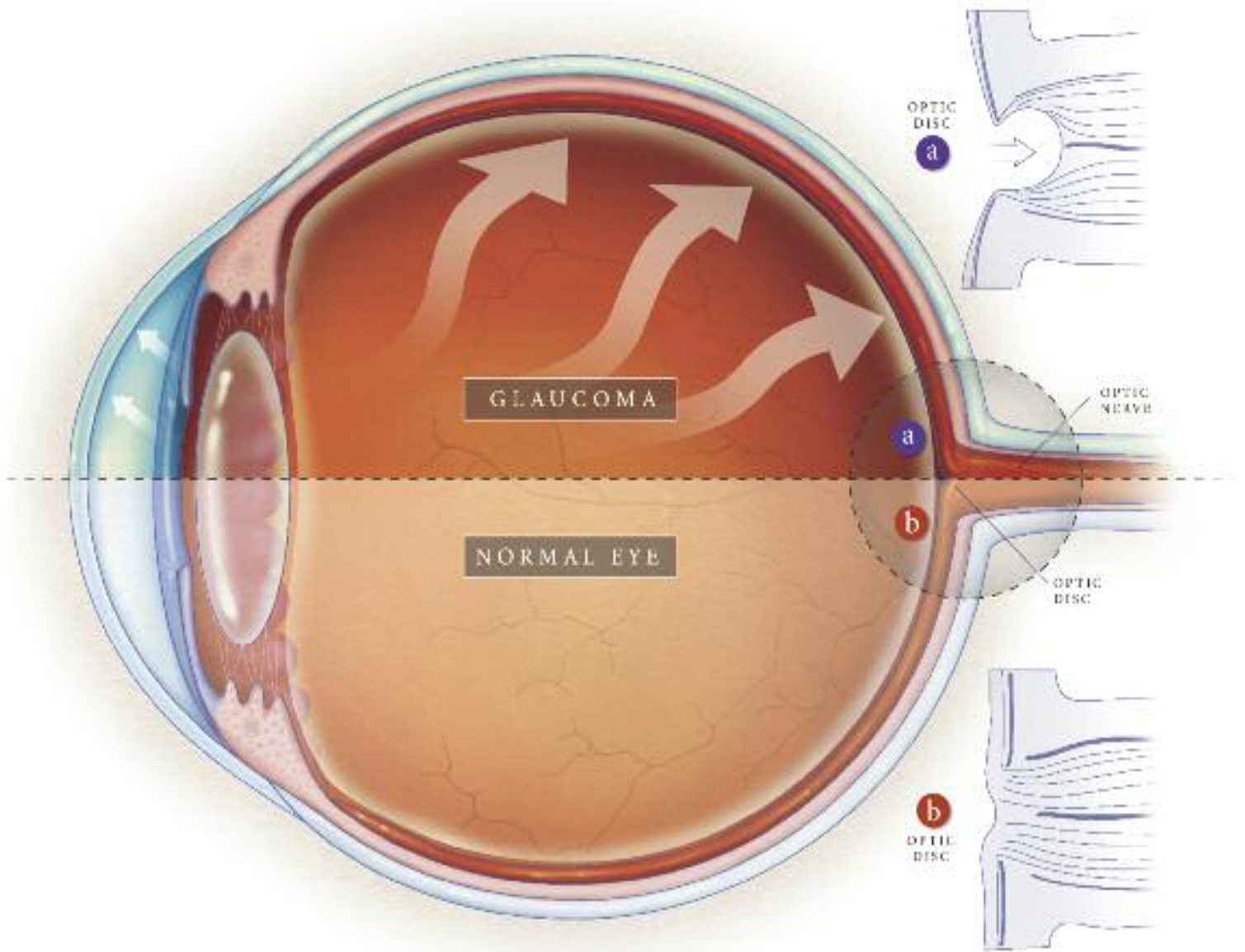


MEMORIAL HERMANN OPHTHALMOLOGY JOURNAL

TEXAS MEDICAL CENTER



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IN THIS ISSUE

FEATURE

02 **Prevention of Vision Loss from
Primary Congenital Glaucoma:
Three Stories**

RESEARCH HIGHLIGHTS

05 **Intravitreal Avastin versus
Laser Surgery for Retinopathy
of Prematurity**

06 **Memorial Hermann and UT
Participate in Phase III Trial
of a New FDA-Approved Drug
for Macular Edema**

07 **Current Research Supported by
the National Institutes of Health**

Behavioral Measures of Vision

Connectivity Patterns of Retinal
Bipolar Cells

Neurogenesis at the Mammalian
Retinal-Ciliary Margin

08 **A Potential Zebrafish Model of
Glaucoma by Genetic Ablation and
Modification of the Annular
Ligament Cells**

