correction of *Ush1c c.216A* pre-mRNA splicing. These effects were sustained for 3 months. Additional ASO treatments increased the duration of efficacy for visual function. Overall, our results demonstrate the therapeutic potential of early ASO intervention to improve gene expression, and cochlear, vestibular, and photoreceptor structure and function in Usher syndrome. Current work focuses on developing ASO-Ush for the treatment of human Usher syndrome including the optimization of delivery and dosing. We are also designing ASOs to target other mutations that cause Usher syndrome in order to expand the repertoire of this class of drug for the treatment of diseases of the eye and ear.

Lentz, J.J., Jodelka, F.M., Hinrich, A.J., McCaffrey, K.E., Farris, H.E., Spalitta, M.J., Bazan, N.G., Duelli, D.M., Rigo, F., Hastings, M.L. (2013) Correction of hearing and vestibular dysfunction in a mouse model of deafness. *Nature Med*, 19: 345-350.

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Funding: NIH/NIDCD, Foundation Fighting Blindness

HUMAN EMBRYONIC STEM CELL-DERIVED EXTRACELLULAR VESICLES (HESEVS) AND THEIR POTENTIAL USE FOR RETINAL REGENERATION

Debora B. Farber, PhD, DPHHC

Human embryonic stem cells (hESCs) release into their culture medium heterogeneous populations of extracellular vesicles (hESEVs) that range in size from 30 nm to 1 µm and contain mRNAs, miRNAs and proteins. After fractionating H9 hESC-derived hESEVs into microvesicles (MVs) and exosomes (EXOs), these nanoparticles were characterized using electron microscopy, dynamic light scattering, total RNA electrophoresis, microarrays of cDNAs and Western blot analysis. MVs and EXOs differ in diameter size and in RNA profiles. MVs carry bigger RNAs than EXOs, which are very much enriched in miRNAs. More than 3,000 genes are differentially expressed in MVs versus EXOs. Expression of surface markers allowed us to differentiate MVs from EXOs. We demonstrated hESEV as well as MV and EXO uptake by cultured Müller cells and then determined how they change the molecular content and morphology of the Müller cells. For example, the pluripotency gene OCT4 from hESEVs or MVs is detected after internalization of the nanovesicles in the mRNA of the

ABSTRACTS

Müller cells, which do not have endogenous OCT4. This is not observed with EXo internalization. Changes suggesting de-differentiation of Müller cells followed by trans-differentiation into other retinal cell types are seen after repeated treatments of Müller cells with hESEVs or MVs: decreased level of Müller cell markers vimentin and GS and increased level of OCT4 and early retinal protein PAX6. Some Müller cells also express marker proteins for ganglion (Brn3a) and amacrine (Calbindin) cells. Control, non-treated Müller cells show none of these changes.

The above data lead us to ask: Do hESEVs/MVs induce in the living retina dedifferentiation of quiescent glial Müller cell progenitors to stem cells, and a retinogenic program leading to regeneration? Results of preliminary experiments show that this seems to be the case.

CHOROIDEREMIA GENE THERAPY

Byron L. Lam, MD

CO-AUTHORS:
Janet Davis, Ninel Gregori, Jennifer Verriotto

Choroideremia (CHM) is a rare, untreatable retinal degeneration that begins in childhood with loss of night and peripheral vision with gradual progression to blindness by middle age. CHM is caused by loss of function of the gene encoding Rab escort protein 1 (REP1) which is located on the X-chromosome. The disease has an X-linked recessive mode of inheritance and affects approximately 1 in 50,000 people, mostly due to loss of function (null) mutations.

In a Phase I/II CHM gene therapy study of 6 subjects using subfoveal injection of AAV2-REP1 ($0.6\text{-}1.0 \times 10^{10}$ genome particles) conducted by MacLaren at UK, good tolerance of the treatment and improved visual acuity were noted at 3.5 years of follow up (MacLaren et al., 2014, 2016). Subsequently, Phase II gene therapy studies using a higher dose of 10^{11} AAV2-REP1 genome particles were initiated in the UK, Canada, USA, and Germany.

