Chicago Alliance to Fund Retinal Research

SIGHT QUEST NEWSLETTER

Autumn 2015

A publication of SEARCH FOR VISION

1011 S. Waiola Avenue, LaGrange, IL 60525 - 847-673-0017 Marla Chorney (Information)

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Parent Petroleum Golf Classic 2015

The 18th annual golf classic benefitted Dr. Michael Grassi and his team of researchers at the Department of Ophthalmology and Visual Sciences, University of Illinois's College of Medicine at Chicago.

Along with raising funds and awareness for retinal degenerative diseases, we were happy to honor our beloved former Chicago Bears linebacker Doug Buffone after his passing earlier this year.

We are grateful for all of his support with hosting the "Bear's Hour" portion during our events and his charismatic personality will forever be missed.

The days sunny forecast provided an ideal setting for 164 donors to enjoy a great day of golf. The evening was highlighted by a wonderful dinner reception full of prizes and passing out of awards.

We should give a big thanks to all the board members with Search for Vision and also give special recognition to our co-sponsors BP and Castrol along with the many vendors, friends and volunteers who help make this event a success.

WINNERS OF THE SEARCH FOR VISION & PARENT PETROLEUM $5,000.00 RAFFLE DRAWING WAS HELD THURSDAY, AUGUST 27, 2015

AT THE PARENT PETROLEUM GOLF OUTING
First Prize - $2,500.00 Pat Racine ticket 0999
Second Prize - $1,000.00 Phillip Lukeose ticket 1091
Third Prize - $550.00 Zack Chacko ticket 1474
Fourth Prize - $250.00 Nancy Spina ticket 0717
Fifth Prize - $250.00 Muhamad Awad ticket 1666
Sixth Prize - $150.00 Drew Rasch ticket 0057
Seventh Prize - $150.00
Alberta Kosik ticket 0972
Eighth Prize - $150.00
Mobil Tel ticket 0197

Dick Lynch Memorial

It is with regret that we report the passing of Dick Lynch a long time supporter of retinal eye research. He will be missed.

Researchers at The University of Illinois, College of Medicine at Chicago, Department of Ophthalmology & Visual Sciences

Dingcai Cao, PhD

Associate Professor of Ophthalmology

Adjunct Associate Professor of Psychology

Human Melanopsin Function

Research Approach:

To measure melanopsin-based responses using a novel, lab-developed photostimulating technology that stimulates melanopsin only, using psychophysical or electrophysiological methods.

Research Goal:

To understand mechanisms in humans that mediate melanopsin's contribution to vision, pupil response or circadian rhythm and to develop effective, melanopsin-based, light therapeutic strategy to improve mental and physical health. Research in nocturnal rodents has shown that melanopsinactivation is important for circadian rhythm, pupil response, perception, cognition, emotion and health.

Mike Grassi, MD

Retina Chemical Genomics Laboratory

Research Associate

Professor of Ophthalmology and Neuroscience

Research Goals:

Identify and better define a biomarker for diabetic retinopathy.

Research Approach:

The aim of our research program is to use cell-based models of retinal disease in genomic and chemical high throughput studies to identify key pathways and novel therapeutic targets for these conditions.

Jason McAnany, PhD

Retinal Function and Structure in Health and Disease

Assistant Professor of Ophthalmology

Adjunct Assistant Professor of Bio-engineering

Research Goals:

Develop novel methods for diagnosing and monitoring the progression of

retinal disease.

Define the relationship between visual dysfunction and underlying disease

processes.

Research Approach:

1. Non-invasive techniques in human subjects including:

1) electrophysiology, 2) retinal imaging, 3) pupillometry, 4) psychophysics.

David R. Pepperberg, PhD

Retinal Neuroscience and Molecular Engineering

Searls-Schenk Professor Ophthalmology & Visual Sciences

Bioengineering

Physiology & Biophysics

Biochemistry &

Molecular Biology

Research Goals:

To develop new molecular therapies that delay the progression of, and restore vision lost in, photoreceptor degenerative diseases such as age-related macular degeneration (AMD).

Research Approaches:

1. Determine the role of amyloid-β in the progression of AMD, and develop technology to control the excessive build-up of amyloid-β in eye tissues.

