

RETINA RESEARCH FOUNDATION NEWSLETTER

Foresight for Sight

Number 1/2013

Research Laboratory of Richard Hurwitz, MD and Mary Hurwitz, PhD

A study published in 1999 in *Human Gene Therapy* by Dr. Richard Hurwitz and Dr. Mary Hurwitz, et.al. titled *Suicide Gene Therapy for Treatment of Retinoblastoma in a Murine Model* describes the successful preclinical studies in the mouse model of retinoblastoma that the Hurwitz laboratory had developed. Retinoblastoma is a blinding disease in young children that is caused by mutations in the retinoblastoma gene.

This early study, leading to further research by the Hurwitz laboratory and other scientific researchers, has ushered in a new era of success in gene therapy in ocular disease. Drs. Hurwitz used suicide gene therapy (an adenoviral vector containing the herpes simplex gene followed by administration of the anti-herpes drug ganciclovir) to successfully reduce the tumor in their mouse model. They then proceeded to treat children with retinoblastoma using a Phase I clinical trial that demonstrated the safety of the technique and potential efficacy of the treatment for patients with vitreous seeding (published in 2005 in the *Journal of Clinical Oncology*).

Currently the Hurwitz laboratory is also exploring the use of gene therapy as a treatment for retinal degenerative diseases such as retinitis pigmentosa, macular degeneration, and Stargardt's Disease. Delivering a normal gene to replace the defective gene is the goal, and solving the challenges of toxicities of these agents and exploring different techniques is the dilemma.

(continued on page 3)



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1. Dr. Richard Hurwitz

2. Dr. Mary Hurwitz

NIH Study: Immune System Could Play a Central Role in AMD

Preliminary research conducted by National Institutes of Health (NIH) investigators indicates that changes in functioning of genes in the immune system may lead to age-related macular degeneration (AMD).

Researchers from the NEI and other NIH institutes, including the National Heart, Lung, and Blood Institute and the National Center for Complementary and Alternative Medicine; the University of Melbourne, Australia; and Oregon Health and Science University, have recently published these findings in *Cell Reports*.

“Our findings are epigenetic in nature, meaning that the underlying DNA is normal but gene expression has been modified, likely by environmental factors, in an adverse way,” said Dr. Robert Nussenblatt, chief of the National Eye Institute (NEI) Laboratory of Immunology. Smoking, diet and aging are environmental factors associated with AMD.

To test whether changes in DNA methylation might play a role in AMD, the investigators evaluated three pairs of twins where only one of the siblings had AMD. When compared with the unaffected twins, methylation patterns were altered in 231 genes of affected twins. This finding is consistent with the hypothesis that environmental exposures may epigenetically regulate expression of many genes and lead to AMD.

The study identified decreased levels of DNA methylation on the interleukin-17 receptor C gene (IL17RC). Changes in DNA methylation, which regulates gene expression, have been implicated in cancer, lupus, multiple sclerosis, and many other diseases.

“Our study also suggests IL17- and IL17RC-mediated immune responses can be crucial in causing AMD,” added Dr. Lai Wei, also of NEI’s Laboratory of Immunology and first author on the paper. “By measuring IL17RC gene activity in at-risk patients, we have also potentially identified an early method to detect AMD.”

“This study strongly implicates epigenetic DNA methylation as another crucial biological pathway for understanding the molecular basis of AMD,” according to Nussenblatt.

www.nih.gov



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3. *Dr. Robert Nussenblatt*

4. *National Eye Institute (NEI)*



Vision Loss Due to Diabetes

Research findings of David Friedman, MD, PhD, of the Wilmer Eye Institute of Johns Hopkins University School of Medicine, indicates that vision loss likely related to diabetes has increased significantly over less than a decade in the United States. Diabetes can lead to vision problems when fluid accumulates in the retina or when lack of oxygen results in new blood vessels growing in the back of the eye.

As diabetes rates continue to rise, some complications tied to the disease are expected to rise as well. Vision loss is especially a concern among people who have had diabetes for 10 years or more.

Friedman's team studied data from a national health and nutrition study and discovered vision impairment in a higher percent of approximately 10,000 people tested in 2005 through 2008 as compared to that same number of people tested in 1999 through 2002. The number of people in the study with diabetes for at least 10 years also increased, especially in adults younger than 40.

"This is a message to vision care providers that they're going to be seeing a lot more of these complications among a younger population," according to David Musch, PhD, an epidemiologist at the University of Michigan Kellogg Eye Center in Ann Arbor. "Hopefully what this article will do is raise awareness and in part increase the screening rate," he said.

www.reuters.com

Hurwitz Research Laboratory

(continued from page 1)

The eye is a particularly successful site for gene therapy; it is relatively easy to introduce the virus into the eye, and the inside of the eye escapes the immune system defense mechanism.

The work of the Hurwitz laboratory (Texas Children's Cancer Center, Baylor College of Medicine, Houston, Texas) has been supported by RRF since 1997. This research is also cited by many other renowned researchers such as the team of Jean Bennett, MD, PhD and Albert Maguire, MD (*Gene Therapy for Retinal Disease*), the RRF Pyron Award recipients for 2011. Dr. Bennett is the inaugural McPherson Lecturer on April 22, 2013 at the McPherson Eye Research Institute.

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5. *Dr. David Friedman*

6. *Fundus – Dry Macular Degeneration*

7. *Classic white pupil of retinoblastoma*



Dr. Nader Sheibani

Awarded NEI Grant

Nader Sheibani, PhD, has received a highly competitive, five-year grant from the National Eye Institute. This grant provides over \$6 million to develop therapeutic molecules to combat wet age-related macular degeneration.

