THE GLAUCOMA FOUNDATION
NEWSLETTER
WINTER 2013

New Focus on Exfoliation Syndrome

The Glaucoma Foundation's Annual International Scientific Think Tank provides a unique opportunity for scientists and clinicians to apply their research and progress to the challenges of glaucoma. For almost twenty years this thought-provoking sharing of ideas has significantly moved the field forward.

Beginning this year, the interdisciplinary Think Tank sharpened its focus on exfoliation syndrome (XFS), an age-related systemic disease characterized by the production and accumulation of a whitish material in many ocular as well as non-ocular tissues. Worldwide, XFS is the most common identifiable cause of open-angle glaucoma, comprising the majority of glaucoma in some countries.

In September, more than 40 experts from the United States, Canada, Ireland, Germany, Japan and Switzerland, representing the vanguard of exploration by medical science into exfoliation syndrome, participated in an intensive two-day meeting, Exfoliation Syndrome: Gearing Up for a Cure, where they shared their knowledge and worked to develop research strategies and goals for the effort ahead.

The precise pathogenesis of XFS remains unknown. But, says Dr. Robert Ritch, TGF's Medical Director and Think Tank organizer, "we feel that the time is ripe and the technology available to begin to consider reversing the formation of exfoliation material, ameliorating the clinical manifestations, and eventually achieving a cure."

Exfoliation syndrome is not a "form" or "type" of glaucoma, but an ocular manifestation of a systemic disease.

Think Tank participants Dr. Masahito Horiguchi and Dr. Branka Dabovic

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

The discovery in 2007 of two distinct mutations, known as single nucleotide polymorphisms (SNPs), in the LOXL1 (lysyl oxidase-like 1) gene was consistent with the systemic nature of this condition. While the etiology of the disease is not yet understood, it appears to depend on risk genetic factors around the LOXL1 gene. LOXL1 is a member of a family of enzymes involved in the synthesis and maintenance of elastic tissues. But these gene defects, while strongly associated with XFS, do not in themselves cause exfoliation syndrome.

(Continued on page 6)

LETTER FROM THE PRESIDENT

Dear Friends:

Since 1984 The Glaucoma Foundation (TGF) has invested some five million dollars in cutting-edge research to find a cure for glaucoma. Now we have sharpened our focus on exfoliation syndrome, the leading identifiable cause of open-angle glaucoma worldwide. We believe a cure for exfoliation syndrome is within reach in the near future.

On these pages you will read about our most recent International Think Tank, which explored the topic "Exfoliation Syndrome: Gearing Up for a Cure" and was pivotal in developing research strategies and goals for the effort ahead. You will also read about our 2012 Black and White Ball benefit, The Foundation's primary fundraising event, which raises vital funds to carry out our programs.

The initiative to find a cure for exfoliation syndrome is the most ambitious project in the Foundation's history. Your continued support is essential to the progress of this major undertaking.

As I write this letter, organizations around the globe are gearing up for educational events, screenings and other observances scheduled to mark World Glaucoma Week in March. The theme for 2013 is "The world is a wonder to see every day – so don't let glaucoma get in the way."

That is a good reminder for all – early detection and ongoing treatment are key to preserving sight. Glaucoma communities can play an important role in helping glaucoma patients understand their disease and learn how to manage it over their lifetime. The Glaucoma Foundation's three free online support groups for young patients, caregivers of young children with glaucoma, and adult patients provide information and mutual support to nearly 1000 members.

These are exciting times for The Glaucoma Foundation. We are most grateful for your support and we value the role that our long-time friends play in all that we do.

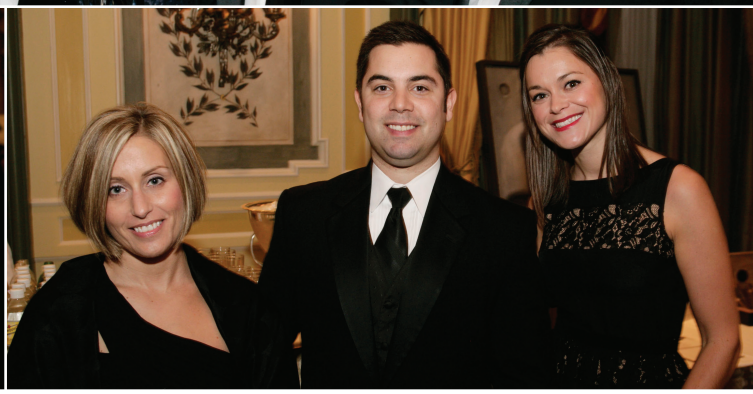
Sincerely,

Scott R. Christensen
President
Chief Executive Officer

Black and White Ball – A Bash

In the elegant setting of New York's Pierre Hotel, friends of The Glaucoma Foundation gathered on December 5th for TGF's 26th Black and White Ball, the Foundation's primary annual fundraising event. The showcase gala benefiting the important work of The Foundation raised $400,000. During the festivities, The Foundation saluted two individuals for their life accomplishments.