2. Engineer light-sensitive nanostructures that interface with remaining healthy neurons of the inner retina, thereby “bypassing” photoreceptor loss.

Retinal Research In Brief

Thanks to Reina International for the following information.

BREAKING NEWS

RetroSense, a biopharmaceutical company has announced FDA approval for the 1st ever Phase clinical trial 1 and 2 for Optogenetic intervention in Retinitis Pigmentosa [RP]. As photoreceptor cells die in Retinal Degeneration [RD], the neural layer remains

relatively intact. Optogenetics is a means of changing these neural cells to become light sensitive to replace the function of the dying photoreceptors with the expectation of some degree of improved or restored vision.

The trial using RST-001 will begin by year end to evaluate safety and efficacy. “This brings us one step closer to realizing our ambition of improving vision in those individuals with currently incurable blindness,” said Sean Ainsworth, CEO of RetroSense Therapeutics. “There is great promise for the clinical application of Optogenetics and this first human clinical trial should provide key insights into the potential for this therapy to treat diseases affecting the eye or brain.” Dr. Zhuo-Hua Pan, the inventor of RetroSense Therapeutics’ optogenetic approach added, “My hope from early on was to see our work improve the lives of people with vision defects. It is great to see the approach moving imminently into human clinical studies.”

RESEARCH NEWS

ARTIFICIAL RETINA

Second Sight, the manufacturer of the Argus Retinal Implant recently announced that the first patient with Age Related Macular Degeneration [AMD] had received a device. This was featured on a recent Carte Blanche production on MNet.

STEM CELLS RESULTS

Ocata, formerly ACT, recently announced positive results in the Phase 1 clinical trial to grow new Retinal Pigment Epithelium [RPE] cells from Stem cells. The cells were implanted into 31 AMD and Stargardt patients up to 4 years ago. None of the patients showed rejection or serious adverse events. They all experienced improved or stable best-corrected visual acuity. They are now planning the second stage of the trial.

It is interesting to note that AMD and Stargardt Dystrophy, for very different reasons, share a common

pathway - that of secondary cone photoreceptor loss due to a build-up of waste materials in the RPE.

RPE65 GENE TRIALS

Early results from the gene replacement therapy trial for Leber Congenital Amaurosis [LCA] were very encouraging. The latest report shows that the demand for RPE65 would not appear to be fully met with the current vectors being used. Professor Robin

Ali stated that " We have concluded that early intervention using a more potent vector expressing higher levels of RPE65 is likely to provide greater benefit and protection against progressive degeneration"

GENE EDITING THERAPY

The CEP290 gene mutation also causes LCA but is too large for delivery via the adeno- associated virus used in the RPE65 trial. Editas, an emerging gene editing company recently announced that it is developing a treatment for the CEP290 form of LCA. It

will be using a "cut and paste" technology known as CRISPR Cas 9 which locates the region in the gene that needs correction and deletes the mutation. Professor Donald Zack at John Hopkins University is using a similar approach for Autosomal Dominant RP.

NOVEL APPROACHES

Low level laser therapy [LLLT] has been shown to improve and maintain vision in an RP patient in Heidelberg, Germany. When Rod Photoreceptors die they send out an "eat me" signal and scavenger cells called microglia engulf the cell and surrounding healthy cells resulting in a feeding frenzy of cell death called apoptosis. Researchers at the National Eye Institute are investigating ways of molecularly inhibiting the microglial action to slow degeneration. Lipid nanoparticles are being investigated for gene delivery at the McGee University in Oklahoma City. RP accounts for 50% of all Inherited RD with more

than 3000 mutations in over 50 genes. A common end stage of RP is the death of cone cells which follows the death of Rod cells. A new intervention strategy is to reprogram rod cells to become more cone-like. Keeping the rod cells alive, even though they are largely dysfunctional seems to support cone cell survival in a mouse model at Washington University. The formation of the waste product lipofuscin in Stargardt Dystrophy results in cone photoreceptor death. In the ABCA4 form a mutation in the gene causes a malfunction in the metabolism of Vitamin A. Researchers at Oxford University have demonstrated that the replacement of Vitamin A with a modified form of the vitamin can prevent vision loss in a murine model of the disease.

