For the past several months, Alexcia Boyd has been a frequent traveler to Portland, where she's enjoyed such popular activities as visiting the zoo and sampling Northwest cuisine, particularly the sushi. But unlike other visitors, the 33-year-old from Chicago spends most of her time in Portland at Casey Eye Institute, where she is the first participant in a landmark gene therapy trial for an inherited blinding eye condition.

The study, conducted by Casey's Translational Clinical Trials Center and the University of Massachusetts, is the culmination of years of academic research of an investigative treatment for Leber's congenital amaurosis (LCA), a degenerative retinal disease that causes severe vision loss at an early age. Participants in this study have a defect in the RPE65 gene, one of 14 genes so far linked to LCA.

Although earlier studies found the gene therapy to be safe and well tolerated, this new trial will evaluate the study drug in a wider range of age groups than before and at dosage levels more in line with its commercial approval.

First Patient Enrolled in Landmark Gene Therapy Trial

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continued on page 2

Dear Friends,

Casey Eye Institute's research groups have made significant discoveries in the areas of cell- and gene-based therapies. Casey faculty and staff exploring the process of cell degeneration at a molecular level are working to unlock the secrets of eye diseases such as macular degeneration, glaucoma and diabetic retinopathy.

We are able to translate these discoveries to the clinic because of the progress being made in technology. Currently, doctors at Casey are participating in a clinical trial that involves replacing a defective gene for Lebers Congenital Amaurosis (LCA), a rare genetic disorder that causes blindness. The implanted gene will be monitored using a unique visual field test designed by Casey's Richard Wieleber, M.D. This trial could lead to Food and Drug Administration (FDA) approval so that the treatment will be available commercially.

There are many similar genetic eye diseases that we plan to treat in this same fashion. Casey is a leader in the progress towards curing eye diseases through cell- and gene-based therapies.

In this edition, you will learn about a community philanthropist who has invested in our research, a scientist who continues to think boldly about transforming technology and our new Translational Clinical Trials Center. Our team believes as did James E. Casey that “our horizon is only as distant as our mind’s eye wishes it to be.”

Sincerely,

David J. Wilson, M.D.
Thiele-Petti Chair, Department of Ophthalmology
Director, Casey Eye Institute
Oregon Health & Science University
potential, says Peter Francis, M.D., Ph.D., one of the study’s investigators. Furthermore, participants will undergo new objective measures of their visual function that will give a better idea if the gene therapy is working (see related story on page 3). Dr. Francis and his team will review and analyze the images, data and visual fields from both clinical sites, which hope to enroll a total of 12 patients.

“This is a beginning of a voyage, the realization that we have set sail on a truly groundbreaking effort,” says Dr. Francis. Alexcia’s own journey with LCA began in early childhood. “I’ve always experienced vision problems but it was hard to convince people that something was wrong with my eyesight,” she says, adding that teachers often attributed her difficulties at school to a behavioral problem. Although a blood test finally confirmed a diagnosis of LCA, Alexcia was told nothing could be done.

“I began handling all my own medical needs and learned how to get around on my own. I even memorized my neighborhood and everything in my house,” says the outgoing Alexcia, who is married and the mother of a two-year-old boy. “I was still convinced something could be done.”

While researching possible treatments for her disease, Alexcia consulted with a retina specialist at the University of Chicago, who referred her to Casey Eye Institute.

After meeting the study’s initial eligibility requirements, Alexcia flew to Portland in early March, where principal investigator Tim Stout, M.D., Ph.D., M.B.A., injected the healthy RPE65 gene underneath her retina during an outpatient procedure. The medication, provided by study sponsor Applied Genetic Technologies Corp., is designed to stimulate retinal eye cells to produce healthy versions of the gene. For the next two years, she will continue to return to Casey for diagnostic testing.

The study is not just significant because of its potential to treat LCA; it represents a defining moment for other eye research, notes Dr. Stout. “Since the early beginnings of medicine, drug discovery has been mostly serendipitous. By understanding the molecular basis for diseases like LCA, we can create therapies highly targeted to address the biological malfunction causing the disease,” he says.

Back home in Chicago, Alexcia is hopeful the pioneering treatment will eventually improve her vision. “If it doesn’t help me, maybe it will help others,” she says.

In the Spotlight
Notes & news from Casey’s divisions

Cornea Services’ faculty published more than 10 articles in 2009. Articles reviewed the use of liquid nitrogen cryotherapy, safety of hydrochloride ophthalmic gels and laser surgery versus long-term contact lens wear.

Rick Fraunfelder, M.D., is the new president-elect of the International Society of Ocular Toxicology and is bringing the international meeting to Portland, Ore. in 2011.

