

From the Director

In the last few years we have made remarkable gains in identifying genes that cause eye disease. In light of this progress, the editors of *Archives of Ophthalmology* have devoted two recent issues to ophthalmic genetics. In the February issue – and in this newsletter – you can read about the results of our own outstanding genetic testing program.

Radha Ayyagari, Ph.D., director of the Ophthalmic Molecular Diagnostic Laboratory at Kellogg, reports on the results of some 350 genetic tests conducted over a five-year period. Through this laboratory, and the efforts of our genetic counselors, we are helping our patients learn more about the nature of their diseases.

Such knowledge is needed if we are to develop gene-based therapies for our patients who face vision loss. And so I am pleased to announce a discovery that has tremendous potential for realizing this goal.

Anand Swaroop, Ph.D., has successfully transplanted precursors to rod photoreceptors in mice. There is more to do, but when the research is fully developed, it could change the lives of people battling diseases like retinitis pigmentosa.

Take a look at these reports, and don't miss the photos that mark our progress in another area: the construction of a greatly expanded Kellogg Eye Center.

Paul R. Lichter, M.D.
Director, U-M Kellogg Eye Center

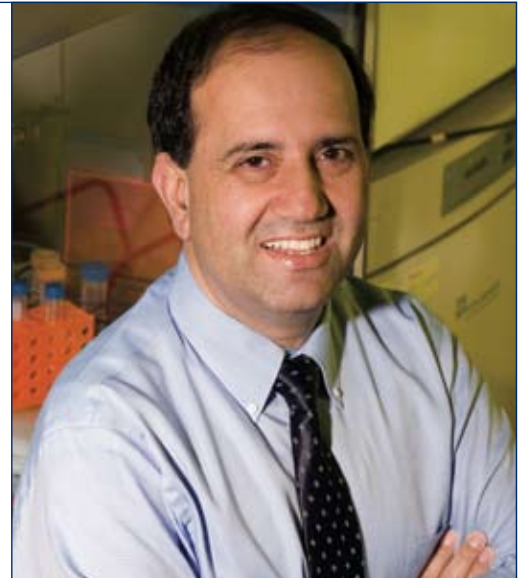
Breakthrough in Cell Transplantation: Timing Is Everything

Sue Smart, R.N., was among the first to congratulate Anand Swaroop, Ph.D., on his newly published research. Her adult son has retinitis pigmentosa, a disease that causes slow but progressive vision loss, and she saw great promise in the news that scientists had successfully transplanted healthy photoreceptors into mouse retinas.

Ms. Smart has followed vision research for years, as do many people who have family members with degenerative eye diseases. As a nurse she understands that a breakthrough in research today may still take many more years before it results in treatments. But for her son's sake, she hopes the research can be developed quickly. "Just hearing about this study and what you have discovered is very uplifting," she says. "When and if you are successful in developing this further, what a wonderful treatment this could be for so very many people."

In the November 9 issue of *Nature*, Dr. Swaroop reported on the successful transplantation of precursors to rod photoreceptors in the mouse retina. The study was the culmination of years of basic science research in the Swaroop lab. Scientists were able to show that transplanted cells survived and were properly integrated into the mouse retina. The mice responded to light, as indicated by pupil response.

The research has profound implications for people who suffer from diseases



Martin Voelt

Anand Swaroop, Ph.D., successfully transplanted rod precursors into mouse retinas.

caused by loss of photoreceptors, the light-sensitive cells that are essential for sight. If scientists could replace those cells, people with macular degeneration or retinitis pigmentosa would most certainly regain some of their lost vision. The current study involved rod photoreceptors, the cells that provide vision in dim light.

As word traveled about the study, Dr. Swaroop, the Harold F. Falls Collegiate Professor of Ophthalmology and Visual Sciences and Professor of Human Genetics, heard from science reporters and from patients wanting to learn more about the research. The Kellogg scientist stresses that it will take time to develop the technology, but he also believes we are entering a period of rapid discovery. "This provides a clear example of how basic fundamental research can contribute to treatment of blinding diseases," he says. "We now have proof of principle that our approach to repairing damaged retina by transplantation of appropriate cells can be successful."

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Beyond LASIK in Vision Correction

The U-M Kellogg Eye Center is one of a handful of eye centers in Michigan offering a new vision correction procedure that can help patients shed their glasses or contact lenses. It consists of implanting lenses, called phakic intraocular lenses (IOLs), into the eye.

Kellogg surgeons use the new Visian Implantable Collamer Lens (ICL), which has been proven effective in patients with a wide range of myopia, or nearsightedness, anywhere from -3.0 to -20.0. Before this procedure, high degrees of myopia could not be corrected.

"This is a great procedure for all those people who have not proven to be good candidates for LASIK surgery," says Shahzad I. Mian, M.D., corneal and refractive surgeon at Kellogg. "Typically, these patients have had to wear thick lenses to correct very high degrees of myopia. Now we can offer them an alternative with potential for excellent quality of vision."

