

This year's International Think Tank was the first in the gathering's 16-year history to focus on one particular glaucoma, exfoliation syndrome (XFS). Some 50 participants from Canada, China, Germany, Hungary, Iceland, Turkey and the U.S. convened in October for the two-day session in midtown New York. The interdisciplinary format brought together research scientists, clinicians, micro-medical engineers, biochemists, molecular geneticists and pathologists.

XFS is an age-related systemic disease characterized by the production and progressive accumulation of a whitish material in many ocular tissues. Worldwide, it is the most common



Ursula Schlotzer-Schrehardt, PhD, a professor from Erlangen, a Think Tank presenter and member of the organizing committee.

identifiable cause of open-angle glaucoma. It is also a cause of angle-closure glaucoma and cataract.

About 25 percent of persons with XFS develop elevated IOP and one-third of them develop glaucoma. However, if you have XFS, your chances of developing

2009 Think Tank Exfoliation Syndrome: The First Potentially Curable Glaucoma

glaucoma are about six times higher than if you don't. An increasing list of associations with cardiovascular and cerebrovascular diseases makes XFS a condition of general medical importance. Recently described associations include stroke, cardiovascular dysfunction, Alzheimer's disease and hearing loss.

"We're learning a lot about the disease," says Dr. Robert Ritch, TGF's Medical Director and Chairman of the Scientific Advisory Board. "At the Think Tank we attempted to relate the current status of our knowledge about XFS in order to develop new approaches to preventing the formation or reversing the deposition of exfoliation material and to explain the origin of its various systemic manifestations."

The discovery in 2007 of two genetic abnormalities in the lysyl-oxidase-like 1 (LOXL1) gene, which is responsible for the formation and maintenance of elastic tissue, is expected to have a major impact not only in understanding XFS but in leading to new avenues of therapy. The protein made by the



Some of the 2009 Scientific Think Tank participants.

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Scott R. Christensen

Letter from the President

Dear Friends:

Partnerships are key to the mission of The Glaucoma Foundation. We hold a strong conviction that all sectors – health professionals, researchers, non-profit organizations, government agencies and corporations – must work together to win the battle against glaucoma.

We are particularly gratified by our strong and growing relationships with corporations that share our goal of developing new treatments that preserve eyesight and prevent blindness for those afflicted with the disease of glaucoma.

The 16th Annual International Think Tank, our important collaborative conference, is a prime example of our partnerships with companies that share our mission and are working to realize mutual goals. The 2009 Think Tank received significant support from eight corporate sponsors. As you will read, Think Tank participants collectively represented the vanguard of exploration by medical science into exfoliation syndrome, a form of glaucoma that was the Think Tank's focus.

We also continue to look for new ways to effectively reach the general public to educate them about glaucoma and to keep glaucoma patients worldwide informed about new therapies and living with the disease.

Most recently, a "Lunch and Learn" program was organized for a group of students, future health care workers in the Los Angeles area. We are reaching others who have the disease through our chapters and our online support communities.

While we have not been spared the challenges created by the recession, we have come through the year strong and more dedicated than ever to our goals of supporting glaucoma patients and their caregivers, educating the public, and funding research that will contribute to better treatments and ultimately eradicating blindness from glaucoma.

We are keenly aware of the important role that you, our long-time supporters, play in these efforts. You, too, are our valued partners and we are grateful for your ongoing commitment.

Sincerely,



Scott R. Christensen
President
Chief Executive Officer



Questions answered by:

Robert Ritch, MD

TGF Medical Director, Vice President & Secretary
Professor & Chief, Glaucoma Service
The New York Eye and Ear Infirmary

How is exfoliation syndrome diagnosed?

Exfoliation syndrome is diagnosed by seeing white flakes of material, which are similar in appearance to dandruff, on the anterior lens capsule and pupillary border during slit lamp examination. The diagnosis is often missed because it usually requires pupillary dilation and examination of the lens after dilation. This is often not done during examination and this plus failure to recognize the material in its earlier phases results in a significant percentage of patients being under diagnosed. When elevated intraocular pressure or glaucoma is present in one eye only in patients over the age of 50, exfoliation syndrome should be suspected until proven otherwise by detailed examination.



