

SPRING/
SUMMER 2003

OPTOMETRIST

THE NEWSLETTER OF
THE GLAUCOMA FOUNDATION

PRESIDENT'S MESSAGE:

In this issue of Eye to Eye, you will find an article by Dr. Robert Ritch about what's new on the glaucoma treatment and diagnosis horizon. Dr. Ritch provides a roundup of the various avenues researchers and physicians are currently exploring as they search for new treatments and work to better understand this complex disease.

Research lies at the heart of The Foundation's agenda. With the support of our friends – individuals and corporations alike – TGF awarded seven seed grants to researchers from as near and far as New Jersey and Hong Kong for an impressive range of projects to be investigated during 2003. Summaries of these research grants begin on page 4.

Not surprisingly, several of these grant projects relate to the topics of our last two Annual Scientific Think Tanks – stem cells and gene therapy. Since its inception 10 years ago, this international gathering of experts from different scientific disciplines has played a major role in charting the direction of glaucoma research. We are now finalizing preparations for our milestone 2003 Think Tank, which will be held in Boston on September 19-20, and will focus on the potential for tissue bioengineering in the eye.

One of the main reasons we continue to move this conference around the country is to give our friends outside New York an opportunity to attend the unique Research Dinner. If you live in or near the Boston area, we hope you will contact us about this function.

As you know, TGF has a dual mission. While our primary focus is to support and promote innovative research, we remain dedicated to helping patients better manage their glaucoma. One of TGF's newer Board members, Mary Jane Voelker, spent several years caring for her mother who was losing vision as the result of glaucoma. On page 5, she shares with our readers some very helpful suggestions about making your home more accommodating for people with limited sight.

Ms. Voelker is not TGF's newest Board member. That designation goes to James Sowers, a resident of Houston, Texas, where he is affiliated with Deloitte & Touche. Jim is committed to issues of eye care and eye health and we welcome him to our Board.

We are grateful of all who support TGF's important work. Our primary fundraiser, the Black & White Ball, will be held this year at The Plaza Hotel in New York City on December 4. It takes the partnership of many to eradicate blindness from glaucoma. We are proud to honor Tim Sear, Chairman, President and CEO of Alcon Laboratories with our 2003 Corporate Visionary Award.

With your continued help, we will reach our goals.



Sincerely,
Scott R. Christensen
President and CEO

tgf
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TGF IS HOLDING ITS SECOND RESEARCH DINNER IN BOSTON ON FRIDAY EVENING, SEPTEMBER 19. THIS IS A RARE OPPORTUNITY FOR TGF FRIENDS TO HEAR FROM SOME OF THE MOST PROMINENT SCIENTISTS WORKING IN THE FIELD OF GLAUCOMA, WHO WILL BE GATHERING THAT WEEKEND FOR OUR 10TH ANNUAL SCIENTIFIC THINK TANK.

IF YOU OR SOMEONE YOU KNOW WOULD LIKE TO ATTEND THIS PRESTIGIOUS EVENT, PLEASE CONTACT KELLY LUNDBERG BY PHONE, (212) 285-0080, OR EMAIL: KLUNDBERG@GLAUCOMAFUNDATION.ORG.

WHAT'S NEW IN GLAUCOMA – A MEDICAL UPDATE

BY DR. ROBERT RITCH
 CHAIRMAN OF THE GLAUCOMA FOUNDATION'S SCIENTIFIC ADVISORY BOARD
 PROFESSOR OF CLINICAL OPHTHALMOLOGY & CHIEF OF GLAUCOMA SERVICE
 THE NEW YORK EYE & EAR INFIRMARY

Progress in glaucoma concepts, research, diagnosis and treatment is being made at an ever-accelerating pace. Glaucoma

is not a single disease associated with elevated intraocular pressure (IOP), but a particular pattern of optic nerve and visual field damage caused by a number of different diseases which affect the eye. Most, but not all, of these are associated with elevated IOP, which is the most important known risk factor for glaucoma, but still remains only a risk factor. We now know, however, that normal tension glaucoma, or glaucoma occurring at statistically defined pressures of 21 millimeters of mercury (mmHg) or less, is quite common, and in fact accounts for about one-third of the glaucoma in the U.S. In Japan, it is three times as common as high-tension glaucoma.