Neurotransmitter Mechanisms in
the Mammalian Retina

Regulation of Retinal Gap Junctions

Houston Area Vision Training Grant

Core Grant for Vision Research

09 **IN PRINT**

**Upcoming Continuing Medical
Education for Ophthalmologists**

PREVENTION OF VISION LOSS FROM PRIMARY CONGENITAL GLAUCOMA: THREE STORIES

JOSIE DURANT

WHEN JOSIE DURANT was delivered preterm at Memorial Hermann Northeast Hospital in Humble, Texas, neonatologist Angel Muñoz, M.D., noted her cloudy corneas and referred her to Helen Mintz-Hittner, M.D., a pediatric ophthalmologist affiliated with Children's Memorial Hermann Hospital in Houston. "We thought she had cataracts," says Josie's mother, Melanie Durant. "But Dr.

"WE WEREN'T EXPECTING JOSIE TO GO TO SURGERY ON THE DAY OF OUR OFFICE VISIT" DURANT RECALLS. "BUT DR. FELDMAN WAS CONCERNED ABOUT THE TWO-WEEK DELAY DUE TO HER NICU STAY AND WANTED TO ACT QUICKLY."

Mintz-Hittner took one look at her, diagnosed primary congenital glaucoma and sent us to Dr. Feldman, who scheduled surgery the same day." Born at 34 weeks, 5-pound, 13-ounce Josie had the classic triad of glaucoma: photophobia, blepharospasm and tearing.

In the operating room, Robert M. Feldman, M.D., an ophthalmologist affiliated with Memorial Hermann-Texas Medical Center and The Cizik Eye Clinic, performed trabeculotomies on both of the infant's eyes, opening the natural pathway to drain the accumulated aqueous humor and reduce the intraocular pressure associated with glaucoma. Dr. Feldman is professor and

chair of the department of Ophthalmology and Visual Science at The University of Texas Medical School at Houston and Richard S. Ruiz, M.D., Distinguished University Chair in Ophthalmology.

Trabeculotomy is the preferred procedure for pediatric patients with primary congenital glaucoma and clouded corneas. The procedure has an 80 percent to 90 percent success rate in children who present between the ages of 1 month to 2 years. In children diagnosed earlier, the success rate is lower.

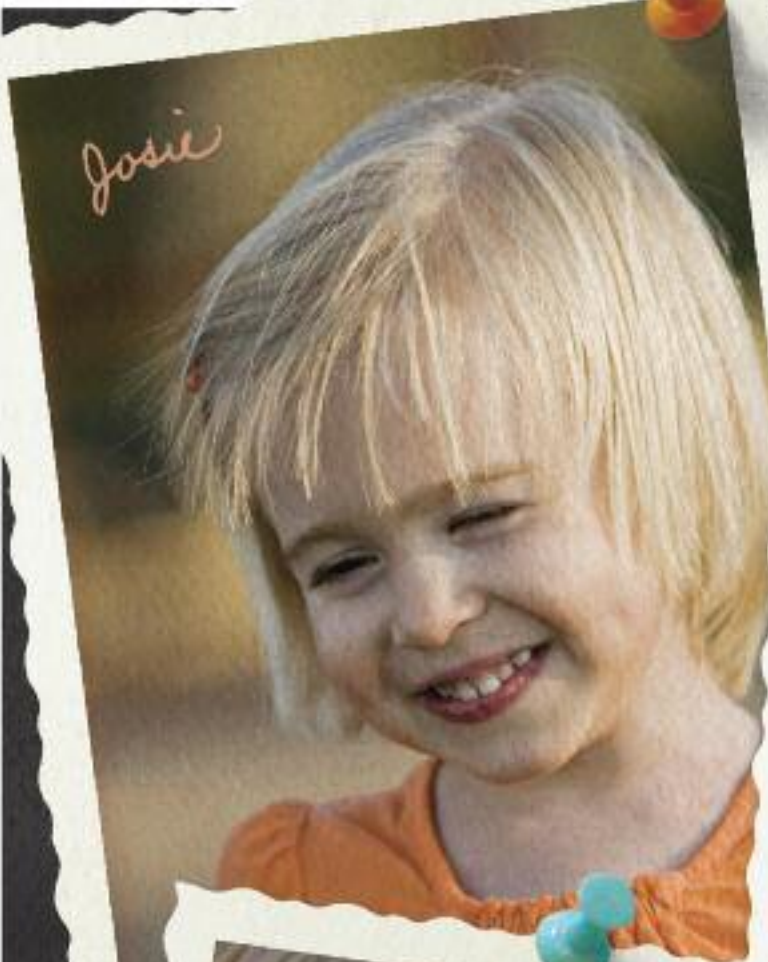
"We weren't expecting Josie to go to surgery on the day of our office visit," Durant recalls. "But Dr. Feldman was concerned about the two-week delay due to her NICU stay and wanted to act quickly."