Producer, songwriter, music supervisor, and vocal artist **Steve Tyrell** received the *2012 Kitty Carlisle Hart Award of Merit for Lifetime Achievement.* Presented personally by Ms. Hart until 2006, the Award was presented in her memory by Ms. Hart's daughter, New York physician **Dr. Catherine Hart,** and son **Christopher Hart. Dr. George L. Spaeth,** a renowned figure in the ophthalmic community, was honored with the *Fifth Annual Robert Ritch Award for Excellence and Innovation in Glaucoma.*



THE GLAUCOMA FOUNDATION
BLACK & WHITE BALL

FACT OR FICTION

Myths About Glaucoma

Untreated, glaucoma can lead to blindness. So it's terribly important for patients to be well-informed. Sifting fact from fiction, here are some common, and not so common, misconceptions about the disease.

I have 20/20 vision, so I couldn't have glaucoma.

Individuals with perfect vision could still have or develop glaucoma since the disease usually affects peripheral vision first and central vision last. Although nearsighted people are at greater risk for the disease, it's also true that farsighted people are more likely to develop narrow angles and ultimately, primary angle-closure glaucoma.

You can't have high eye pressure if you don't have high blood pressure.

Blood pressure and eye pressure are independent of one another. Controlling blood pressure does not mean elevated intraocular pressure (IOP) is controlled. While high blood pressure can be associated with elevated IOP, low blood pressure is strongly associated with some types of glaucoma, for example normal-tension glaucoma, a type of glaucoma that occurs even though the pressure inside the eye is not elevated. Patients with any progressive glaucoma need to make sure their blood pressure is not dropping to very low levels while they sleep.

You can test your own peripheral vision to see if you have glaucoma.

Many people think they can test their peripheral vision by closing one eye and trying to look at side objects. But it is impossible to evaluate the state of your vision without a true visual field test conducted in your doctor's office. Loss of peripheral vision can often go undetected until significant damage has occurred. A complete examination for diagnosing glaucoma includes measuring the (IOP), testing the peripheral vision, looking at the optic nerve head, examining the angle in the eye where the iris meets the cornea, and measuring the thickness of the cornea.

Glaucoma is always inherited.

Some forms of glaucoma are inherited, and researchers are actively investigating the genes responsible. But absence of glaucoma in one's family doesn't mean a person is risk-free as in many cases glaucoma is not inherited. Increased intraocular pressure (IOP) is a well-known significant risk factor. African, Latino and Asian-American ancestry, age, thin central corneas, a serious eye injury, nearsightedness and extremely high or low blood pressures are among other potential risk factors.

Smoking marijuana is good for glaucoma.

We quote the position statement of the American Glaucoma Society: "Although marijuana can lower the intraocular pressure (IOP), its side effects and short duration of action, coupled with a lack of evidence that its use alters the course of glaucoma, preclude recommending this drug in any form for the treatment of glaucoma at the present time."

Glaucoma is curable.

Glaucoma is a chronic condition that needs ongoing treatment and monitoring. If damage has occurred, at this time it is irreversible. Early detection and treatment minimize the risk of permanent vision loss.

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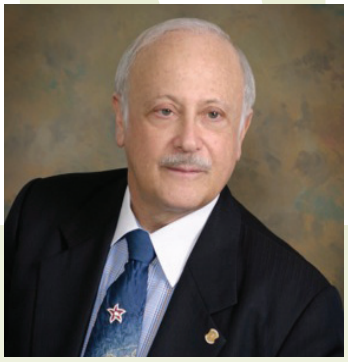
Doctor, I Have a Question



QUESTIONS ANSWERED BY:

Robert Ritch, MD

TGF Medical Director
Professor and Chief, Glaucoma Service
New York Eye & Ear Infirmary

Are alternative therapies being studied for their role in glaucoma?

Many available natural compounds used as non-pharmaceutical therapy have been reported to show beneficial effects on circulation, the immune system and neuroprotective activities. The mechanism of action of neuroprotection most common to natural compounds is antioxidant/free radical scavenging activity, anti-inflammatory activity, beneficial actions on the immune system, and improvement in ocular blood flow. Many different actions are present and some extracts, such as Ginkgo biloba and curcumin, have widespread activity on a number of enzyme systems involved in cell death in glaucoma. There has been a paucity of clinical trials examining neuroprotective effects of these compounds on ocular diseases. More are warranted.