For about the last 15 years, there has been increasing interest in the blood flow to the eye as an important determinant of ocular health. Non-IOP-dependent risk factors for glaucoma seem to be most commonly associated with defective regulation of the blood supply to the eye or insufficient blood flow to the eye. Decreased blood flow is thought to be a risk factor for glaucomatous damage. Conditions that are associated with decreased blood flow, or vasospasm, such as migraine, Raynaud's phenomenon, atrial fibrillation, anemia, sleep apnea and low blood pressure, are associated with normal tension glaucoma.

Throughout the 20th century, all we were able to do therapeutically was to lower IOP. At the present time, we still do not have any proven treatments aside from lowering IOP. Calcium channel blockers have been shown to increase blood flow to the eye, but they also lower blood pressure and, although there was a flurry of interest in these in the early 1990s, their use has not become widespread or standard. Ginkgo biloba extract, which has been used in Chinese traditional medicine for 5000 years, improves the blood flow to the eye and the brain and improves the symptoms of Raynaud's disease in many patients. It has been reported to slow the progression of Alzheimer's disease, and it may benefit glaucoma.

Inhibition of retinal ganglion cell death, or neuroprotection, is the newest area of interest. Much investigative effort is being put into this area, not only in glaucoma but in other eye disorders and

in neurological diseases as well. The concept of neuroprotection is based upon strengthening the nerve cells against toxic injury. When nerve cells are damaged, they become more porous to calcium which, when it enters the cell in too great a concentration, triggers a series of genetically determined events which lead to the death

of the cell (apoptosis). When the cell dies, it releases toxic materials which damage healthy cells, initiating a domino effect. At the present time, there are no neuroprotectants that have been proven to benefit glaucoma.

Memantine, which has been used in Europe for over 20 years for cerebral vascular disease and Alzheimer's disease, is being tested in a world-wide clinical trial for glaucoma, but the results will not be in for a few years. In the next decade, we expect to see major advances in our abilities to provide neuroprotection to the optic nerve cells in glaucoma.

“New imaging tools promise improved accuracy in diagnosis and in following the progression of glaucoma damage.”

The results of several clinical trials have been published recently. The Ocular Hypertension Treatment Study (OHTS) has shown that topical medication to lower IOP is effective in delaying or preventing the onset of primary open angle glaucoma in persons with elevated IOP (ocular hypertension). Patients with elevated IOP and no glaucomatous damage were divided into two groups — one of which was followed untreated and the other of which was treated to lower IOP. Twice as many patients in the untreated group developed glaucoma, compared to the treated group. However, it must be recognized still that over 90 percent of patients in the study

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over five years did not develop any damage, and this study does not imply that all patients with elevated IOP should be treated. The factors that predisposed to development of glaucoma damage were older age, thinner corneas, and higher IOP.

Corneal thickness has received much recent attention. The actual IOP in patients with thicker corneas is lower than what is read on the scale of the tonometer in the doctor's office, while in patients with thinner corneas, the actual IOP is higher. This calculation of IOP may be a factor in the greater susceptibility of patients with thinner corneas to glaucomatous damage. But it is also possible that patients with thinner corneas have other tissue factors in the eye which make the eye more susceptible to glaucomatous damage at any pressure level. This has yet to be proven.