When the trabeculotomies failed over time to maintain normal pressure in Josie's eyes, Dr. Feldman took the infant back to the OR for tube-shunt surgery. The flexible plastic tubes Josie has in both eyes help maintain normal intraocular pressure by draining aqueous humor to attached silicone plates.

Nan Wang, M.D., an assistant professor in the department of Ophthalmology and Visual Science at the UT Medical School and a partner at The Cizik Eye Clinic, removed a cataract in Josie's left eye and performed an iridectomy to improve vision in the left eye.

Josie was back in the operating room two more times in late 2008 and early 2009, when Dr. Feldman cleared accumulated debris from the tube in her left eye and, later, repositioned the tube shunt in her right eye to accommodate growth. After multiple surgeries, Josie is doing well. Vision in her right eye is normal.

"With one good eye, we expect Josie to do very well developmentally," says Dr. Feldman, who sees her regularly to track her pressures and monitor progress. "Like most young children with primary congenital glaucoma, she'll need future surgeries to adjust the position of the tube shunts as her eyes grow."



Now 2 1/2, Josie is speaking in complete sentences and developing an extensive vocabulary. “She has the vocabulary of a 20-year-old,” Durant says. “She’s constantly surprising us.

“I don’t know what we would have done without Dr. Feldman,” she adds. “He understands the urgency of the situation and sees us at the drop of a hat.”

JACOB DURANT

PRIMARY congenital glaucoma is relatively rare, estimated to affect fewer than 0.05 percent of all ophthalmic patients, and previous to Josie’s birth, there had been no history of glaucoma in the Durant family. But when Jacob Durant was born with clouded corneas, his parents knew exactly what to do. Delivered by cesarean section on a Monday in late June 2009, Jacob was in Dr. Feldman’s office by Thursday of the same week.

He underwent trabeculotomies on both eyes that same day. When the procedure failed to lower intraocular pressure in Jacob’s right eye, Dr. Feldman connected a tube shunt in August.

“Jacob is still a very young infant but he appears to be doing well,” Dr. Feldman says. “The left eye is clear and good.”

What is unusual is that both Durant children were born with the disorder, given the relatively low frequency of primary congenital glaucoma and the sporadic nature of its occurrence. “Different modes of inheritance may be involved in the transmission of congenital glaucoma,” Dr. Feldman says. “A few genetic markers have been identified but they aren’t commonly seen in the population, and there isn’t a single

gene that drives the development of the disease. With only two children in one generation with congenital glaucoma, we can’t really gather much information about the cause. We suspect that there’s a *de novo* mutation in an autosomal dominant gene in at least one of the parents.”

For the Durants, who have decided they are happy as a family of four, genetic testing is a moot point. “One or both of us carries the gene,” Melanie Durant says. “Having given birth to two out of two children with congenital glaucoma, we think it’s a good bet that it would happen again.”

GRACE SPEER

BORN in September 2007 with cataracts in both eyes, Grace Speer exhibited elevated intraocular pressure in a follow-up exam under anesthesia (EUA) conducted at the age of 3 months, after removal of her cataracts. She had developed uveitis in her right eye following the surgery and required a vitrectomy to clear blood and debris left by the inflammation. A few weeks later, her mother, an anesthesiologist, noticed that her cornea was cloudy.

By February 2008, less than six months after her birth, Grace displayed the classic triad of glaucoma: photophobia, blepharospasm and tearing. When the ophthalmologist who diagnosed Grace at another hospital couldn’t see her earlier than two weeks out, her mother turned to pediatric ophthalmologist Helen Mintz-Hittner, M.D., who is affiliated with Children’s Memorial Hermann Hospital and holds the Alfred W. Lasher III Professorship in Ophthalmology at the UT Medical School. Dr. Mintz-Hittner referred Grace to David A. Lee, M.D., a professor in the department of Ophthalmology and Visual Science at UT Medical School.

“Dr. Lee saw us on a Friday and noted that her pressures were abnormally elevated to about twice the normal range,” says Grace’s mother, Bryce Speer, D.O., L.T., U.S.N. “He scheduled her for surgery the following Monday.”

In the operating room, Dr. Lee placed a tube shunt in Grace’s right eye; her left eye has remained stable on Cosopt®.

“She takes drops in both eyes and is doing really well,” her mother says. “We have our routine EUAs every three months and continue to see improvement at each visit. Because she was only 5 months old when the tube shunt was placed, it will have to be revised at some point to accommodate growth of her eye.”

While Dr. Lee doesn’t anticipate the need for additional interventions for glaucoma, he notes that Grace is at risk of developing amblyopia. “It takes about five years for all the connections between the eye and the brain to form,” he says. “If one eye is better than the other, the brain will select the image it produces and ignore the image produced by the other eye. The eye producing the unselected image will tend to turn in more.” Grace has worn contacts since the age of 8 months to maintain good vision and reduce the risk of amblyopia.

