2016 Scientific Think Tank Scheduled for June

The 23rd Annual International Think Tank, this year returning to the subject of exfoliation syndrome (XFS), will take place on June 10-11 in New York City. Much has happened in XFS research since TGF made the condition its primary focus four years ago. TGF Founder and Think Tank organizer Dr. Robert Ritch estimates that the number of researchers active in the field has tripled in recent years.

R. Rand Allingham, MD, professor at Duke University Medical Center and a Think Tank participant, concurs. “These are exciting times for exfoliation syndrome research that should be of interest to a broad segment of the lay public,” says Allingham. “There is a dominant genetic player for XFS that revolves around the gene LOXL1. New information about this gene, and its regulation by the gene LOXL1-antisense, is receiving growing interest as an important clue in the pathogenesis of this disease.”

Another area of interest is the growing appreciation of the systemic nature of exfoliation. It has been known for decades that exfoliation material can be found in most tissues. There is now a growing appreciation for diseases that are directly associated with XFS, including atrial fibrillation, pelvic organ prolapse, hernia, central nervous system disease, chronic lung disease and others. Says Dr. Allingham, “The benefit of targeted treatment of XFS may extend well beyond those affecting the eye and vision, and may include mitigating tissue failure, cardiac malfunction and other common maladies affecting large segments of the population as we age.”
Dear Friends:

As I write this message, The Glaucoma Foundation is preparing for its 23rd Annual International Think Tank. Each year, we involve clinician-scientists, researchers in glaucoma, researchers in other areas of the eye and scientists totally uninvolved with the eye in order to cross-fertilize ideas and identify important areas for future research and funding.

On these pages you will read about last year’s Think Tank, which served as a forum for discussing what’s new in the rapidly evolving field of Regenerative Medicine for Cornea and Trabecular Meshwork.

The 2016 Think Tank will again take up the disorder called exfoliation syndrome, the focus of TGF’s efforts. Current and future research is the theme; finding a cure is the goal. It is most gratifying that the number of researchers working on exfoliation syndrome has tripled in recent years.

In related news, a prominent researcher in that field has just been selected as this year’s recipient of the Robert Ritch Award for Excellence and Innovation in Glaucoma. We are honoring Ursula Schlötzer-Schrehardt, PhD, Associate Professor and Senior Scientist in the Department of Ophthalmology at the University of Erlangen-Nürnberg. Dr. Schlötzer-Schrehardt has contributed greatly to the understanding of exfoliation syndrome and the growing body of knowledge about this disease.

I’m also delighted to welcome Dr. Louis Pasquale as the newest member of our Board of Directors. Professor of Ophthalmology at Harvard Medical School and Director of the Glaucoma Service at the Mass. Eye and Ear Infirmary in Boston, he serves on TGF’s Medical Advisory Board and Think Tank Organizing Committee and is an active Think Tank participant.

Our efforts simply could not be achieved without the support of so many individuals. We extend our heartfelt thanks to each and every one of you.

Sincerely,

Scott R. Christensen
President
Chief Executive Officer
High-Tech for Low Vision

Advances in consumer electronics are improving the quality of life for people with low vision. For many, mobile devices such as smart phones and tablets can provide lower-cost alternatives to high-priced specialty equipment and have features that make them powerful assistive devices.

**Smartphones and More**

Both Apple and Android-based smartphones and tablets offer a range of apps and built-in functions to help people with low vision:

On **iOS devices**, such as the iPhone, iPad, or iPod touch, numerous assistive features are on the apps that come with the devices and are easily accessible by going to Settings > General > Accessibility.