The surgery is similar to cataract surgery, but the new ICL does not replace the eye's natural lens. Instead it is placed behind the iris, leaving the lens intact. The incision required to implant the ICL is small and located at the far edge of the cornea. After the lens is in place, sutures typically are not necessary to close the incision.

Mary Ruppenthal, 47, of Ypsilanti, was severely nearsighted and not a candidate for LASIK. In the summer of 2006, she had this new surgery performed on both eyes. "Once the lenses were in place, I could see so clearly right away. My recovery has been great and my vision is crystal clear."

To learn more about phakic IOLs, please contact us at 734.615.6914 or lasik@umich.edu

KELLOGG JOINS NEI GENETIC TESTING NETWORK

For the past seven years, Radha Ayyagari, Ph.D., has performed genetic testing for individuals with inherited retinal eye disease. Her laboratory was one of the first to receive the necessary federal approval, allowing patients with forms of macular degeneration and retinitis pigmentosa to receive precise descriptions of their diseases. Both of these conditions cause gradual vision loss that can result in legal blindness.

Now Dr. Ayyagari has joined a network created by the National Eye Institute (NEI) to make diagnostic gene testing more widely available. The National Ophthalmic Disease Genotyping Network, or eyeGENE, launched its nationwide research and testing program last fall.

The Kellogg laboratory is one of ten labs across the country participating in the eyeGENE network. Individuals tested at the Kellogg Eye Center who also participate in the NEI program do not pay testing fees.

As a result of her early involvement in ophthalmic genetic testing, Dr. Ayyagari has a unique perspective on its uses. In the February issue of *Archives of Ophthalmology* she reports on 350 genetic tests conducted over five years. Of these, 266 were performed to confirm a clinician's diagnosis, 75 sought to determine whether an individual was a "carrier" of a disease, and 9 were used to assess the likelihood that an individual with a family history of a given eye disease would go on to develop that disease.

The most common use, confirming a diagnosis, is not as straightforward as it may



Radha Ayyagari, Ph.D., Director of the Ophthalmic Molecular Diagnostic Laboratory

seem. Many retinal diseases present similar symptoms, and it is sometimes difficult for even the most skilled specialist to distinguish one from the other. Genetic testing, which reveals the molecular blueprint of the disease, can provide the information needed to confirm or rule out a diagnosis.

"EyeGENE is a nationwide program that will enhance our ability to connect genes to specific diseases, quicken the pace of gene discoveries, and speed research on treatments for blinding eye diseases."

-Paul A. Sieving, M.D., Ph.D.
Director of NEI

Patients have much to gain from having a molecular diagnosis on file, observes Dr. Ayyagari. "When treatments begin to emerge for these complex genetic diseases," she says, "the individual's genotype may determine whether a new treatment will be the one that works for that patient."

Patients who wish to be tested must be referred by a physician, genetic counselor, or other health professional. The U-M laboratory, the Ophthalmic Molecular Diagnostic Laboratory, can help patients set up an appointment with a Kellogg genetic counselor.

LEARN MORE

Genetic Testing at Kellogg 734.647.6347
www.kellogg.umich.edu/research/eyegenetest.fop.html
email: eyegenetest@med.umich.edu

NEI eyeGENE 301.496.2234
www.nei.nih.gov/resources/eyegene.asp

TEACHING THROUGH TEAMWORK

A 72-year-old woman sees her ophthalmologist because she has severe headaches. One week later she complains that she is frequently drowsy. The CT scan shows hemorrhaging in her brain.

After neuro-ophthalmologist Jonathan D. Trobe, M.D., makes his diagnosis – his patient has an aneurysm — he must select a specialist to perform the correct procedure — and soon. The aneurysm, a weakness in the artery, could burst, threatening not only the patient’s vision, but her life.

Dr. Trobe and colleague Wayne T. Cornblath, M.D., presented this and other case studies at Kellogg’s annual Mid-Winter Symposium. They asked six specialists from other departments of the U-M Health System to discuss how they would treat various neurological disorders.

According to Dr. Trobe, the discussions were typical of the give and take that goes on when physicians analyze neurological disorders that often appear first as vision problems. “Collaboration is such an important part of our work,” he says. “We’re fortunate to have such a deep reservoir of expertise.”

Dr. Trobe selected the case of the woman with the aneurysm to illustrate a

remarkable new technique practiced at Michigan. Dheeraj Gandhi, M.D., assistant professor of radiology, repaired the aneurysm by threading a thin catheter with titanium coils at its tip through the woman’s arteries, all the way from groin to brain. Once the catheter had reached the weakened bulge, Dr. Gandhi signaled the coils to unfurl. The coils conform to the shape of the aneurysm and stay in place, strengthening the artery.