AGE RELATED MACULAR DEGENERATION

Studies at Duke University in the USA show that Vitamin D deficiencies were more prevalent in patients with “wet” AMD when compared to patients with “dry” AMD and controls. New studies show that past smokers and current smokers develop the advanced “wet” form of AMD on average nearly 5 years earlier than their never smoked counterparts. Patients carrying the high risk gene factors in the CFH and ARMS2

genes developed “wet” AMD 12 years earlier.

PATIENT BASED EVIDENCE

The voice of the patient in research is becoming more important. Researchers are examining ways of interpreting patient reported outcomes and of accessing patient’s opinions and expectations. Incorporating all of these into the organization and design of clinical trials will mean less patient drop out and more realistic expectations and outcomes.

Reina International was represented at a Patients Based Evidence Course at Harvard University, Boston, to learn the techniques of accessing the patient voice. Thanks to Novartis International who funded the 30 delegates from worldwide patient groups.

Stem Cells Allow Nearly Blind Patients to See

Embryonic stem cells can be turned into a therapy to help the sight of the nearly blind.

In a report published in the journal Lancet, scientists led by Dr. Robert Lanza, chief scientific officer at Advanced Cell Technology, provide the first evidence that stem cells from human embryos can be a safe and effective source of therapies for two types of eye diseases—age-related macular degeneration, the

most common cause of vision loss in people over age 60, and Stargardt's macular dystrophy, a rarer, inherited condition that can leave patients legally blind and only able to sense hand motions.

In the study, 18 patients with either disorder received transplants of retinal epithelial cells (RPE) made from stem cells that came from human embryos. The embryos were from IVF procedures and donated for research. Lanza and his team devised a process of treating the stem cells so they could turn into the RPE cells. In patients with macular degeneration, these are the cells responsible for their vision loss; normally they help to keep the nerve cells that sense light in the retina healthy and functioning properly, but in those with macular degeneration or Stargardt's, they start to deteriorate. Without RPE cells, the nerves then start to die, leading to gradual vision loss.

The transplants of RPE cells were injected directly into the space in front of the retina of each patient's most damaged eye. The new RPE cells can't force the formation of new nerve cells, but they can help the ones that are still there to keep functioning and doing their job to process light and help the patient to see. "Only one RPE can maintain the health of a thousand photoreceptors," says Lanza.

The trial is the only one approved by the Food and Drug Administration involving human embryonic stem cells as a treatment. (Another, the first to gain the agency's approval, involved using human embryonic stem cells to treat spinal cord injury, but was stopped by the company.) Because the stem cells come from unrelated donors, and because they can grow into any of the body's many cells types, experts have been concerned about their risks, including the possibility of tumors and immune rejection.

MORE: Early Success in a Human Embryonic Stem Cell Trial to Treat Blindness

But Lanza says the retinal space in the eye is the ideal place to test such cells, since the body's immune cells don't enter this space. Even so, just to be safe, the patients were all given drugs to suppress their immune system for one week before the transplant and for 12 weeks following the surgery.

While the trial was only supposed to evaluate the safety of the therapy, it also provided valuable information about the technology's potential effectiveness. The patients have been followed for more than three years, and half of the 18 were able to read three more lines on the eye chart. That translated to critical improvements in their daily lives as well—some were able to read their watch and use computers again.

"Our goal was to prevent further progression of the disease, not reverse it and see visual improvement," says Lanza. "But seeing the improvement in vision was frosting on the cake."

Lack of Exercise, Smoking and Genes Play Role in AMD Risk

NIH/National Eye Institute

Between 2010 and 2050, the estimated number of people with AMD will more than double from 2.1 million to 5.4 million. National Eye Institute people with a genetic predisposition for age-related macular degeneration (AMD) significantly increased their odds of developing the blinding eye disorder if they had a history of heavy smoking and consistently did not exercise or eat enough fruits and vegetables, according to an observational study of women funded by the National Eye Institute, part of the National Institutes of Health.