**VoiceOver** is a screen reader that speaks items on the screen and helps to navigate. If you have a hard time reading the text on your device, **Speak Screen** can read your email, iMessages, web pages, and books to you. **Siri**, Apple’s assistant, can send messages, place phone calls, and even turn on and off such features as **VoiceOver**, **Guided Access** and **Invert Colors**. And because **Siri** is integrated with **VoiceOver**, you can ask where the nearest sushi restaurant is and hear the answer read out loud. **Zoom** is a built-in magnifier that works wherever you are on your device. You can also convert your contacts, mail, messages, etc. to a larger size and choose bold text to make it heavier. If a higher contrast or a lack of color helps you better see what’s on the display, **iOS** lets you invert the colors or enable grayscale onscreen. **Dictation** lets you talk wherever you would type.

On an **Android phone**, in Settings > My Device > Accessibility or Settings > Accessibility, there are options to customize your phone, including large font, bold text, screen zoom, text to speech, Braille keyboard integration and more.

**E-Readers**

If a back-lit tablet screen is a strain on the eyes, an e-reader, such as a Kindle or Nook, might be a better reading option. These devices with E Ink screens do not emit light. Instead, like regular books and printed material, light is reflected off the surface.

The Kindle Paperwhite and Nook GlowLight don’t require an outside light source to read them and allow users to easily change font size and read outdoors without the glare one would normally experience with a tablet. While they do not have text to speech capability, if you already own an iPad or Android tablet there are free apps you can download from the App Store or Google Play which support the voice over accessibility feature.

**Low-Tech Reading Tips**

In addition to special lighting equipment available from numerous manufacturers, a gooseneck lamp with at least a 60 watt light bulb directed over a page or directed onto a task can be helpful for reading and close-up work. LED pocket lights or a flashlight app on a smartphone will help reading menus in restaurants and more.

**Resources**

- For detailed articles on how to use the assistive capabilities of the devices discussed here, and a searchable database of assistive technology products, American Foundation for the Blind has comprehensive information online at [afb.org/info/living-with-vision-loss/using-technology/12](http://afb.org/info/living-with-vision-loss/using-technology/12)

- Prevent Blindness provides a comprehensive list of resources for people with low vision, including 1600 links and contacts to US agencies, centers, organizations and societies (by state), assistive technology products, services and much more. Go to [Lowvision.preventblindness.org](http://Lowvision.preventblindness.org)
22nd Annual
Glaucoma Foundation
Think Tank

Regenerative Medicine for Cornea and Trabecular Meshwork

Think Tank participant Ursula Schlötzer-Schrehardt, PhD, giving a presentation.

Forty-seven glaucoma and cornea investigators and clinicians, biologists, stem cell researchers, geneticists and bioengineers convened in New York City last September to participate in TGF’s 22nd Annual Think Tank. In attendance at the 2015 gathering were scientists from throughout the US, as well as from Belgium, Canada, England, Germany, Ireland, Japan, and Singapore.

The presentations focused on tissue regeneration in the eye, with researchers reporting on cutting edge topics that ranged from the status of stem cell-based therapies and the possibilities for bioengineering corneal and trabecular meshwork (TM) tissue to the potential for biological uses of 3-dimensional printing.

Dr. Robert Ritch, Founder and Medical Director of The Glaucoma Foundation and Think Tank organizer since its inception, greeted participants at the opening session. "Our goal is to foster new relationships that will lead to continued communication across disciplines and between laboratories - long after the meeting has ended," said Dr. Ritch. "Moving forward with the creative and novel ideas that originate in these discussions can help us unlock the mysteries of glaucoma and restore vision lost from optic nerve damage."

The program was unique in bringing corneal and trabecular meshwork regenerative research together, looking at advances in both. While there has been significant progress in the area of corneal regeneration, stem cell-based therapy to regenerate the trabecular meshwork and reduce IOP is a newer direction for glaucoma.

A large body of evidence links the cornea with various aspects of intraocular pressure and glaucoma. Among relevant attributes are corneal thickness, elasticity, viscosity and hysteresis, which is associated with risk of progression of visual field loss. Presenters reported on the status of current investigations into using patients’ own stem cells to regenerate damaged corneal tissue,
which may lead to corneal repair replacing corneal transplants.