Illustration of exfoliation material.

Many physicians recommend that cataracts be removed once they cause a decrease in corrected vision rather than waiting because operative complications increase with the density of the lens due to weakness of the zonules, which hold the lens in place.

Is there a connection between exfoliation syndrome and cataracts?

Yes, there is an etiological association. When unilateral cataract and unilateral exfoliation syndrome are present, they almost invariably co-exist in the same eye. It is extremely rare to find them in opposite eyes. Both conditions are thought to have components of oxidative damage. Normally there is a very high concentration of ascorbic acid in the aqueous humor, which serves as an important anti-oxidant for the eye. In exfoliation syndrome the amount of ascorbic acid is significantly decreased and other markers of oxidative damage are increased.

Are diabetics at greater risk for glaucoma?

Diabetics with retinopathy are prone to developing neovascular glaucoma. Aside from this, there has been many years of controversy as to whether primary open-angle glaucoma is associated with diabetes. This has not been substantiated. In the ocular hypertension treatment study, it was initially thought that diabetes protected against the development of glaucoma but this was later found to be a result of patient selection. At the present time, it does not appear that there is any direct correlation.

Do some glaucoma medications cause hair loss?

Yes, beta blockers have been associated with hair loss for a long time. This applies both to selective beta blockers such as Betaxolol and all of the non selective beta blockers used in treating glaucoma. Discontinuation of the drug leads to regrowth of hair.

Glaucoma Surgery – Beyond Trabeculectomy

When medications, usually the first course of treatment for glaucoma, no longer adequately lower IOP, laser surgery is often recommended (e.g. laser trabeculoplasty). Should glaucoma continue to progress, the step usually taken involves conventional surgery called trabeculectomy.

Trabeculectomy, or filtering surgery, has been the standard for a long time. It is a procedure whereby the doctor makes a tiny hole in the eye. The surgery creates a bleb (blister) whereby aqueous fluid can seep out, thereby reducing pressure. This can be very effective, but patients must be followed regularly because the presence of the filtering bleb makes the eye susceptible to infection.

Should the trabeculectomy fail, a drainage implant (i.e. tube shunt implant) can be placed in the eye. These devices consist of a small silicone tube that extends into the anterior chamber of the eye. The tube is connected to one or more plates, which are sutured to the surface of the eye, usually not visible. Fluid is collected on the plate and then absorbed by the tissues in the eye. This type of surgery is thought to lower IOP less than trabeculectomy, but is preferred in patients whose IOP cannot be controlled with traditional surgery or who have previous scarring.

Newer nonpenetrating glaucoma surgery, which does not enter the anterior chamber of the eye, shows great promise in minimizing postoperative complications and lowering the risk for infection. However, such surgery often requires greater surgical acumen and generally does not lower IOP as much as trabeculectomy. Furthermore, long-term studies are needed to assess these procedures.

There are several new and promising surgical alternatives. The ExPRESS mini glaucoma shunt, released in 2002, is a stainless steel device that is

inserted into the anterior chamber of the eye and placed under a scleral flap. It lowers IOP by diverting aqueous humor from the anterior chamber. The ExPress offers the glaucoma surgeon an alternative to either performing repeat trabeculectomy or placing a tube shunt implant.

Another of the new less invasive treatments, the Trabectome, was approved by the FDA in 2004. It is a thin, probe-like device that is inserted into the anterior chamber through a tiny incision in the cornea. The procedure delivers thermal energy to the trabecular meshwork, reducing resistance to outflow of aqueous humor and, as a result, lowering IOP. Eye pressures with the Trabectome are not lowered as much as with traditional trabeculectomy.

Canaloplasty, a recent advancement in non-penetrating surgery, is designed to improve the aqueous circulation through the trabecular outflow process, thereby reducing IOP. Unlike traditional trabeculectomy, which creates a small hole in the eye to allow fluid to drain out, canaloplasty has been compared to an ocular version of angioplasty, in which the physician uses an extremely fine catheter to clear the drainage canal, enhancing outflow facility without creating an artificial bleb.