Eating a healthy diet and getting exercise have been shown in earlier studies to protect against AMD, a leading cause of vision loss among people age 50 and older. Findings from this latest study, conducted by a team of investigators at the University of Wisconsin-Madison, suggest that genetic and lifestyle factors may contribute to AMD in a synergistic way. The findings were published online in the journal Ophthalmology.

"If you have a family history of AMD, the good news is that the study findings suggest that there are things you can do to potentially lower your risk of developing AMD yourself," said Julie A Mares, Ph.D., of the University of Wisconsin-Madison. The study teams were led by Dr. Mares and Barbara A. Blodi, M.D., in the Department of Ophthalmology and Visual Sciences, in collaboration with investigators from the University of Iowa, Iowa City, and Oregon Health Science University, Portland.

The researchers studied the risk among women ages 50 to 79 years who had participated in the Carotenoids in Age-Related Eye Disease Study (CAREDS), an ancillary investigation of the much larger Women's Health Initiative, an observational study that has tracked the health-related behaviors and outcomes of more than 160,000 women since 1991.

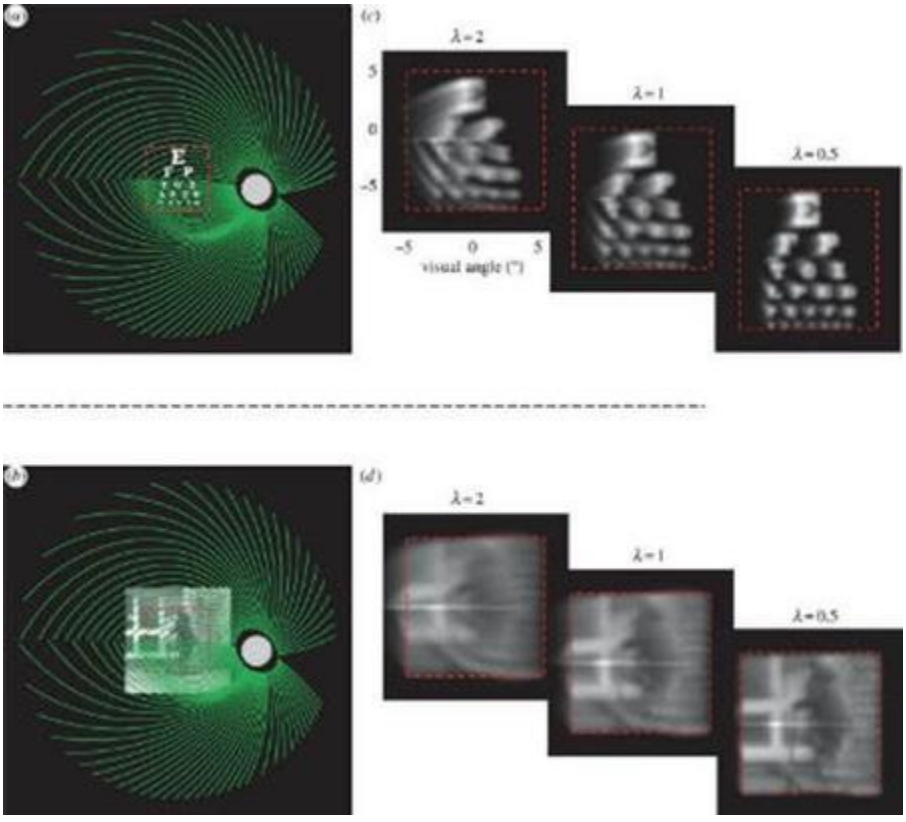
For the current study, first author Kristin J. Meyers, Ph.D., and her team evaluated the diet and exercise patterns of 1663 women and categorized them into lowest, moderate- and highest risk groups. They also evaluated whether the women smoked and, if so, how many years they smoked a pack of cigarettes or more each day. They also assessed genetic data from the women to determine whether they carried known genetic risk factors for AMD. They looked most closely at an allele (version) of the complement factor H (CFH) gene that is known to be associated with greater AMD risk, probing whether the women had zero, one, or two copies of the allele.

A total of 337 women in the study developed AMD, of whom 91 percent had early-stage disease.