One of the presenters, Ursula Schlötzer-Schrehardt, PhD, from the University of Erlangen-Nürnberg in Germany, discussed limbal stem cell (also called corneal epithelial stem cell) transplantation for corneal surface regeneration. Long-term success is still not satisfactory, she reported, which may be caused by a gradual loss of stem cells during cultivation and transplantation. She provided an overview of the present understanding of the molecular anatomy of the limbal stem cell niche as well as current tissue-engineering approaches for corneal surface regeneration.

The stem cell-based challenges are still greater where trabecular meshwork is concerned. Elevated intraocular pressure (IOP) is the main risk factor for primary open-angle glaucoma and the only proven modifiable risk factor for glaucoma. Blockage of aqueous humor outflow through the trabecular meshwork and its inner lining – the juxtacanalicular meshwork and Schlemm’s canal endothelial cell layer – lead to elevated IOP. The goal continues to be to lower the pressure.

Studies have been underway to see whether replacement of damaged or lost trabecular meshwork cells with healthy stem cell derived TM-like cells can induce functional restoration and lower IOP following transplantation into glaucoma eyes. Mary Kelley, PhD, of the Casey Eye Institute, Oregon Health & Science University, reported on her laboratory’s work in this area. Using a model for cell loss in the TM, a notable feature associated with glaucoma, she found compelling experimental evidence that this cell loss compromises the regulation of IOP in the human eye. Upon transplantation of stem cells differentiating to a trabecular meshwork-like cell, they were able to fully restore this function, providing a potential novel alternative treatment option for open-angle glaucoma.

The Think Tank discussion considered a different route as well – the feasibility of employing nanotechnology and bioengineering to recreate an implantable trabecular meshwork for restoring biological function lost from disease and injury.

The 2015 Think Tank, like earlier meetings, aimed at stimulating new collaborative research efforts. Said participant Yutao Liu, MD, PhD, associate professor of cellular biology and anatomy at Georgia Regents University in Atlanta: “It was a great success, especially in bringing corneal and trabecular network regenerative research together. The format of short presentations followed by long integrative discussion provided plenty of insightful comments and promoted more interaction between clinical and basic researchers.”

That interaction has promoted new collaborations among the laboratories of Think Tank presenters, including a developing collaboration on human genetics and cornea molecular biology between Dr. Liu and Dr. Winston Kao at the University of Cincinnati.
Doctor, I Have a Question

QUESTION ANSWERED BY:
Philip P. Chen, MD
Professor and Grace E. Hill Chair, Department of Ophthalmology,
University of Washington
Chief of Ophthalmology, UW Medicine Eye Institute

Is blood pressure related to glaucoma?

It turns out this question is a little tricky. The first thing that patients should know is that eye pressure is not correlated with blood pressure, and that is in fact what many patients are wondering about. However, blood pressure can play a role in other aspects of glaucoma, mainly because it is important in the amount of blood flow that gets to the optic nerve. The optic nerve is like the cable carrying information from the eye to the brain, and is an important part of the eye that actually gets damaged in any kind of glaucoma. Several studies have actually shown that low blood pressure, in particular low diastolic blood pressure (the bottom number of a blood pressure reading), is a risk factor for the development of glaucoma. One way to quantify this is to calculate the blood flow to the eye (called the ocular perfusion pressure). This calculation involves taking into account both the systolic and diastolic blood pressure, and the eye pressure (intraocular pressure). You can think of the ocular perfusion pressure as the amount of blood that the heart can pump to the eye, with the intraocular pressure pushing against that blood flow and making it harder for blood to reach the eye. So having blood pressure that is very low can make it more likely that someone might get glaucoma, especially if that person also has eye pressure that is high.

In recent years, worsening of glaucoma has also been related to low blood pressure and ocular perfusion pressure. Often a person’s blood pressure will run very low at night during sleep, and this causes a problem because the ocular perfusion pressure can go very low. We think that this causes the optic nerve to become more damaged.