A type of new implant called the suprachoroidal drainage shunt is designed to lower IOP by draining aqueous fluid from the anterior chamber to the suprachoroidal space. One that is commercially available is called the Gold Shunt. Another prototype is currently being tested. These implants are very thin and are placed through a single micro-incision in the sclera. Data is not yet available on the long-term efficacy and risk of complications of some of these newer procedures.

The Lifestyle Connection

The Importance of Passion
By Catherine Duffek

It is 6:00 a.m. Wisps of my brown hair are plastered to my forehead as I madly pedal. I am gerbil-like on the elliptical at my fitness club. To pass the time, I plan the program for the next meeting of the New England Chapter of the Glaucoma Foundation (TGF). Thanks to Gregory K. Harmon, M.D. and Scott Christensen, I have found my passion. Greg is my ophthalmologist, as well as Chairman of the Board of The Glaucoma Foundation. He treats me for congenital glaucoma. Scott is the President of TGF.

It is now three years since they enticed me to volunteer and found the New England Chapter of TGF. I am continuously thrilled and honored by this opportunity.

Congenital glaucoma, as its name implies, is a life-long eye condition. Unlike other forms of glaucoma, it manifests itself in infants and small children, generally within their first or second year of life. No one definitively knows how or why it develops.

Unlike the adult onset glaucomas which are asymptomatic, congenital glaucoma expresses specific symptoms, including red eye, excessive tearing without discharge, sensitivity to light, and eye pain.

Pediatricians and general practitioners, now as in the 1940's when I was born, often view glaucoma as an eye condition of adulthood. When they see children with these symptoms, they often dismiss them as routine childhood ailments. As in my case, the condition can remain undiagnosed until irreversible optic nerve and corneal damage permanently destroy vision.

In my case, the lapse in treatment caused me to lose enough vision to become legally blind. Specifically, this means that I am able to see only objects at 20 feet, while the average person can see those same objects from 200 feet.

Early in life, I lost all the vision in the right eye



Catherine Duffek while traveling in Italy.

after high intraocular pressure and complications stretched the eyeball, causing the retina to detach.

In my left eye, the long durations of elevated intraocular pressure led to corneal damage, for which I received a successful corneal transplant. However, the left eyeball was also stretched, causing retinal complications, including a macular hole which is inoperable.

Though my vision forces me to straddle two worlds, that of the seeing and that of the blind, it has not deterred me from living an active, "normal" and fulfilling life.

I work full time, run the New England Chapter of TGF, and work as a part-time freelance medical writer. For relaxation, I cook and knit, and my husband and I enjoy traveling. We have a special affection for Italy, its art, architecture and food.

Today, there is sophisticated medical technology and a vast array of therapeutic drugs to treat intraocular pressure, the primary symptom of glaucoma. However, how glaucoma behaves is still a mystery. Because of this, glaucoma specialists are still a long way from preventing or curing this potentially ravishing eye condition.

My goals for the New England Chapter of TGF are to help others diagnosed with glaucoma learn about available treatments, advances in research, issues with medications and, most of all, realize that they are not alone in their struggles with this serious eye condition.

If you would like to get involved with a glaucoma support and education chapter near you, please contact Kira Zmuda at (212) 285-0080.

Research Grants - Spring 2009

TGF has approved the funding of the following four new research projects.

Erin B. Lavik, SB, SM, ScD

Associate Professor, Biomedical Engineering
Case Western Reserve University, Cleveland, Ohio

A Minimally Invasive Drug Delivery Approach to Modify the ECM and Promote Neural Regeneration in a Model of Glaucoma

Neural degeneration in glaucoma arises from the loss of retinal ganglion cells (RGCs) and is accompanied by extensive remodeling of the extracellular matrix (the external environment of the optic nerve cells) that inhibits repair. This project proposes to make the environment permissive for repair by delivering a drug, AG1478, that has been shown to alter this environment and promote optic nerve regeneration. The drug will be delivered from injectable microspheres. The project hypothesizes that the combination of neural progenitor cells to replace lost RGCs cells with sustained delivery of AG1478 will promote regeneration.