In the US Phase II single-arm clinical trial, sponsored by the Bascom Palmer Eye Institute, 6 adult patients (age 32 to 72 years) with CHM were recruited. The worse eye was treated and the pre-treatment visual acuity ranged from 20/32 to 20/160. At three month follow up, visual acuity of the treated eye returned to the same or better than the baseline levels in all patients. No serious adverse events were encountered. Postoperative inflammation occurred rarely and resolved rapidly.

Preliminary results of the US Phase II CHM gene therapy clinical trial show reasonable safety and suggest efficacy. The results support the progression to a Phase III clinical trial with a large sample size to determine the efficacy of CHM gene therapy.

BIOCOMPATIBILITY OF A NOVEL BIOPOLYMER SCAFFOLD FOR RETINAL CELL TRANSPLANTATION IN THE SUBRETINAL SPACE OF PIGS

Elliott H. Sohn, MD

PURPOSE:
Photoreceptor cell replacement has demonstrated potential for restoring vision in retinal degenerations, but only a small fraction of transplanted cells survive and integrate into the host retina. This failure is largely due to lack of physical support for the cells after injection. We tested the biocompatibility of a hydrogel-based polymer scaffold, poly(caprolactone) (PCL), suitable for patient-specific iPSC-derived retinal cells, in the subretinal space of a large animal model.

METHODS:
Methacrylate-functionalized PCL scaffolds were polymerized at 50 wt% with Irgacure 651 by exposure to UV light. Complex prototype structures with varying pore sizes were created using two-photon polymerization with Irgacure 369 as the initiator. Compressive modulus was measured using dynamic mechanical analysis. Four month old Yucatan mini pigs (n=5 eyes from 5 animals) had 23G three-port vitrectomy and hyaloid induction. A subretinal bleb was raised with BSS, followed by placement of a 1.25 x 4mm PCL scaffold in the subretinal space, then fluid-air exchange. Five pig eyes underwent control surgery (i.e. same as experimental arm except no subretinal polymer). Animals were sacrificed 1 month after surgery at which time ophthalmoscopy and spectral-domain OCT (SD-OCT) were performed; eyes and other tissues were collected. Histological analysis was performed on paraffin sections of control and experimental retinas.

RESULTS:
At 1 month after surgery, ophthalmoscopy revealed all 10 eyes had complete, spontaneous retinal reattachment. PCL polymer implants were detectable by ophthalmoscopy in 5/5 treated eyes, and their anatomic location in the subretinal space was confirmed *in vivo* with SD-OCT. On SD-OCT the surface of the polymer was hyper-reflective while the body was hypo-reflective compared to the retina. No eyes had evidence of intraocular inflammation or vitreous opacities. Hematoxylin-eosin stained sections through a subset of injected eyes demonstrated subretinal location of the implanted polymer, and preservation of retinal layers adjacent to the implant.

CONCLUSIONS:
PCL polymer can be successfully delivered to the subretinal space and is well-tolerated ophthalmoscopically. This knowledge will be fundamental to the development of effective autologous cell-based sub-retinal transplantation grafts for retinal degenerative diseases.

GENE DELIVERY OF SECRETED CELL PENETRATING PEPTIDES TO PREVENT RETINAL DEGENERATION IN A MOUSE MODEL OF OXIDATIVE STRESS IN THE RETINAL PIGMENT EPITHELIUM

Alfred S. Lewin, MD

CO-AUTHORS:
Cristhian J. Ildefonso, Qiuhong Li, Henrique Jaime, William W. Hauswirth