Among natural compounds and extracts of great interest for glaucoma are curcumin, omega-3 fatty acids and Ginkgo biloba. **Curcumin**, a component of the commonly used spice, turmeric, is a potential neuroprotective candidate for glaucoma. Curcumin studies have increased greatly in recent years, with over 5000 papers published since 2000. Curcumin has shown possible beneficial effects in most of the mechanisms thought to be involved in the development and progression of glaucoma. A pilot study has shown that it slows disease progression.

Omega-3 fatty acids, found most notably in fish oil, play an important role in reducing oxidative damage in the retina, improving ocular blood flow and protecting against retinal ischemia (decrease in the blood supply) induced by increased IOP. While studies have not specifically addressed glaucoma, it has been suggested that fish oil may reduce IOP and be relevant to glaucoma because of its protective effect on the macula and its benefits for other eye problems.

Ginkgo biloba extract has been claimed effective in the treatment of a variety of disorders associated with aging. It appears to have many qualities applicable to the treatment of non-IOP-dependent risk factors for glaucomatous damage. It is believed to improve central and peripheral blood flow, reduce spasm of the blood vessels, and have protective effects against free radicals because of its antioxidant property.

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Top: Think Tank organizer Dr. Robert Ritch (Center) and participants Dr. Jeffrey Liebmann (left) and Dr. Rand Allingham (right). Bottom: Think Tank participants Dr. Michael Anderson (left) and Dr. Louis Pasquale (right). Center: Kathi Anderson.

New Focus on Exfoliation Syndrome

(Continued from Cover)

The exact disease mechanism of XFS-associated glaucoma is unknown; the vast number of people with these SNPs will never develop exfoliation syndrome. Further work on the LOXL1 gene is revealing aspects of its molecular structure, its regulation and its role in the production of exfoliation material that will help in understanding exfoliation syndrome and in leading to new avenues of therapy.

It is believed that both genetic and non-genetic factors may cooperate in the accumulation of exfoliation material. Several studies have set out to find out how demographic and geographic risk factors are associated with the prevalence of XFS, which is highly variable among different racial and ethnic groups. More work is needed to determine how environmental factors conspire to contribute to exfoliation syndrome.

Continuing our search for a cure, exfoliation syndrome will again be the subject of the Think Tank in 2013.

Myths About Glaucoma

(Continued from 4)

Eye drops have to be instilled at the exact time every day, or exactly 12 hours apart.
It is important to make your glaucoma medications a part of your daily routine. Most patients plan their eye drops at a time that closely approximates what the prescription indicates, but around a daily event such as getting out of bed, brushing their teeth, or before bedtime. The exact time of instillation is less important. If you forget to take a dose of your medication, it is best to instill the drop as soon as you think of it, even if the next dose is due shortly. What's important is consistency over a long period of time.

Doctor, I Have a Question

(Continued from 5)

It has been shown to be effective in treating Raynaud's disease, which is strongly associated with normal-tension glaucoma. A recent study in Korea [Lee et al. 2012] concluded that Ginkgo biloba extract administration slowed the progression of visual field damage in patients with normal-tension glaucoma. These and other properties raise the possibility that this herb may be a potential antiglaucoma therapy.

Dr. Ritch suggests interested patients join the FitEyes.com discussion group and the glaucoma group at groups.yahoo.com run by David Shields and Sherry Holthe, respectively, as there are often discussions about this subject and a lot of relevant information is posted. Before considering incorporating complementary therapy into your treatment regimen, consult your doctors to make sure that that it will not interfere with medications you are already taking. It is important to keep your doctors abreast of any therapies you try.

Help Us Find a Cure for Glaucoma

Together, we can find a cure for exfoliation syndrome and hasten the day when blindness from glaucoma is eliminated. The timing is right: TGF is uniquely positioned to succeed. Won't you partner with us in our campaign to find a cure and make a donation today? Your donations are vital for The Glaucoma Foundation to fund promising and innovative research projects that will bring us closer to our goal. 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.