Dr. Sheibani's project, *Novel Antiangiogenic Peptides for Treatment of Exudative AMD*, is a collaborative effort including fellow McPherson ERI members Dr. Christine Sorenson (Pediatrics) and Dr. Daniel Albert (Ophthalmology and Visual Sciences), as well as investigators from Northwestern University and the University of Nebraska.

Researchers at Northwestern University are developing the peptides and those at the University of Nebraska are developing the drug delivery nanotechnology. Dr. Sheibani and his staff will test whether the treatments work in preclinical models of the disease for its translation to humans.

Treatments currently available inhibiting the growth of new blood vessels (anti-VEGF treatments) currently help save vision in patients with AMD, but this study aims to develop treatments mimicking the body's own inhibitors of angiogenesis. Angiogenesis, the growth of new blood vessels that leak, leads to vision loss in patients with AMD if unchecked.

A cause of vision loss in this type of AMD is associated with angiogenesis, the growth of new blood vessels which are leaky with severe consequences to vision

www.med.wisc.edu

Dr. Sheibani holds the RRF Chair at University of Wisconsin-Madison Department of Ophthalmology & Visual Sciences and is a member of McPherson Eye Research Institute.

Dr. Albert was founding Humble Director of UW Eye Research Institute (now renamed McPherson Eye Research Institute).

Dr. Sorenson is one of RRF's 2013 Pilot Study Grant recipients.



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8. and 9. Dr. Nader Sheibani



Avoid Eye Fatigue

Eye fatigue can result in tired, itching, and burning eyes. Although rarely serious, a few precautions may prevent eye fatigue. If eye fatigue persists despite taking simple precautions, see your doctor, especially if associated with headaches or with certain eye or vision problems.

Some Causes

- Extended periods of reading, writing, or driving.
- Exposure to bright light or straining to see in dim light.
- Staring for long periods at digital devices such as computer screens or cell phones.
- This type of eye fatigue or eye strain is sometimes known as computer vision syndrome. Some estimates say computer-related eye symptoms may be responsible for millions of primary care eye examinations each year.
- Digital devices may also be linked to eye fatigue because of a tendency to blink less often when staring at a computer screen.
- Blinking refreshes the eyes, but studies indicate that people only blink about half as often while using a computer.
- During sleep, the eyes are replenished with essential nutrients.
- Lack of sleep may result in persistent eye irritation.
- Eye fatigue may also be due to a need for a change in your present eyeglass prescription.

What to do?

- Try setting your computer screen about 20-26 inches from your eyes and a little below eye level.
- Rest your eyes several times an hour by looking in the distance (through a window for example).
- Don't forget to blink!

www.webmd.com/eye-health

Finally, many websites including ours (www.retinaresearchfnd.org) allow you to change font size to view the web pages more comfortably if needed.



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10. *Sore eyes*

11. *View out window*

12. *Text size selection*

13. *Blink*

New Pilot Studies Funded by RRF in 2013

Three new pilot studies have been funded by RRF this year, bringing the total number of pilot studies funded in 2013 to thirteen.

Christine M. Sorenson, PhD

University of Wisconsin Dept. of Pediatrics and
McPherson Eye Research Institute
Madison, WI

Research Project: *Retinal Vessel Rarefaction and Bim Expression*

14.

WISCONSIN



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Timothy W. Corson, PhD

Indiana University School of Medicine
Indianapolis, IN

Research Project: *Cellular Targets of a Candidate AMD Therapy*

Ming Zhang, MD, PhD

Georgia Regents University
Augusta, GA

Research Project: *Autophagy and NLRP3 Inflammasome
in Acute Retinal Necrosis (ARN)*

*For more detailed information about all pilot studies, awards,
fellowships, and research or educational programs funded by RRF
please view our website www.retinaresearchfnd.org*

14. Wisconsin flag

15. Indiana flag

16. Georgia flag



Meet the Advisory Trustees

Suzanne Miller

Personal

- Born and raised in Shreveport, Louisiana;
- Attended the University of Texas at Austin;
- Following her marriage, moved to Houston;
- Houston resident since 1957;
- Has two children and five grandchildren.

Career in retail and design:

- First with a family-owned chain of jewelers;
- Then in the development of Walden on Lake Conroe;
- And for almost 20 years in the 1980s and 1990s as co-owner of the Traditions antique shop located in the Museum District.

Memberships and Affiliations include:

The Houston Symphony, Museum of Fine Arts, Juvenile Diabetes Foundation, Tourette's Foundation, M.D. Anderson Hospital, and Seven Acres, where she has been involved in fundraising and planning special events; active in numerous philanthropic organizations, primarily in the arts and medical research.

Petros E. Carvounis, MD

Career and Professional Affiliations

- Director, Vitreoretinal Fellowship Program, and Assistant Professor, Cullen Eye Institute, Baylor College of Medicine;
- Trained 7 vitreoretinal fellows and 48 ophthalmology residents;
- Author of over 95 papers, book chapters and presentations at national and international conferences;
- Fellow of American Academy of Ophthalmology & Royal College of Surgeons of Canada;
- Graduate of the University of Cambridge (preclinical medicine) and the University of Oxford (clinical medicine).

Personal

- Born in Vancouver, Canada, and raised in Athens, Greece;
- Fluent in Greek, Spanish and French;
- Competitive tennis player;
- Enjoys windsurfing, snowboarding, sailing, horseback riding and swimming;
- Opera lover: on Board of Directors of the Opera at the Heights (Oh!);
- Avid traveller (visited 28 countries).



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17. Suzanne Miller

18. Dr. Petros Carvounis



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 HANDICAPPED

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Call the office for more information: 713-797-1925

Additional memorials received will appear in the next issue.