The Collaborative Initial Glaucoma Treatment Study (CIGTS) was designed to evaluate whether medical therapy or trabeculectomy is the better initial treatment for patients with open angle glaucoma. In addition to examining effects on visual field progression, IOP control, and visual acuity, this study also examined the effects of medical and surgical treatments on quality of life. After five years, there was no significant difference in visual field loss between the medically and surgically treated patients. Patients in the trabeculectomy group had lower IOP, but also had three times the rate of cataract progression. Patients in the surgically treated group had local eye symptoms, such as discomfort and tearing. The results of this study do not support altering our current treatment practices in the initial management of patients with primary open angle glaucoma and do not support the initial use of surgery.

In the Early Manifest Glaucoma Trial (EMGT), patients were randomized to laser treatment and one medication or no immediate treatment. After six years, the progression of glaucoma was reduced by 50 percent in the treated eyes. Factors which predisposed to progression were higher IOP, exfoliation syndrome, glaucoma in both eyes and older age. Corneal thickness was not measured in this study. The presence of disc hemorrhage, which is most common in normal tension glaucoma, was strongly associated with progression of glaucoma damage.

New imaging tools promise improved accuracy in diagnosis and in following the progression of glaucoma damage. The gold standard of white-on-white computerized perimetry (visual field test) is less sensitive than newer tests, which examine specific categories or classes of optic nerve cells. New tests include short wavelength automated perimetry and frequency doubling perimetry. Multifocal visual evoked potentials (or mfVEP), is like a visual field test in which the patient does not have to push the button. The machine measures the electrical activity of the retina and prints out a map similar to the visual field. This device shows great promise as an objective visual field test. All of these new modalities appear to be more sensitive than standard perimetry. However, further knowledge and analysis of results is necessary before they can replace it.

Examination of the optic disc and retinal nerve fiber layers is best done by examination and stereo photography. An objective diagnostic imaging device has been a long sought goal. Optical coherence tomography (OCT), scanning laser polarimetry (SLP/GDx), and scanning laser tomography (HRT) have greatly improved in accuracy with the introduction of new software and hardware improvements. They are excellent additional tools for confirming suspicious optic disc and visual field findings, but at the present time they should not be relied upon for making a diagnosis of glaucoma in the absence of other clinical evidence.

In the not-too-distant future, gene therapy and stem cell transplantation will be added to our array of treatment options. At that time, reversal of blindness from glaucoma will become a possibility. ■

*For a glossary of terms, please visit the
"About Glaucoma" section of The Foundation's website at
www.glaucomafoundation.org*

SAVE THE DATE
for THE SEVENTEENTH ANNUAL BLACK & WHITE BALL
Thursday, December 4, 2003
THE PLAZA HOTEL, New York, NY

2003 RESEARCH AWARDS

RAYMOND CHUEN-CHUNG CHANG, PhD -
University of Hong Kong

IMMUNE RESPONSES AND DEGENERATION OF RETINAL GANGLION CELLS IN EXPERIMENTAL GLAUCOMA (RENEWAL)

The goal of this continuing project is to clarify how immune responses affect the degeneration and death of retinal ganglion cells (RGCs) in glaucoma. This study attempts to further explore whether immune responses in the eye via incoming activate macro-phages (scavenger white blood cells that remove dead tissues and debris), have direct effects on determining the fate of neurons. Previous findings show that immune responses can either harm or protect the central nervous system, depending on the experimental models. Understanding the biological mechanisms of immune responses related to the degeneration of RGCs can open a new avenue for glaucoma treatment.

ADRIANA DI POLO, PhD - University of Montreal

PROTECTION OF RETINAL GANGLION CELLS IN GLAUCOMA: A GENE THERAPY APPROACH

Glaucoma is characterized by the selective death of RGCs. There is strong evidence that a novel neuroprotective strategy, based on gene transfer of the neurotrophin receptor TrkB, effectively sustains the survival of RGCs. This study will test the efficacy of this approach in an experimental rat model of chronic pressure-induced optic nerve damage that resembles human glaucoma. The results of this study may have implications in the design of gene transfer therapies, which when combined with treatments such as lowering intraocular pressure, may promote optic nerve production in glaucoma.