Among women with stable diets, those who carried two high-risk genetic alleles, smoked at least seven pack years, and were in the highest risk diet and exercise categories were more than four times more likely to have AMD compared to those women who did not have genetic risk factors and who ate a healthy diet and got at least 10 hours/week of light exercise (such as housework or walking at a pace you could sing to) or at least eight hours of moderate activity (such as brisk walking).

In addition to lifestyle contributions, vitamin D levels may play a synergistic role with genetic factors, according to the findings of another study by the same team involving 913 CAREDS participants. Amy E. Millen, Ph.D., that study's first author, found that blood levels indicating vitamin D deficiency (less than 12 ng/mL of 25 hydroxyvitamin D) were associated with a 1.8-fold increase in the odds of having AMD among women with no risk alleles, but a 6.7 fold increase in the odds of having AMD among women with two risk alleles, compared with women who had no genetic risk alleles and adequate levels of vitamin D. The findings of the vitamin D study, which was also funded by NEI, were published in JAMA Ophthalmology.

"The findings of both studies support the notion of biologic synergy. That is, that one's genes, lifestyle factors and nutrition all come together in a synergistic way to mediate inflammation, which is a key mechanism involved in AMD," said Mares. "There's a large body of evidence that unhealthy lifestyle habits are associated with inflammation and that CFH risk alleles augment inflammatory responses. Vitamin D is believed to suppress inflammation, which is thought to enhance the AMD disease processes both directly and indirectly.



The black and white images show visual distortions that might result from electric prostheses that enable vision by stimulating the retina. (Credit: Ione Fine and Geoffrey Boynton / University of Washington).

Various sight recovery therapies are being developed by companies around the world, offering new hope for people who are blind. But little is known about what the world will look like to patients who undergo

those procedures.

A new University of Washington study seeks to answer that question and offers visual simulations of what someone with restored vision might see. The study concludes that while important advancements have been made in the field, the vision provided by sight recovery technologies may be very different from what scientists and patients had previously assumed.

In a paper published Aug. 3 in the journal Philosophical Transactions B, UW researchers used simulations to create short videos that mimic what vision would be like after two different types of sight recovery therapies.

Lead author Ione Fine, a UW associate professor of psychology, said the simulations are unprecedented. “This is the first visual simulation of restored sight in any realistic form,” she said. “Now we can actually say, ‘This is what the world might look like if you had a retinal implant.’”

Fine said the paper aims to provide information about the quality of vision people can expect if they undergo sight restoration surgery, an invasive and costly procedure.

“This is a really difficult decision to make,” she said. “These devices involve long surgeries, and they don’t restore anything close to normal vision. The more information patients have, the better.”

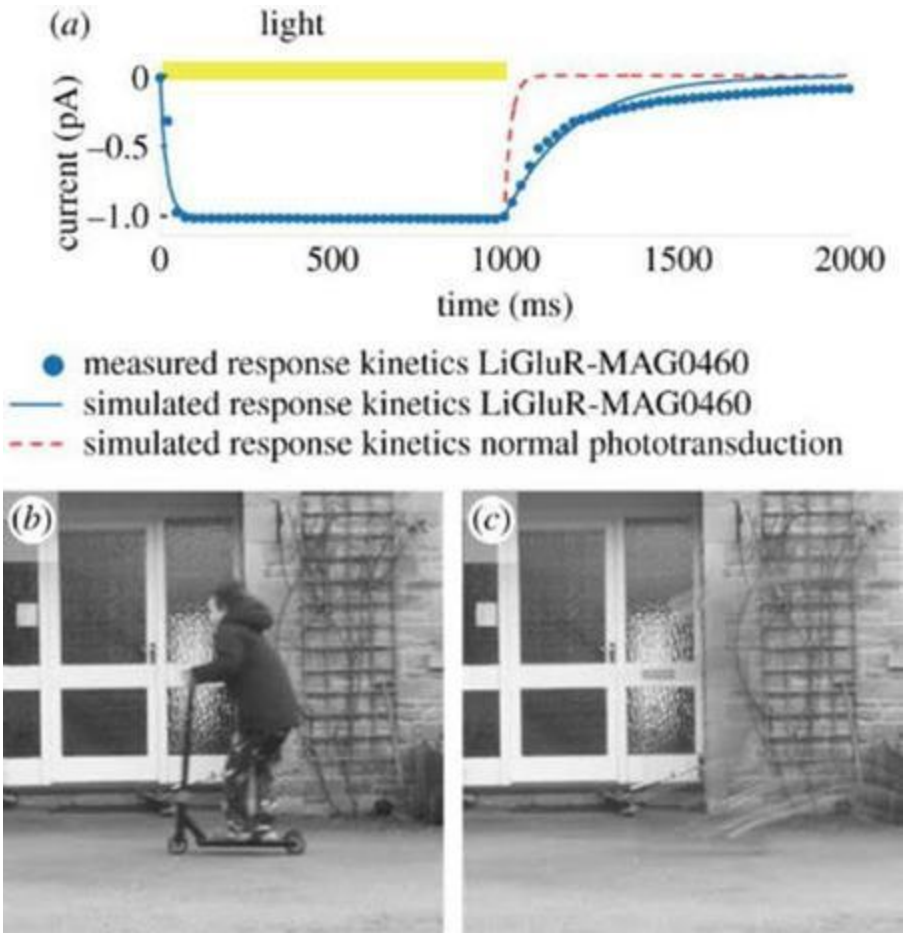
More than 20 million Americans aged 18 and older have experienced vision loss, according to the American Foundation for the Blind, and rates of vision loss are expected to double by 2030 as the nation’s population ages.