Damage caused by reactive oxygen species is believed to contribute to the damage to the retinal pigment epithelium (RPE) and choroid leading to the development of age related macular degeneration (AMD). To model this process in a shortlived animal and to test the hypothesis that mitochondria are a source of RPE oxidative stress, we generated a mouse model in which *Sod2*, the gene for mitochondrial superoxide dismutase, is deleted in the RPE. These mice exhibit some of the salient features of dry AMD including accumulation of lipofuscin, disorganization of Bruch's membrane, atrophy of RPE cells and death of associated photoreceptors. We have used this model to test gene therapies for geographic atrophy, the advanced form of dry AMD. Adeno-associated virus (AAV) vectors were designed to deliver secreted, cell penetrating peptides to block the activation of the NLRP3 inflammasome or to induce the production of antioxidant enzymes in the RPE. These vectors reduced inflammatory stress in the retina in the endotoxin induced uveitis model and protected the retina in an acute model of oxidative injury caused by injection of sodium iodate. AAV expressing a caspase activation and recruitment domain (CARD) peptide reduced the rate of retinal degeneration in the *Sod2* deletion model of geographic atrophy. We anticipate that these gene delivery approaches will have benefit in preventing advanced dry AMD in human patients.

ABSTRACTS

OPTOGENETIC GENE THERAPY FOR VISION RESTORATION

Zhuo-Hua Pan, PhD

Severe loss of photoreceptor cells in inherited or acquired retinal degenerative diseases, such as retinitis pigmentosa and age-related macular degeneration, can result in partial or complete blindness. Research in my lab is focused on the development of optogenetic approaches to restoring vision by expressing microbial rhodopsins, especially channelrhodopsins (ChRs), to convert second- or third-order retinal neurons into photosensitive cells. Proof-of-concept studies have demonstrated the restoration of light responses in surviving retinal neurons and visually guided behaviors in animal models. The first Investigational New Drug (IND) application of optogenetic gene therapy has been approved by US FDA for clinical trials. Our ongoing studies are aimed at improving the optogenetic technology, including the development of more light sensitive and/or red-shifted ChRs and the development or improvement of AAV-mediated retinal cell-types or subcellular compartment-specific targeting.

OPTOGENETIC VISION RESTORATION

John G. Flannery, PhD

CO-AUTHORS:
Benjamin Gaub, Michael Berry, Amy Holt, Ehud Isacoff

Afflicting people of all ages, Retinitis Pigmentosa causes a gradual loss of vision, akin to losing pixels in a digital camera. Sight is lost from the periphery to the center, usually leaving people with the inability to navigate their surroundings. Some 100,000 Americans suffer from this group of inherited retinal diseases. We are developing a therapy based on an AAV virus that inserts a gene for a common neuronal receptor into normally blind cells of the retina that survive after the light-responsive rod and cone photoreceptor cells die as a result of disease. The receptor either uses the vitamin A derivative, retinal, that is freely available in the eye, or a synthetic chemical photoswitches that the physician supplies, and thereby becomes responsive to light. In this way, the cells in which the receptor is located respond to light with a change in neural firing, and this reanimates the retina and sends information to the brain to restore vision.

To date, versions of this approach that were developed the Flannery laboratory[1], as well as others in the field, have employed receptors that are rather insensitive to light or very slow in response and so could not support normal vision. We now propose a new strategy that uses natural amplification properties of cell signaling to dramatically increase sensitivity (by 1000 times) and speed. We also pursue a discovery that enables a combinatorial approach that uses several photoreceptors at a time in order to recreate the natural diversity of retinal signaling that had earlier been missing. Finally, we employ sophisticated behavioral analysis to, for the first time, test not simply the restoration of the ability to tell light from dark or flashing from steady light, but to determine if the animal is able to see images.

[1] Optogenetic Vision Restoration Using Rhodopsin for Enhanced Sensitivity. Gaub BM, Berry MH, Holt AE, Isacoff EY, Flannery JG. *Mol Ther* 2015 Oct;23(10):1562-71. doi: 10.1038/mt.2015.121. Epub 2015 Jul 3.

TREATMENT STRATEGIES FOR DHDDS–ASSOCIATED RP: CAN SMALL COMPOUNDS WORK?

Rong Wen, MD, PhD

CO-AUTHORS:
Ziqiang Guan[2], Byron L. Lam[1], Yiwen Li[1]

Mutations in *DHDDS* gene cause retinitis pigmentosa (RP). DHDDS (dehydrodolichol diphosphate synthase), a key enzyme for biosynthesis of dolichols, catalyzes the dolichol chain elongation reaction using IPP (isopentenyl pyrophosphate) as substrate. IPP is the product of the mevalonate pathway and also a substrate for squalene synthase, the first step of committed step of cholesterol biosynthesis after the mevalonate pathway. Since *DHDDS* mutations alter the function of the enzyme, we reasoned that inhibiting squalene synthase might increase the substrate pool of IPP and thus influence dolichol biosynthesis. Specifically, an increase in IPP might lead to an increase in dolichol production.