Shannath Merbs, MD, PhD

Associate Professor, Department of Ophthalmology
Johns Hopkins University, Baltimore, MD

DNA Methylation Changes Associated with Ganglion Cell Injury

Alterations in the expression of genes can lead to disease. One way to alter gene expression without changing the DNA sequence of a gene, is to chemically modify the DNA by methylation. Abnormal DNA methylation leads to some cancers, and it is possible that methylation changes could also contribute to the development of non-neoplastic diseases like glaucoma. This project will look for DNA methylation changes associated with RGC death. Drugs to manipulate DNA methylation have been used in the treatment of cancer and might someday prove useful for the treatment of glaucoma.

Xiuqian Mu, MD, PhD

Assistant Professor, Department of Ophthalmology
State University at Buffalo, NY

Math5 Target Genes in Retinal Ganglion Cell Formation

This proposal focuses on the function of a transcription factor named Math5 in RGC formation. Transcription factors are proteins that regulate the activities of other genes. Genetic studies have shown that Math5 is required for RGC formation, but how it functions is not known, in that we do not know what genes are turned on and off by Math5. The objective of this proposal is to identify these genes. The project will utilize a recently developed technology, ChIP-seq, which uses specific antibody and ultrahigh-throughput DNA sequencing to identify the genes Math5 controls. This information will help future efforts to generate RGCs in cell culture for cell replacement therapy for glaucoma.

David W. Sretavan, MD, PhD

Professor of Ophthalmology
University of California San Francisco

Micro & Nanotechnology-Based Bioplatforms for High-Throughput Analysis of Axon-Glial Interactions in Glaucomatous Neuropathy

Improved management of glaucoma requires better understanding of disease mechanisms that damage the axons of RGC cells at the optic nerve head. This work is aimed at developing a new type of highly versatile microplatform that incorporates advances in micro and nanotechnology to provide researchers with unprecedented control over key experimental parameters. This renewal grant proposes to use this bioplatfom to conduct high-throughput experimentation on RGC axons to investigate whether axon biology and survival may be affected by the presence of Eph/ephrin signaling molecules. This cellular signaling system was recently demonstrated to be closely linked to onset of RGC axon damage in disease.

2009 Think Tank *continued from page 1*

LOXL1 gene helps build the network of fibers and elastin that weaves the body's tissues together. The effect of the genetic variants, which appear in 100 percent of XFS cases, seems to be to lower the production rate of the protein it specifies. This protein appears to play a role in the accumulation of microfibrillar deposits that causes XFS.



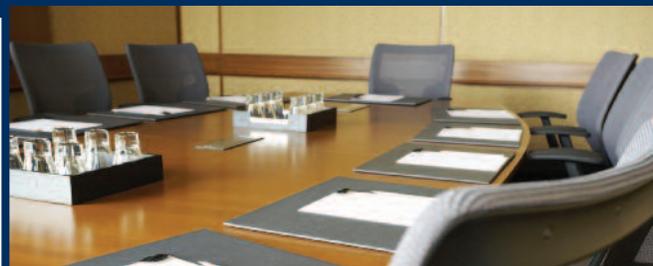
Left to right: Gregory K. Harmon, MD; Paul L. Kaufman, MD; Robert Ritch, MD; Scott R. Christensen.

Both genetic as well as external factors are required for XFS processes to occur. Scientists are now learning about the molecular processes that lead to the production and accumulation of the exfoliation material. They are investigating what triggers the cell types producing these materials to enter a highly active fibrotic pathway.

Several ocular stress conditions – oxidative stress, impaired blood flow to the eye, and low-grade inflammation – have been identified. The cells in the eye fail to respond appropriately because they have impaired stress defense mechanisms. By interfering with this stress response, scientists hope to develop new therapeutic strategies to treat patients with exfoliation syndrome earlier and before damage to the optic nerve has occurred.

“We seem poised to make rapid strides,” said Dr. Ritch after the Think Tank. “Exfoliation syndrome has the potential to become a preventable and curable disease.”