For many of these patients, vision loss occurs after light enters the eye and lands on the retina, a thin layer at the back of the eye that contains millions of nerve cells. Among those are cells called rods and cones, which convert light into electrical impulses that are transmitted to vision centers in the brain. Loss of rods and cones is the primary cause of vision loss in diseases such as macular degeneration or retinitis pigmentosa.

But those diseases leave most remaining neurons within the retina relatively intact, and various technologies under development aim to restore vision by targeting the surviving cells.

This is a pivotal time for the industry, Fine said, with one company that has a device on the market and several others set to enter the market in the next five to 10 years.

What would the world look like to someone with a bionic eye?



Limitations in sight recovery technologies can cause fast-moving objects to seemingly disappear, as shown in the above image of a child on a scooter. (Credit: Ione Fine and Geoffrey Boynton / University of Washington). Two of the most promising devices, she said, are electric prostheses, which enable vision by stimulating surviving cells with an array of electrodes placed on the retina, and optogenetics, which insert proteins into the surviving retinal cells to make them light-sensitive.

But the devices have a major shortcoming, co-author Geoffrey Boynton said, since stimulating the surviving cells in a retina is unlikely to produce vision that is close to normal.

“The retina contains a vast diversity of cells that carry distinct visual information and respond differently to visual input,” said Boynton, a UW psychology professor.

“Electrically stimulating the retina excites all of these cells at the same time, which is very different from how these cells respond to real visual input.”

There are similar issues with optogenetics, Boynton said. “The optogenetic proteins that are currently available produce sluggish responses over time, and they are limited in the number of different cell types that they can separately target,” he said. These limitations in both technologies mean that patients may

see fuzzy, comet-like shapes or blurred outlines, or they may experience temporary visual disappearances if an object moves too fast.

Previous simulations of restored vision have used a “scoreboard model,” a grid of dots similar to the scoreboard at a football game, in which each electrode produces a visible dot in space. Together, that collection of dots is intended to demonstrate what someone with restored vision will see.

Fine said the new simulations show that the scoreboard model, which is sometimes used to test devices, doesn’t provide a good representation of the quality of vision sight restoration technologies are likely to produce. More realistic models are needed, she said, to give patients, clinicians and researchers a better idea of how those technologies will work in the real world.

Fine said better simulations can provide valuable information about how implants need to be improved to produce more natural vision. “As these devices start being implanted in people, we can compare different types of devices and the different perceptual outcomes of each,” she said. “The path to fully restored eyesight is an elusive target. We need to start developing more sophisticated models of what people actually see.

“Until we do that, we’re just shooting in the dark in trying to improve these implants.”

NOTICE

Anyone wishing to receive Sight Quest Newsletter can contact Jay or Lorraine Popek at popek@att.net or call 708-652-4614.

Jay & Lorraine Popek

Co-presidents

Search for Vision