Be Social and Find us at –

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TGF_Glaucoma

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Editor: **Gabrielle Bamberger**

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Recent Research Grants

Christopher Kai Shun Leung, MD, MB ChB, BMedSc, MSc
Associate Professor, Ophthalmology and Visual Sciences
University Eye Center
The Chinese University of Hong Kong

In Vivo Imaging of Retinal Ganglion Cells – A New Model to Study Neuroprotection in Glaucoma (Renewal Grant)

The goal of this project is to investigate the use of a novel imaging technique to monitor the longitudinal profile of retinal ganglion cell (RGC) damage in glaucoma and to study the treatment response of a neuroprotective agent, brain-derived neurotropic factor (BDNF). An experimental model of glaucoma is induced in a strain of genetically modified mice (Thy-1 CFP) that express yellow fluorescent protein under the control of a Thy-1 promoter. Using a confocal scanning laser ophthalmoscope, RGC damage is detected as progressive loss of fluorescent signals. This imaging model offers a unique opportunity to study RGCs longitudinally and non-invasively, and will provide a new paradigm to study neuroprotection in glaucoma.

Richard T. Libby, PhD
Asst. Professor of Ophthalmology
University of Rochester Medical School
Rochester, NY

JNK Signaling is Critical for Retinal Ganglion Cell Death after Axonal Injury

Loss of vision in glaucoma is caused by the death of a specific type of neuronal cell, the retinal ganglion cell (the neuron that sends information to the brain). Presently there are no widely available treatments aimed at neuroprotection. This project aims to determine the molecular signaling pathways responsible for killing retinal ganglion cells in glaucoma. Identifying these molecules will provide important information about the complexity of the signaling pathways active in glaucoma, indicate which pathways could be targeted for glaucoma therapies, and identify potential genes that could account for the variability in susceptibility to glaucoma in different people.

Steven Roth, MD
Professor and Director, Neuroanesthesia
Dept. of Anesthesia and Critical Care
University of Chicago Medical Center, IL

Rescuing Retinal Ganglion Cells by Survival Signaling

Using a rat model of glaucoma, this project will test a novel and innovative method of providing factors that could promote survival and repair of injured retinal ganglion cells. Bone marrow-derived stem cells that have been modified to carry a viral vector containing the survival factor Ak1 will be injected into the vitreous of rats with glaucoma. The ultimate goal of this research is to understand the mechanisms of action of Akt1 signaling in glaucoma and to optimize delivery strategy in an animal model, leading to clinically translatable treatment of glaucoma. This project could provide a method using a person's own cells with a modification to prevent or even reverse the nerve injury of glaucoma.

Mansoor Sarfarazi, PhD
Professor of Human Molecular Genetics
Molecular Ophthalmic Genetics Laboratory
University of Connecticut Health Center
Farmington, CT

Exome Sequencing of Families with Exfoliation Glaucoma

Exfoliation syndrome (XFS) is a systemic condition with or without manifestation of glaucoma. Because it is a late-onset condition, large families with multiple affected subjects are extremely rare. Over the past 15 years, the laboratory has been ascertaining such families and has identified two provisional genetic locations. But the identity of the defective gene has remained elusive mainly due to the large size of these locations. This project will scan the entire genome of these families with multiple affected subjects by whole-genome exome sequencing. This, together with existing association studies will significantly increase our chance of identifying a defective XFS gene.

The Art of Research

Dr. George L. Spaeth was the 2012 recipient of The Glaucoma Foundation's *Robert Ritch Award for Excellence and Innovation in Glaucoma.* The award recognizes the contributions of individuals who have played a significant and unique role in promoting the medicine and science of glaucoma and was officially presented at TGF's Black & White Ball benefit on December 5.

A luminary in the forefront of glaucoma research for decades, Dr. Spaeth was Director of the William and Anna Goldberg Glaucoma Service and Research Laboratories at the Wills Eye Institute/Jefferson Medical College from 1968 to 2007 and has held the Louis J. Esposito Research Professorship there since 2000.

Acknowledging the award, Dr. Spaeth spoke about the challenges of research. We share a portion of his remarks here:

> *In the office of Francis Moore, revered by many as a clinician scientist at Harvard Medical School, was a plaque that said, 'You only see what you look for; you only look for what you know. ' I thought it brilliant. And I had the words put up in a nice font and hung it on a plaque on the wall of the fellows' room where I taught. There is certainly truth in it – an important truth. But as I became more deeply involved in trying to answer questions, which is what research does, I came to realize that if you only see what you know, you will never learn anything new. The challenge in research or investigation is to see what you don't know…And the methodology of great research is better expressed in a poem by William Butler Yeats than any of the many scholarly articles in research technique. [Like the character in Yeats' The Song of the Wandering Angus,] Angus had a fire in his head. And he was looking for something. That's what great researchers do, they have fires in their head and they look for something important.*

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