Winston Chamberlain, M.D., is performing keratoprosthesis implantation, which is used when a standard corneal transplant has failed or when it would be unlikely to succeed. The implantation is a procedure designed to help patients whose conditions are the most difficult to treat.

OHSU’s largest community event, the Macular Degeneration and Low Vision Expo, will be held on Saturday, May 22 at the Doubletree Hotel/Lloyd Center. The all-day program features updates on research, treatments and low vision topics. For more information visit www.caseyamd.com.

The Uveitis Clinic is participating in two new clinical trials for patients with uveitis. One is a multicenter study utilizing an antibody against IL-17; the other is an OHSU-only study of a small molecule blocking PDE4 (IL-17 and PDE4 are both molecules that regulate inflammation and autoimmunity).

Eric Suhler, M.D., is a new graduate of the American Academy of Ophthalmology Leadership Development Program. This program facilitates the promotion of graduates into leadership positions in ophthalmology both locally and nationally.

The Neuro-Ophthalmology Clinic is looking at a potential association between the use of erectile dysfunction drugs and the development of anterior ischemic optic neuropathy (AION). The clinic is also involved with a National Institutes of Health sponsored multicenter clinical trial studying potential genetic factors involved in the development of idiopathic intracranial hypertension, as well as visual outcome of this condition when treated with weight loss only versus weight loss and medication.
Innovative Diagnostic Tools a Mainstay of Casey Research

In the search to find better treatments for inherited retinal diseases, researchers are finding great potential in the microscopic world of cells and genes. However, along with this groundbreaking work comes the need to use the most innovative methods possible to learn if these novel therapies are effective.

At Casey Eye Institute, experts such as Mark Pennesi, M.D., Ph.D., are meeting this challenge by employing and refining sophisticated diagnostic techniques at the Translational Clinical Trials Center. Tools such as electroretinography (ERG), visual field tests and optical coherence tomography (OCT) can tell doctors if retinal cells are responding to the subtle changes brought about by gene replacement therapy or cell-based treatments such as stem cell therapy.

“As this type of research progresses, it is vital to have objective methods such as electrophysiology and imaging to capture minute changes in retinal cells,” explains Dr. Pennesi, who holds both a medical degree in ophthalmology and a doctorate in neuroscience.

“Traditional tests of vision may not be able to detect improvements in patients with retinal diseases such as retinitis pigmentosa. Diagnostic tests give us an easy, non-invasive way to objectively and accurately measure the remaining vision,” he says.

For example, an ERG, which measures the retina’s electrical activity through electrodes placed on the eye, can detect problems with the eye’s photoreceptor cells. These light-sensing cells, composed of rods and cones, are responsible for transmitting images to the brain. When damaged by retinal disease, they cause vision loss.

Because conventional ERGs can’t pick up on smaller areas of the retina affected by disease, a newer technology called multifocal ERG is particularly useful in certain cases, such as in gene replacement therapy for inherited retinal disorders. “Multifocal ERG provides a more detailed look at the retina, and allows us to determine if vision is returning in a specific location as a result of the experimental treatment,” says Dr. Pennesi. Casey is the only eye center in the region that offers both conventional and multifocal ERG testing.

The ERG has also become a valuable tool in pre-clinical studies for degenerative retinal disease in animal models. At Casey, Dr. Pennesi has customized an ERG device to evaluate visual function in rodents. “The structure of the rodent eye on a microscopic level is very similar to humans,” he says, adding that scientists are able to manipulate genes to simulate human ocular diseases such as retinitis pigmentosa in rats and mice. “The degeneration that we see in these animals is very similar to the degeneration observed in humans.”

Not only are state-of-the-art diagnostic tools paramount in research, they also are a critical part of Casey’s clinical care services. In recognition of their growing importance, Dr. Pennesi recently was appointed Casey’s first medical director of Imaging Services, where he oversees ophthalmic photography, fluorescein angiography, ocular coherence tomography and ultrasound among other services.

Mark Pennesi, M.D., Ph.D., with an electroretinogram (ERG) he customized for rodent studies of degenerative retinal diseases.
Casey Eye Institute Increases Patient Access in Southwest Washington

In fulfillment of Casey’s mission to reach new communities with the best eye care, we are proud to announce the opening of two new locations in Southwest Washington. Casey now has offices in Vancouver and Longview, Wash. The opening will give Washington residents increased access to ophthalmology services and offer a more seamless referral process for patients who need to travel to the Casey Eye Institute in Portland for surgery or services not available locally. To schedule an appointment at one of our new locations please call the Casey Eye Institute main line at 503 494-3000.

**Casey Eye Institute – Vancouver**
16701 S.E. McGillivray Blvd.
Vancouver, WA 98683

**Casey Eye Institute – Longview**
600 Triangle Center, Suite 400
Longview, OR 98632

Casey Eye Institute Vancouver offers a full range of optical services.