Mice harboring the K42E DHDDS mutation exhibit several retinal phenotypes, including photoreceptor degeneration and suppressed ERG b-wave. The flat b-wave could be an outcome measurement for a trial of a potential treatment. We thus designed experiments to investigate whether inhibition of squalene synthase could have effects on the dolichol production and ERG b-wave. Inhibition of squalene synthase was achieved by oral administration of lapaquistat acetate (TAK-475, a generous gift from Takeda Pharmaceutical). Dolichol levels in the retina were measured after treatment for 1 month. ERGs were measured after lapaquistat treatment for 2 months. The levels of dolichol-17 and dolichol-18 were not significantly altered by the treatment. However, there was a significant improvement of the ERG b-wave after lapaquistat treatment. These results indicate that inhibition of squalene synthase with lapaquistat could potentially improve retinal function for DHDDS-associated RP.

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TOO LITTLE VS. TOO LATE IN TREATING RETINITIS PIGMENTOSA

Stephen Tsang, MD, PhD

LAY ABSTRACT:
Gene therapy is a promising approach for treating retinal degeneration. However, this therapeutic strategy can to be hampered by either insufficient gene-transduction efficiency and/or the disease being too advanced at diagnosis (the so-called "point of no return"). We developed a mouse model of retinitis pigmentosa (RP) in which the mutant gene, cGMP phosphodiesterase 6b (Pde6b), can be inducibly repaired in all diseased photoreceptor cells. With gene-transduction optimized, they were able to determine the therapeutic window for rescue. In fact, gene restoration in these mice halted photoreceptor degeneration at early, mid or late stage disease (see accompanying image). Our findings indicate that RP is treatable using gene therapy, even at advanced disease stages, and suggest that efforts in this area should focus on improved gene delivery.

SCIENTIFIC ABSTRACT:
Hereditary retinal degenerative diseases, such as retinitis pigmentosaloss of rod photoreceptors followed by cones. While retinal gene therapy clinical trials temporarily improved visual function, this approach has yet to achieve sustained functional and anatomical rescue after disease onset in patients. The lack of sustained benefit could be due to insufficient transduction efficiency of viral vectors ("too little") and/or because the disease is too advanced ("too late") at the time therapy is initiated. Here, we tested the latter hypothesis and developed a novel mouse RP model what to the best of our knowledge that permits restoration of the mutant gene in all diseased photoreceptor cells, thereby ensuring sufficient transduction efficiency. We then treated mice at early, mid, or late disease stages. At all three time points, degeneration was halted and function was rescued for at least 1 year. Not only do our results demonstrate that gene therapy effectively preserves function after the onset of degeneration, our study also demonstrates

that there is a broad therapeutic time window. Moreover, these results suggest that RP patients are treatable, despite most being diagnosed after substantial photoreceptor loss and that gene therapy research must focus on improving transduction efficiency to maximize clinical impact.

GLIAL CELL DERIVED NEUROTROPHIC FACTOR FOR PHOTORECEPTOR RESCUE: DIRECT AND INDIRECT NEUROPROTECTION STRATEGIES

Petr Baranov, MD, PhD

Retinitis pigmentosa and age-related macular degeneration are characterized by the progressive and irreversible loss of retinal cells. Several growth factors, including glial cell derived neurotrophic factor (GDNF), have been shown to rescue several types of retinal neurons – photoreceptors and ganglion cells, in various animal models. The advancement in biotechnology led to the successful development of several delivery systems for GDNF and other neurotrophic factors. They have been administered as recombinant proteins, overexpressed in transplanted or encapsulated cells or produced in host cells by the adeno-associated viral vectors and other genetic engineering tools. The major challenges driving the evolution of such systems are the ability to deliver to exact location in the retina with the precise control of the dosage and the duration of the growth factor expression.