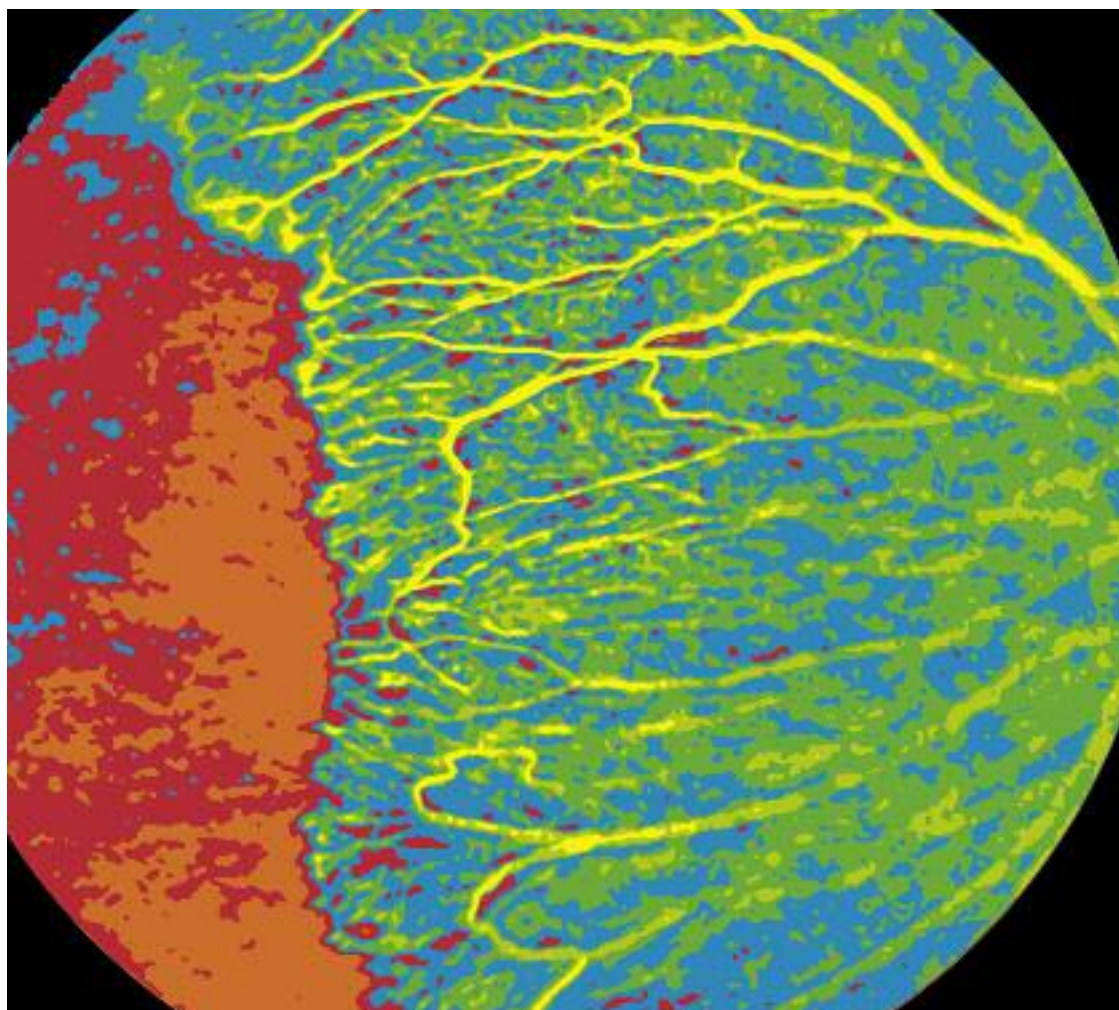
“I’m not exaggerating when I say that Dr. Lee saved her eye,” says Dr. Speer, who is currently serving a tour of military duty in North Carolina. “She had all the classic symptoms of primary congenital glaucoma. He was willing to see us immediately and take care of it. We’re so fortunate to have found doctors who listen to parents and believe them. Parents always know when something isn’t right with their children.”

INTRAVITREAL AVASTIN VERSUS LASER SURGERY FOR RETINOPATHY OF PREMATURITY

A NATIONAL, PROSPECTIVE, RANDOMIZED, CONTROLLED, MULTI-CENTER PHASE II CLINICAL TRIAL LED BY RESEARCHERS AT CHILDREN'S MEMORIAL HERMANN HOSPITAL AND THE UNIVERSITY OF TEXAS MEDICAL SCHOOL AT HOUSTON INVESTIGATES THE EFFICACY OF INTRAVITREAL AVASTIN™ INJECTIONS TO IMPROVE OUTCOMES IN INFANTS WITH RETINOPATHY OF PREMATURITY.

principal investigator in a Phase II trial comparing the use of intravitreal bevacizumab (Avastin) injections to conventional laser surgery to improve structural and functional outcomes of vision-threatening retinopathy of prematurity (ROP). The University of Texas Health Science Center at Houston is the lead center in the national study, which began in March 2008 and will enroll 150 patients at centers in Texas, California, Colorado, Illinois and South Carolina. Researchers expect to complete the study in October 2010.