JAREMA MALICKI, PhD -
Massachusetts Eye and Ear Infirmary / Harvard Medical School

ANALYSIS OF RETINAL GANGLION CELL-SPECIFIC TRANSCRIPTS IN ZEBRAFISH (RENEWAL)

To identify genetic factors involved in the development and maintenance of retinal ganglion cells, this study will search for genes that are either exclusively or entirely restricted to this cell type. Earlier analysis of over 8,000 randomly chosen genes revealed that over 11 genes are entirely or partially restricted to ganglion cells within the retina. Those genes provide an attractive opportunity to gain insight into the molecular circuitry underlying specification and differentiation of ganglion neurons. The aim of these studies is to reveal the

early mechanisms of ganglion cell development and provide new methods of treatment for ganglion cell disorders such as glaucoma.

TAT FONG NG, PhD - Schepens Eye Research Institute

TRANSPLANTATION OF NEURAL STEM CELLS FOR TREATMENT OF GLAUCOMA

Stem cells isolated from the blood and other tissues are being used in the attempt to alleviate disease processes in a number of pathological conditions. Using mice with hereditary glaucoma, Dr. Ng will study the impact of transplanted neural stem cells (NSCs) on the survival of RGCs in the diseased retina. His team will determine if NSCs can improve the survival of RGCs in the diseased retina using specialized, specific labeling techniques, and whether the transplanted NSCs can function as RGCs by connecting to the target. It is anticipated that observations made during the course of this research will lead to novel therapies for the treatment of glaucoma.

DONALD SAKAGUCHI, PhD - Iowa State University

NEURAL STEM CELL TRANSPLANTS: NEW STRATEGIES FOR THE TREATMENT OF GLAUCOMA (RENEWAL)

One approach being investigated in the quest for effective therapies to halt or reverse neuronal loss in disorders of the nervous system, such as glaucoma, is transplantation of stem cells to provide a source of new neurons for regeneration of the retina and optic nerve. The long-term goal of this continuation study is to gain a more complete understanding of the mechanisms regulating the control of neural stem cell development and differentiation, and to determine if neural stem cells can integrate functionally in the glaucomatous retina. Transplantation of neural stem cells to replace lost cells, or to act as support cells to facilitate rescue, may ultimately become a practical approach to treating blinding diseases in the future.

ERNST R. TAMM, MD - University of Erlangen-Nurnberg

STEM CELLS IN THE PRIMATE TRABECULAR MESHWORK

Impaired function of the trabecular meshwork (TM) contributes to increased intraocular pressure, the most important risk factor in primary open-angle glaucoma (POAG). The application of adult TM stem cells to compensate for the TM cell loss in glaucoma appears

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A DAUGHTER HELPS LIGHT THE WAY

Mary Jane Voelker, who joined The Glaucoma Foundation's Board of Directors last year, does not herself have the disease. But she learned first hand what it takes to live with diminished eyesight, while sharing the family home and caring for her mother who was losing her vision. Dorothy Voelker died at the age of 91 in 2001. She had learned about The Glaucoma Foundation a few years earlier, when she received a direct mail letter soliciting support for our sight-saving work. Soon thereafter, she arranged for a generous gift to TGF through her estate.

Dorothy Voelker was living an extremely active and independent life for a woman in her late 80s, her age at the time she was diagnosed with normal-tension glaucoma in 1999. "Even then," says her daughter, "my mother was one of those women who lived by the motto, 'shop till you drop.' She wore me out, never wanting to stop."

"Her sight deteriorated very quickly, in spite of laser surgeries," says her daughter. "I was determined to allow her to continue staying at home alone, and living the normal life she was used to. "I changed my work schedule so that I worked only three days a week and could spend more time at home. But the real challenge was making our home easier to navigate," she recalls. "We just took it day by day, experimenting to see what worked and what didn't. We constantly altered the vision aid devices to meet her changing needs. That's how she continued to stay at home alone. You just do what you have to do!"