If low blood pressure is possibly dangerous for patients for glaucoma, should you ignore your family doctor, internist, or cardiologist when they tell you that you must control your hypertension (high blood pressure)? No. You cannot ignore high blood pressure, because it is known to cause major health problems such as heart attacks and strokes. So you must continue to monitor your blood pressure, and take any blood pressure medication that you have been prescribed. However, if you are on blood pressure medication and you feel lightheaded or dizzy when you stand up, you might discuss your situation with the doctor who prescribed that medication, to make sure you are not being overmedicated for hypertension. Avoid taking hypertension medication right at bedtime, since it might make your blood pressure run too low overnight.

Also, if you are taking any beta-blocker eyedrops for your glaucoma (including drops such as timolol, Timoptic, Betagan, Betimol, betaxolol, Betoptic, Combigan, Cosopt, Dorzolamide-Timolol, or levobunolol), you should know that these drops can lower your blood pressure and perhaps should be used in the late afternoon or around dinnertime rather than at bedtime. You can discuss this with your ophthalmologist.

We don’t understand enough about how blood pressure works in the eye to recommend trying to raise your blood pressure, nor do doctors have any experience trying to do that for glaucoma patients. So don’t try to raise your blood pressure. Just work on using your drops and hypertension medications correctly, and with an eye towards preventing the blood pressure from dropping too low, especially overnight.
Five Key Questions to Ask Your Doctor

If you've recently been diagnosed with glaucoma, communicating with your eye doctor is essential to successfully treating the disease. Here are some tips that will help you work in partnership with your doctor to preserve your vision.

1. If you are a new glaucoma patient, ask what type of glaucoma you have. There are many forms of glaucoma.

2. If medications are prescribed, make sure you understand why you need to take the medication, what the medication will do for you, how often and when you need to take the medication.

3. Ask your doctor or your doctor's assistant to show you how to take your eye drops properly, and what to do if you miss a dose.

4. Ask about the risks and side effects associated with the recommended treatment, and if there are any foods, drugs or activities you should avoid. Report any side effects or allergic reactions to your doctor promptly.

5. Ask the names and purposes of tests you may undergo. Ask if there are any changes since your last exam and ask to see test results, for example the print-out of your visual fields - with an explanation of what those black spots mean.

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LIVING WITH GLAUCOMA
A Thirst for Life... An Appeal for Research Funding

“I try to focus on what I have and remind myself I’m healthy in other ways. I try to be prepared for what would happen if I go completely blind. And I try to stay on top of the latest information.”

David works in sales for an IT company and spends his days in front of a computer screen working from home. “I have limits on how long I can work without a break. But I find ways to cope. Technology can help people like me. Things are progressing so quickly.

“Glaucoma is constantly on my mind. It absolutely affects the quality of your life. No, it’s not life-threatening, but it is life-altering. It’s a constant battle. My goal is to maintain what I have.

“There are so many diseases out there that need funding for research,” says David. “Glaucoma is an important one. It’s a disease that can go undetected — that’s why we need more early diagnoses and better diagnoses. TGF needs money for research because we have to help people maintain their sight and maybe someday bring back sight to people who have lost it. The holy grail is the cure.”

David Rosenblatt of Nashville, Tennessee, age 38, was diagnosed with elevated IOP at the age of 13 and has been on a varying regimen of eye drops ever since.

When he was 27, he had the first of six major eye glaucoma surgeries. In February, 2015, the residual wear and tear from the glaucoma surgeries contributed to cornea failure in his left eye. Three months later they removed his cornea and iris and implanted a donated cornea.