Retinopathy of prematurity, originally called retrolental fibroplasia, remains a common cause of retinal detachment and blindness. When the disease was first described in 1943, there was no recommended treatment for any stage of progression. In 1984, following a national, prospective, randomized, controlled, multi-center clinical trial, cryotherapy for advanced Stage 3 ROP was approved. In the early 1990s, laser therapy came into use following the publication of multiple case studies, and in 2003 laser therapy for early Stage 3 ROP was approved based on the results of a national, prospective, randomized, controlled, multi-center clinical trial. In 2007, the use of an intravitreal anti-VEGF (vascular endothelial growth factor) injection for advanced Stage 3 in Zone I and for Stages 4a and 4b was suggested by a few case reports and



Retinopathy in premature infant. Retinal fluorescein angiogram showing hypoxia of the retinal periphery.

Helen Mintz-Hittner, M.D., a pediatric ophthalmologist affiliated with Children's Memorial Hermann Hospital and the Alfred W. Lasher III Professor of Ophthalmology at The University of Texas Medical School at Houston, is

case series.

The advantages of Avastin include avoidance of laser complications, including no reintubation of infants for treatment, an immediate response compared to a seven-to-14-day delayed response for laser therapy, no unneces-

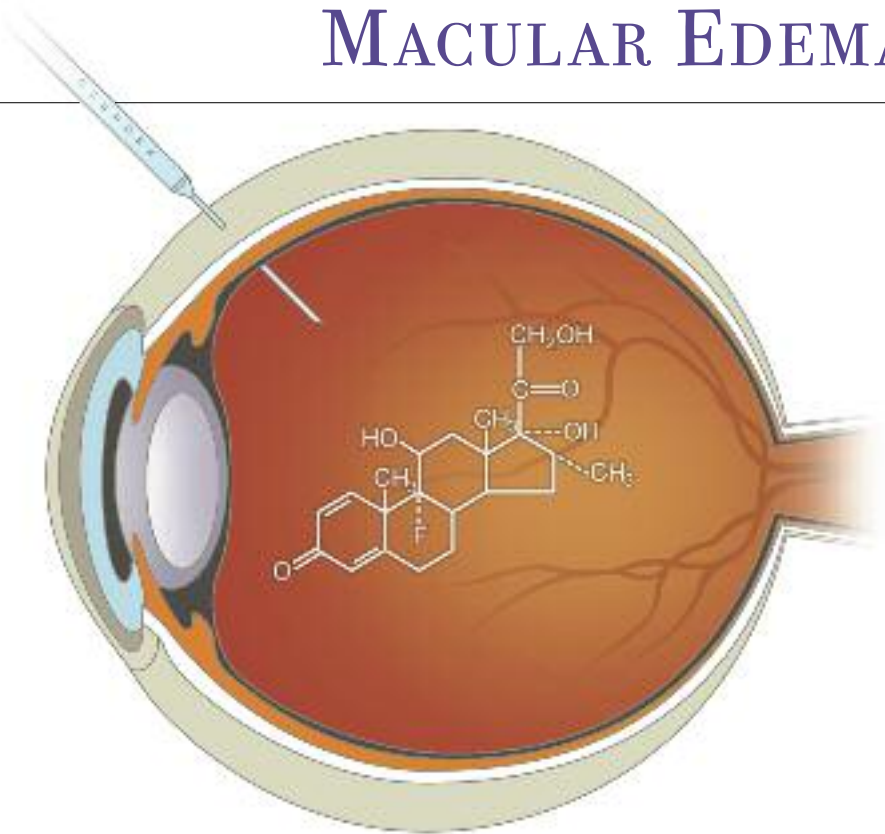
sary loss of visual field and a decrease in the amount of severe nearsightedness related to ROP. The FDA has approved intravenous administration of Avastin for metastatic cancer of the colon and lung and has not approved its use in the eyes of adults or premature infants. Intravitreal Avastin has been used off label for age-related macular degeneration, diabetic retinopathy and multiple other neovascular ocular disorders in adults around the world. The new study seeks to gather evidence-based data to determine the efficacy and safety of Avastin intravitreal injection compared to conventional laser surgery for ROP: off label (new route of administration: intravitreal) - off label (new population: neonates). Eligible infants include those who weigh less than 1,500 grams at birth and were born at less than 30 weeks gestation and develop vision-threatening Stage 3 ROP in Zone I or posterior Zone II.