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New Scientific Advisory Board Member

Uday B. Kompella, PhD

Dr. Uday B. Kompella is a professor in the department of Pharmaceutical Sciences at the University of Colorado Denver. Before joining the University of Colorado, he served on the faculty at the University of Nebraska Medical Center.

The recipient of numerous awards, Dr. Kompella was recognized with a “Distinguished Scientist” award from the University of Nebraska Medical Center in 2006. He has authored or co-authored 100 scientific papers and book chapters and co-edited two books. He is the current editor of *Pharmaceutical Research* and sits on the editorial boards of five other journals. He previously served as an editor for the journal *Clinical Research and Regulatory Affairs*.

Dr. Kompella’s key areas of research are nanotechnology for drug delivery, gene delivery and imaging; supercritical fluid technology for delivery systems; anti-angiogenic and anti-inflammatory therapeutics for diabetic retinopathy, age related macular degeneration, corneal angiogenesis and lung cancer.

Dr. Kompella received his B. Pharm from BITS, Pilani, India, his M. Pharm from Jadavpur University, Kolkata, India, and PhD (Pharmaceutical Sciences) from the University of Southern California, Los Angeles.

Your Support is Critical

Your donations are vital for The Glaucoma Foundation to fund promising and innovative research projects that can lead to federal government funding and bring us closer to finding new treatments and eventually a cure for glaucoma.

Our grant recipients continue to underscore the importance of private funding to their efforts. One TGF-funded researcher from California stressed that the public needs to understand the important role of private foundations in the current NIH climate. "The NIH is unable to meet the funding demand requirements, so we have to make up the difference," he wrote.

Another reported that our seed grant allowed his research team at the University of Michigan Medical School to develop what was a reasonable hypothesis, but for which substantiating data were lacking. TGF funding allowed him to develop critical proof that contributed directly to significant NIH funding.

The message is clear. The generosity of longtime and new friends is more important than ever if we are to fund the types of novel projects that TGF has historically encouraged. We urge your renewed support.

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CHAPTER CORNER

New England Chapter

The New England Chapter of TGF held a support group meeting in September. At this meeting patients shared their experiences about having glaucoma.

By popular request, Christine Finn, Pharma D, Chief Pharmacist at the Massachusetts Eye and Ear Infirmary, again honored the New England Chapter support group on November 21 with a talk about "Glaucoma Medications and Other Resources."

On Saturday, January 30, Allen Taylor, PhD, Director of the Laboratory for Nutrition and Vision at Tufts University School of Medicine, will share research findings on eye health and nutrition. This presentation will be held at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, MA.

Chapter meetings are free. Anyone interested in learning more about glaucoma is welcome to participate. **Dates and speaker information will be available on The Glaucoma Foundation website or by emailing cduffek@glaucomafoundation.org.**

New York City Chapter

The Glaucoma Support and Education Group meets on the 3rd Saturday of each month from September through June, except for December. In November, nutritionist Dolores Perri discusses the latest thinking on nutrition as it relates to the glaucoma patient. In January, there will be a lecture by Chris Teng, MD, on blood flow and glaucoma.

Group members who attend these meetings often request special workshops. In April such a request will be met by Dr. Mindy Levine, who will conduct a group session on psychological insights of living with glaucoma, a factor that governs many of those in various stages of glaucoma.

An outstanding feature of the Group's activities is the publication of "Living with Glaucoma," a quarterly newsletter, which

reprises the lectures. The newsletter enables those unable to attend the lectures to participate vicariously in the activities of this vital group. Persons who wish to receive all publications and notices online are also accommodated. **If you would like to be involved with the NYC Chapter please email kzmuda@glaucomafoundation.org.**

Chicago Chapter

The fourth meeting of the chapter's Madison, Wisconsin Glaucoma Support and Education Group met in October for an open forum featuring guest speaker, Dr. J. Agapov, on the subject of visual fields. November marks the launching of another glaucoma group in the Glenview, Illinois area. Additional support groups are planned for Evanston and Chicago. On the drawing board is a project to work with the Hispanic community in the Chicago area, with the goal of launching a small group. **If you would like to be involved with the Chicago Chapter please email kzmuda@glaucomafoundation.org.**