“Losing my cornea was a real scare. I have a thirst for life. Getting a new cornea renewed that thirst,” says David, who thanks the doctors, nurses, and staff at Vanderbilt University Eye Clinic. The transplant was successful; a contact lens now gives him 20/40 vision in that eye.
Recent Research Grants

Audrey Bernstein, PhD
Icahn School of Medicine at Mount Sinai, NY

Impaired Lysosomal and Mitochondrial Function in Exfoliation Syndrome

In exfoliation syndrome (XFS), frontal interior parts of the eye start accumulating white fluff deposits composed of protein aggregates. The aggregates eventually float away with the fluid flow and block the fluid exit, causing glaucoma. We have discovered that cells obtained from these eyes may have a problem degrading these protein aggregates inside the cell leading to a buildup of “cellular trash” that becomes toxic to the cells. In this proposal we will test methods to improve the degradation of this cellular waste to improve the health of the XFS cells.

Simon W. John, PhD
The Jackson Laboratory, Bar Harbor, Maine

Determining the Genetic Basis of Exfoliation Syndrome in a Large Pedigree Using Next-Generation Sequencing

Determining the genetic basis of exfoliation syndrome in the general population has proven challenging similar to other complex, age-related diseases. This study aims to determine the genetic basis of exfoliation syndrome in a large family with a strong pattern of inheritance. Affected family members’ genomes likely contain a causal or high risk disease variant(s). Genetic signatures will be obtained by sequencing the DNA of affected and unaffected individuals. Knowledge of how exfoliation syndrome is inherited can help with diagnoses and may provide novel approaches to treatment.

Chien Chuen KHOR, PhD
Genome Institute of Singapore

Unlocking the Hereditable Basis of Exfoliation Syndrome

Until today, investigators were unable to localize the specific genetic variants responsible for XFS due to limited patient collections. We are now in a strong position to address this after building an international XFS genetic consortium across six continents. This study is part of this global effort to fully understand the hereditable basis of XFS by performing systematic genome-scans on multi-ethnic XFS patient collections. We anticipate this global effort to be able to definitively identify and implicate a robust network of XFS genes which will provide dramatic insights into the disease process of XFS and inform drug discovery.

W. Daniel Stamer, PhD
Duke University Medical Center, Durham, North Carolina

Mechanisms in Exfoliation Glaucoma: Effect of Genetic Risk Variants and Ocular Cell Stressors on LOXL1 Expression

It is known that genetic variants in the gene LOXL1 increase risk for developing a particularly severe form of glaucoma called exfoliation glaucoma. In addition, environmental factors such as UV exposure can influence disease risk in genetically susceptible individuals. However, the precise mechanism for how these factors contribute to disease development is poorly understood. We are working to better understand how an individual’s genetic makeup and environment interact to cause exfoliation glaucoma. With this new knowledge, it will be possible to develop novel therapies to treat and possibly even cure this blinding disease.

Deborah Wallace, BSc, PhD
University College, Dublin, Ireland

To Investigate the Role of Methylation in the Regulation of Lysyl Oxidase-Like 1 Expression in Pseudoexfoliation Glaucoma

Genetic studies have identified a gene called lysyl oxidase-like 1 (LOXL1) which is thought to be important for an individual’s predisposition to developing pseudoexfoliation syndrome. Other studies have shown that levels of LOXL1 can vary between normal and disease patients and also in disease progression. This study addresses the question of how levels of LOXL1 are altered as glaucoma develops and progresses. We will investigate the role of epigenetics in controlling LOXL1 expression.

Aparna Rao, MD, FRCS
LV Prasad Eye Institute, Bhubaneswar, India

Tear Cytokine and MMP Assay in Different Stages of Pseudoexfoliation Syndrome

Diagnosis of this disease still depends on clinical examination of the unique deposits in the anterior segment. There is no current system for identifying it in the earliest stage before the onset of glaucoma. We have recently characterized the clinical features that may be seen in the earlier and later stages of the disease process. Tear evaluation for markers is known to predict severity of a disease or even presence of a particular condition in the eye. Study of tears would therefore be a useful noninvasive and easy tool for identifying the earlier stages of the disease as well as predicting progression.