Dr. Trobe, a highly-respected neuro-ophthalmologist with years of experience, is amazed by the procedure. “Just five years ago, major surgery would have been the only option. The catheterization has risks, of course, but it is far less invasive than surgery.” Dr. Trobe marvels at the skill of the physician who guides the catheter, no thicker than a strand of spaghetti, through arteries and their ever-thinner branches.

By the end of the day, the physicians had reviewed eight cases. “A problem-solving approach is the best way to teach



Jonathan D. Trobe, M.D., and resident Hilary Grabe, M.D., talk about the signs of neurological disorders in patients with vision problems.

medicine,” says Dr. Trobe. “It is far more effective than a lecture because this is the way doctors work.” He adds, “There is an extra level of intensity when you are discussing conditions that are not just vision-threatening, but life-threatening as well.”

Timing Is Everything

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As reported in *Nature*, it appears that timing of the transplanted cells has everything to do with the success of the procedure. And this is a concept that has evolved directly from the Swaroop lab.

About a year ago, Dr. Swaroop demonstrated that as rods develop, there is a point at which the cells are rod precursors; they are “programmed” to be, but have not yet become, functionally mature rod photoreceptors. In the most recent study, only the cells transplanted during this specific window of time were able to survive and

become integrated into the retina. If the cells were introduced too soon, while they were still undifferentiated stem cells, they were unable to create the connections needed to restore vision.

As Ms. Smart says, the hope that this finding could one day lead to human therapies is “huge.” She has watched her son deal with the challenges of vision loss. “You can become very isolated when you begin to lose vision,” she observes. “Job opportunities are often limited for people with visual impairments.” Her son, Shawn, has a degree in history, but is now studying for advanced training in computer science. He plans to develop adaptive technologies and websites to help others with low vision,

but he also wishes to use his programming skills in a wider range of areas. “Any vision my son could get back would make a tremendous difference in his life,” she says.

Dr. Swaroop’s research is supported by grants from the NIH, Foundation Fighting Blindness, Sramek Foundation, and Research to Prevent Blindness.

PATIENT RESOURCES

U-M Kellogg Eye Center
Retina Clinic 734.763.5906
Low Vision Clinic 734.764.5106

Low Vision Resource Guide

www.ewashtenaw.org/government/departments/library/li_resource_guide.html

MARCH MADNESS

Against Blindness Benefits Kellogg Research

Now a healthy four-year-old, Brendan Hepner lost his eye to retinoblastoma when he was only nine months old. His parents, Myron and Karen, are grateful to the physicians and staff at the University of Michigan Kellogg Eye Center for all they've done – and continue to do – for Brendan.

"The doctors and staff were a shining light to us when Brendan's diagnosis of retinoblastoma was made," said the Hepners. "Their caring attitude towards us went far beyond just being patients, and we have been grateful for their sincerity throughout all the follow-up visits. They are a blessing to our family!"

To show their appreciation, the Hepners organized the two-day inaugural *March Madness Against Blindness* to raise awareness and funds to support research at Kellogg. It was held at Damon's Grill in Ann Arbor during the first round of the NCAA men's basketball tournament in March. Last year, while watching the tournament, Myron had decided to put his basketball viewing to good use. He spoke with the owners of Damon's and this year's fundraiser was born.

Myron pledged to watch all 32 games of the first round in exchange for donations. In



Brendan Hepner at 10 months, one month after his surgery

addition to direct donations, the restaurant contributed 10 percent of dining receipts from both days to the fundraiser.

All proceeds from the inaugural *March Madness Against Blindness* will go toward Kellogg's vision research program. As the Hepners await the final tally, they are already making plans for next year's event.



Building our Vision: Kellogg Begins the Expansion

Photo 1: The formal groundbreaking celebration took place in September, with Department Chair Paul R. Lichter, M.D., hosting a crowd of over 300 faculty, staff, and supporters of the Eye Center Expansion. Among the distinguished speakers were U-M Regent Olivia P. Maynard, President Mary Sue Coleman, Robert P. Kelch, M.D., Executive Vice-President for Medical Affairs, Douglas L. Strong, CEO, U-M Hospitals and Health Centers, and James O. Woolliscroft, M.D., Interim Dean of the Medical School. Dee and Bill Brehm spoke about the diabetes research and analysis center they have created to accelerate research toward a cure for Type 1 diabetes. The W.K. Kellogg Foundation was represented by C. Patrick Babcock, Interim Vice President for Programs, who reflected on the role the Foundation played in establishing the Eye Center in 1985.

Photo 2: For the moment we are looking at mud-filled craters, bulldozers, and cement trucks — all with great hope and expectation. We can see the beginnings of the greatly expanded eye center our patients, faculty, and staff have been waiting for.

Photo 3: Rendering of the Kellogg Eye Center Expansion, a 222,000 square-foot state-of-the-art center for patient care, vision research and education.

Watch our progress at www.kellogg.umich.edu/expansion

Advances

To learn more about the Kellogg Eye Center or if you wish to be added to our mailing list, contact the marketing staff at:
aboutkellogg@umich.edu
or 734.647.5586

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