“We are proud to support Dr. Mintz-Hittner’s important study at Children’s Memorial Hermann Hospital and await the results of this clinical trial to better understand the outcomes of these two forms of treatment to prevent blindness in neonates with retinopathy of prematurity,” says Craig Cordola, CEO of Children’s Memorial Hermann Hospital.

“This is the first prospective randomized, controlled study to compare these two very different forms of treatment for this condition in neonates,” says Robert M. Feldman, M.D., professor and chair of the department of Ophthalmology and Visual Science at the UT Medical School and Richard S. Ruiz, M.D., Distinguished University Chair in Ophthalmology. “Memorial Hermann and UT Medical School recognize the critical importance of this clinical trial and the value that the study findings will have for neonatology practice.”

FOR MORE INFORMATION ABOUT THE TRIAL, CONTACT DR. MINTZ-HITTNER AT 713.704.2345 OR HELEN.A.MINTZ-HITTNER@UTH.TMC.EDU.

MEMORIAL HERMANN AND UT PARTICIPATE IN PHASE III TRIAL OF A NEW FDA-APPROVED DRUG FOR MACULAR EDEMA



Memorial Hermann-Texas Medical Center and The University of Texas Medical School at Houston participated in a multi-center Phase III trial that led to United States Food and Drug Administration approval of Ozurdex™ (dexamethasone intravitreal implant) 0.7 mg as the first drug therapy indicated for the treatment of macular edema following branch retinal vein occlusion or central retinal vein occlusion. Retinal vein occlusion (RVO) is the second most common retinal vascular disease after diabetic retinopathy and a significant cause of vision loss.

Ozurdex is a first-of-its-kind therapy administered through intravitreal injection delivering dexamethasone, a potent corticosteroid, via a proprietary delivery

system developed by Allergan. A biodegradable implant that allows for extended release of dexamethasone is placed in the vitreous cavity in the back of the eye, treating the macular edema associated with retinal vein occlusion and improving visual acuity. Release takes place over a period of approximately six months, a significant advance over previously available treatment, which required a monthly injection.

The first injectable, sustained-release steroid implant that provides prolonged efficacy and a favorable safety profile, Ozurdex produced a three-line improvement in best-corrected visual acuity in 20 percent to 30 percent of patients with RVO with an onset of effect within the first two months following therapy.

CURRENT RESEARCH SUPPORTED BY THE NATIONAL INSTITUTES OF HEALTH

Behavioral Measures of Vision

Principal Investigator:

Louvenia Carter-Dawson, M.D.