I will discuss two approaches for GDNF delivery into the retina: PLGA microsphere-based slow release systems and induction of GDNF in endogenous cells by small molecules. We have demonstrated that single intravitreal injection of GDNF-VitaminE loaded microspheres can partially rescue photoreceptors in a rhodopsin-knockout mouse model of retinitis pigmentosa. The effect on the overall photoreceptor survival was moderate and comparable to the previously published approaches: the amount of cells in outer nuclear layer of treated animals was 1.7 fold higher compared with the sham-injected controls. However, the treatment preserved the outer segments of cones, as confirmed by opsin blue staining, and also led to better preservation of synapses in the outer plexiform layer. It is also notable that the observed effect was pan-retinal, compared to subretinally delivered GDNF vectors.

For the second approach – indirect neuroprotection, we have used a novel small molecule, previously found to induce GDNF in ES-derived astrocytes and C6 rat glioma cell line. We have shown that it can induce GDNF in several retinal cell lines, miPSC-derived retinal tissues in vitro; and in healthy mouse retina following intravitreal injection in vivo. We have also demonstrated its superior photoreceptor rescue efficacy in rhodopsin knockout mouse model and Royal College of Surgeons rat model of retinal degeneration. This greater potency may be related to the better tissue distribution profile of small molecule in comparison to exogenous recombinant GDNF.

Overall, our findings warrant the further development of GDNF-based neuroprotective therapies for retinal degenerative diseases. We have also demonstrated the power of an alternative strategy for photoreceptor rescue – indirect neuroprotection.

COMPLEXITY OF THE RETINAL DEGENERATION IN RP CAUSED BY RHODOPSIN GENE MUTATIONS

Samuel G. Jacobson, MD, PhD

Among the earliest discoveries of the genetic bases of monogenic retinal degenerations was that mutations in the *rhodopsin* (*RHO*) gene can cause retinitis pigmentosa (RP). Further identifications of molecular causation of RP continue to this day. In parallel, characterization of the newly-identified diseases occurred – a gene would be discovered and interest peaked to re-examine these patients with mechanism in mind. Now, we have entered an era when therapies (many gene-specific) are emerging and we need to understand the phenotypes with a different purpose – to determine smart outcome measures for clinical trials. Among others, we grappled with the phenotypes in the many RP-causing *RHO* mutations and classified them into broad understandable categories. We have now re-examined a cohort of the class of *RHO* mutations that retains rod function, because some of the potential therapies are targeting rod photoreceptors. This revisiting of 'Class B' patients revealed new features that need to be recognized in order to deliver therapy (if focal) to regions of rod cell vulnerability or to monitor for efficacy (and safety) rod-rich regions in retina-wide treatment strategies.

DEVELOPING NEW TREATMENTS FOR BLINDNESS IN THE MACLAREN RESEARCH TEAM

Alun Barnard, BSc, PhD

I work in a group dedicated to finding new treatments for blindness, particularly in patients with incurable retinal diseases, such as retinitis pigmentosa, choroideremia and Stargardt disease. We combine clinical studies and laboratory research to investigate and develop a range of different potential treatments. We have explored the use of different types of gene therapy (gene replacement, neuroprotection and optogenetics) to retain and reverse visual loss; investigated repairing the retina through photoreceptor transplantation; looked at restoring vision with an electronic retinal implant and studied an oral drug treatment to slow down retinal disease. I will try to give an overview of our ongoing programme and highlight some particularly exciting findings and recent successes.

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{ MY HEART TO JACQUE, LAURA, JANIS AND ROZI. YOUR LOVE MAKES ALL THINGS POSSIBLE. }

HOPE for VISION
www.hopeforvision.org

“SOMETIMES THE DIFFERENCE BETWEEN SUCCESS OR FAILURE IS HOW MUCH OR HOW LITTLE ENCOURAGEMENT WE GIVE OR GET.”

– AUTHOR UNKNOWN,
ADAPTED BY BETTI LIDSKY

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...and our founding angel, Adrienne Arsht

SAVE THE DATE:

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