Long Island (NY) Chapter

The chapter has been devoting all its efforts planning a major November event – a free morning of lectures, discussions and a Q&A session. "All About Glaucoma" was organized by chapter president Diana Falk with ophthalmologists Craig H. Marcus, MD and Janet B. Serle, MD. They joined with physicians Ronald Caronia, MD, Lawrence F. Jindra, MD, Arnold Prywes, MD and Demetrios Halikiopoulos, DO, giving presentations on such subjects as target intraocular pressure, the optic nerve, laser and filtration surgery, and medications and side effects. All participated in the Q&A session. **If you would like to be involved with the Long Island Chapter please email kzmuda@glaucomafoundation.org.**



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Lunch and Learn in Los Angeles

TGF's Lunch and Learn Program is a new way for the Foundation to work with organizations or business groups by providing an expert guest to educate members about glaucoma.

On October 2, TGF Board Member Dr. Maurice Luntz made a presentation to members of the "Pre-Health Society" at the Los Angeles Trade-Technical College (LATTC).

The society was formed to help students become more educated and familiarized with various healthcare professions and careers. Its members are primarily students who plan to pursue careers in health and eventually become healthcare providers.

The event was spearheaded by the society's president, Sara Heikali, who plans to attend optometry school. "I

made it my goal to learn more about the four main ocular ailments," she says, "and began my search by looking online and reading information on the TGF's site. As I learned more, I came across the L&L program, and thought it would be a great idea to plan an event to educate students and faculty. Because anyone at any age can get glaucoma, it made the most sense to have a lecture on glaucoma for students and faculty," she says.

"Dr. Luntz was a very inspirational speaker," she reports. "Most of the students had no idea what glaucoma was until they heard the lecture; the feedback was very positive. Thank you on behalf of our group for helping us organize all the material for this event."



*Funding for this newsletter generously provided by **DORRIS M. MENDELSON***

A copy of The Glaucoma Foundation's annual financial report may be obtained upon request by writing to The Foundation at 80 Maiden Lane, Suite 700, New York, NY 10038 or by residents of the states listed below from the appropriate state agency. Florida: A copy of the official registration and financial information may be obtained from the Division of Consumer Services by calling toll-free within the State. Registration Number - CH7263. Registration does not imply endorsement, approval, or recommendation by the State. Maryland: Information filed under the Maryland Charitable Organizations Laws can be obtained for the cost of postage and copies from the Office of the Maryland Secretary of State, Statehouse, Annapolis, MD 21401 or by calling 410-974-5534. Mississippi: Mississippi Secretary of State's Office, Charities registration, PO Box 136, Jackson, MS 39205-0136, 601-359-1633. New Jersey: Information filed with the Attorney General concerning this charitable solicitation may be obtained from the Attorney General of the State of New Jersey by calling 201-504-6215. Registration with the Attorney General does not imply endorsement. New York: A copy of the last annual report filed may be obtained upon request in writing to the Office of the Attorney General, Department of Law, Charities Bureau, 120 Broadway, New York, NY 10271. North Carolina: A copy of the license to solicit charitable contributions as a charitable organization or sponsor and financial information may be obtained from the Department of Human Resources, Solicitation Licensing Branch, by calling 919-733-4510. Registration does not imply endorsement, approval, or recommendation by the State. Pennsylvania: The official registration and financial information of The Glaucoma Foundation may be obtained from the Pennsylvania Department of State by calling toll free, within Pennsylvania, 1-800-732-0999. Registration does not imply endorsement. Virginia: Official registration and financial information of The Glaucoma Foundation may be obtained from the State Division of Consumer Affairs, Department of Agriculture & Consumer Services, P.O. Box 1163, Richmond, VA 23209. Washington: Registration and financial report information may be obtained from the Charities Division, Office of the Secretary of State of Washington, Olympia, WA 98504-0422 or by calling 1-800-332-4483. West Virginia: West Virginia residents may obtain a summary of the registration and financial documents from the Secretary of State, State Capitol, Charleston, WV 25305. Registration does not imply endorsement.