Associate Professor, Department of

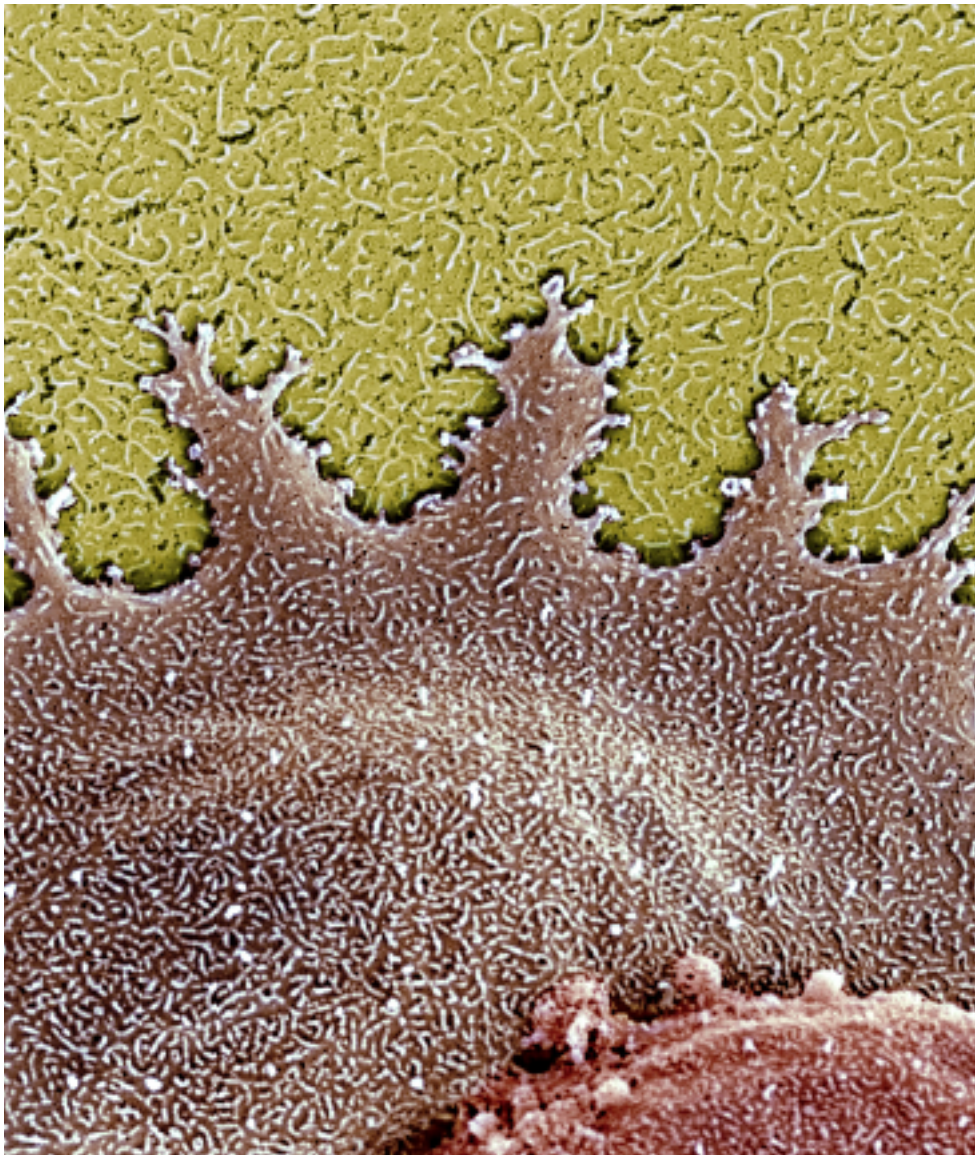
Ophthalmology and Visual Science

*The University of Texas Medical School
at Houston*

This quantitative and histological analysis of glaucomatous damage in monkeys with monocular experimental glaucoma is being conducted by Dr. Carter-Dawson,

after assessments of visual field and OCT evaluation of retinal nerve fiber layer thickness (RNFL) by Ronald Harwerth, O.D., Ph.D., of the University of Houston College of Optometry. Retinal ganglion cells are being quantified in 16 specific

Colored scanning electron micrograph (SEM) of two human retinal stem cells (brown and red) on their feeder cells (yellow).



visual field test sites in histological sections to further investigate the relationship between the degree of visual defects and number of retinal ganglion cells. RNFL thickness is being evaluated in histological sections and compared to that obtained by OCT. In addition to RNFL thickness, the researchers are identifying the neural and non-neural components of the layer and quantifying them in control and glaucomatous monkey retinas using immunohistochemistry and confocal microscopy. These data will allow prediction of remaining retinal ganglion cells in eyes with known visual field defects and the relative contribution of glia to the RNFL with severity of glaucoma damage.

Connectivity Patterns of Retinal Bipolar Cells

Principal Investigator:

Stephen L. Mills, Ph.D.

*Professor, Department of Ophthalmology
and Visual Science*

*The University of Texas Medical School
at Houston*

Dr. Mills and his team are using novel labeling techniques to identify and record from mammalian retinal ganglion cells. The goal of the research is to identify unknown visual processing pathways and also to understand the effect on visual perception of ganglion cells firing in synchrony rather than independently.

Neurogenesis at the Mammalian Retinal-Ciliary Margin

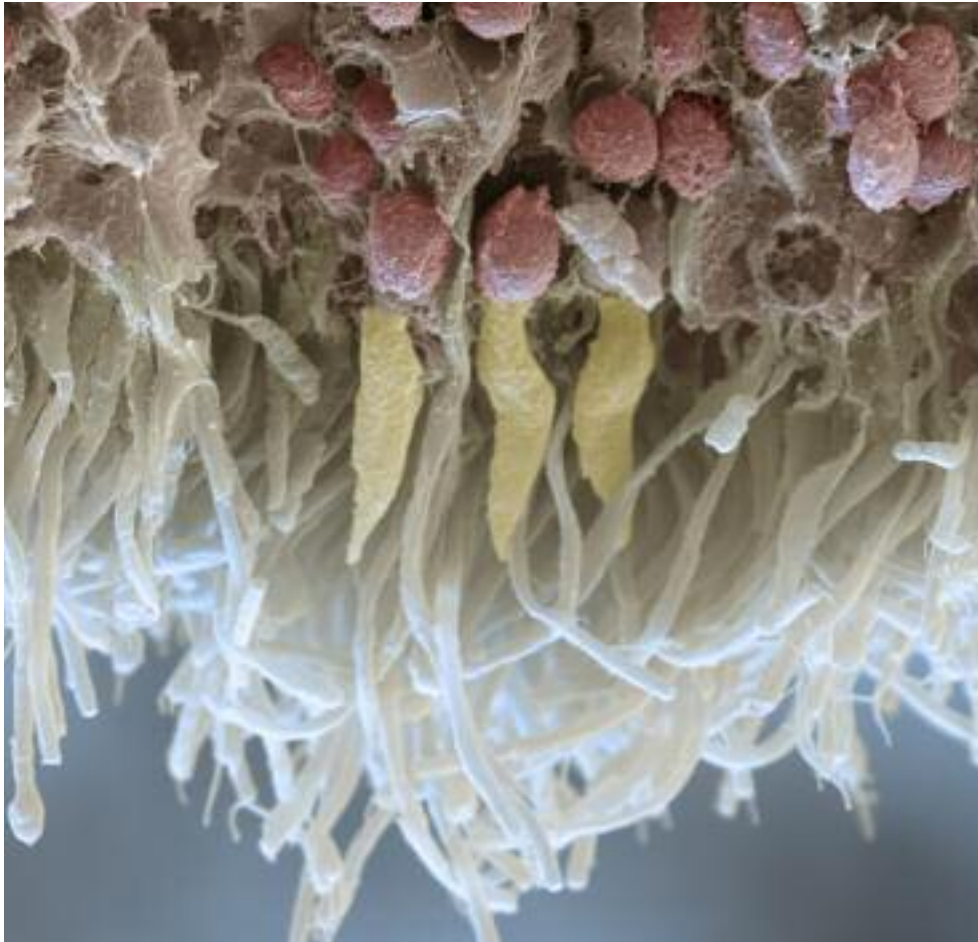
Principal Investigator:

Steve Wang, Ph.D.

*Assistant Professor, Department of
Ophthalmology and Visual Science*

*The University of Texas Medical School
at Houston*

This research study is using advanced genetic engineering techniques to explore the potential of retinal-ciliary margin for producing stem cells capable of forming retinal ganglion cells, amacrine cells and horizontal cells.



The picture shows a section through the human retina. From top to bottom are shown bipolar neurons and cones of the receptor cells (red) and under that the rod cells (white) and cone cells (yellow).

A Potential Zebrafish Model of Glaucoma by Genetic Ablation and Modification of the Annular Ligament Cells

Principal Investigator:
Xinping C. Zhao, Ph.D.

*Assistant Professor, Department of Ophthalmology and Visual Science
The University of Texas Medical School at Houston*

Researchers are using genetic and transgenic approaches to ablate and modify the annular ligament cells of the zebrafish eye, the zebrafish equivalent of human trabecular meshwork, to increase intraocular pressure, which may lead to development of glaucoma or a glaucoma-like phenotype in the transgenic animal.

Neurotransmitter Mechanisms in the Mammalian Retina

Principal Investigator:
Steve Massey, Ph.D.

*Professor and Elizabeth Morford Chair in Ophthalmology, Department of Ophthalmology and Visual Science
The University of Texas Medical School at Houston*

In the laboratory, researchers are investigating how the retina processes visual information and how it adapts so rapidly to the visual scene to optimize the process. To this end, they are using high-resolution imaging to reconstruct neuronal circuits in the retina and injecting single neurons with fluorescent dyes and labeling other cell types with antibodies. A laser-driven confocal microscope is used to scan the retina in three color channels to visualize neuronal connections. By reconstructing the circuits in 3D, researchers can reconstruct specific pathways used for color vision or night vision, as well as other pathways.

Regulation of Retinal Gap Junctions

Principal Investigator:

John O'Brien

*Associate Professor and Frederic B. Asche Chair in Ophthalmology, Department of Ophthalmology and Visual Science
The University of Texas Medical School at Houston*

The goal of this project is to identify the molecular mechanisms that control gap junction coupling between retinal neurons. Gap junctions form one of the major routes for communication between neurons, and regulation of coupling is critical to adapting the retina to function under different lighting conditions. Study of these mechanisms will help to explain how humans see efficiently at night but prevent signals from swamping out the visual image during the day when rods are saturated.

Houston Area Vision Training Grant

Principal Investigator:

Steve Massey, Ph.D.

*Professor and Elizabeth Morford Chair in Ophthalmology, Department of Ophthalmology and Visual Science
The University of Texas Medical School at Houston*

Four graduate students and one postdoctoral fellow in the Houston area are supported by this NIH grant, which is held in collaboration with the University of Houston College of Optometry. Laura Frishman, Ph.D., of the University of Houston, is co-principal investigator.

Core Grant for Vision Research

Principal Investigator:

Steve Massey, Ph.D.

*Professor and Elizabeth Morford Chair in Ophthalmology, Department of Ophthalmology and Visual Science
The University of Texas Medical School at Houston*

This multi-faceted infrastructure grant supports core facilities for ophthalmology and visual science research at the UT Medical School.

IN PRINT

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UPCOMING CONTINUING MEDICAL EDUCATION FOR OPHTHALMOLOGISTS

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United States Army Eye Surgeon
Fort Bragg, North Carolina
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