We asked Ms. Voelker to share some of her specific ideas for making the home more accessible and user-friendly for the vision impaired with our readers. Here's what she had to say.

"The main task was to discover which colors worked best at a particular time. I remember the first thing we did was changing mother's shoes to white," since she had difficulty making out darker colors.

"Probably our most important device was fluorescent tape," she says. "I used it on the door jams, along the edges of counter tops, at the top and bottom of each step, all around the garage. And we constantly changed colors. Sometimes a white strip did the job; at other times, a bright color worked better. Flexibility was the key to selecting colors that helped define edges.

"Then we bought a white cordless phone that had large numbers on it, and – increasingly important as her sight

deteriorated further – a memory redial button that was clearly placed on the phone.

"In the kitchen, I color-coded bottles with strips of a certain color. Mother continued to use the microwave, to cook her meals when I was not home," Ms. Voelker says. "I cooked sufficient meals in advance for the week, and froze them, color-coded according to their contents so my mother could get what she wanted and then cook it in the microwave. Beef was one color, turkey another.

"Probably our most important device was fluorescent tape," she says. "I used it on the door jams, along the edges of counter tops, at the top and bottom of each step, all around the garage."

"Too often, older people who live alone get bored with their meals, and don't eat properly. I always made sure she had what she liked, and we devised a system for stocking the freezer, so she could find everything. The top of the freezer had beef; the next section was turkey, and so on. The shelf stored frozen food products."

Asked about all the effort involved, Ms. Voelker was quick to answer. "We had a wonderful life together. I wanted to make sure my mother would have no problem and I didn't want to spend every day worrying whether she was eating. Knowing she was content meant a lot to me."

When asked if she had any more advice, she offered these suggestions:

- Don't change the furniture around. We all get used to where things are and that helps getting around when vision is diminished.
- In the bedroom, as elsewhere, instead of moving furniture, pad sharp corners. For example, on a bed or dresser.
- Replace loose rugs with non-skid flooring.
- Eliminate needless electrical cords.
- Keep experimenting and changing to make your home a safe and accessible environment for your sight-impaired family member. ■

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THE NEWSLETTER OF
THE GLAUCOMA FOUNDATION



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2003 RESEARCH AWARDS

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to be a novel, promising therapeutic approach. Dr. Tamm proposes to identify adult TM stem cells in the eyes of higher primates (monkeys) and to develop novel detection methods that will enable researchers to isolate TM cells and grow them in culture systems. This will be a critical first step for a rational stem cell therapy of the trabecular meshwork.

MENGQING XIANG, PhD -

UMDNJ-Robert Wood Johnson Medical School

ROLE OF BRN3 GENES IN AXON OUTGROWTH OF RETINAL GANGLION CELLS

The studies proposed by Dr. Xiang are designed to test the hypothesis that the Brn3 genes (Brn3a, Brn3b, and Brn3c) may play a redundant role in RGC survival and axon outgrowth by regulating a common set of target genes. His research will investigate axon outgrowth and pathfinding defects of RGCs in mice deficient for both Brn3a as well as in mice deficient for Brn3a and Brn3b. The long-term objective of this study is to understand the molecular mechanisms underlying the development and maintenance of RGCs. Together, these proposed studies will provide important insights into the molecular mechanisms underlying optic nerve damage and RGC loss in glaucoma. ■

A copy of The Glaucoma Foundation's annual financial report may be obtained upon request by writing to The Foundation at 116 John Street, Suite 1605, 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.

SHARING THE VISION — SUPPORTING RESEARCH

The Glaucoma Foundation is proud of the growing interest in our research initiatives. More scientists are approaching TGF in pursuit of research funding for their critical and novel investigations than ever before. We are also pleased to report that the grant applications we receive come from both glaucoma specialists and scientists working in other disciplines who have been encouraged to apply their expertise to the enigmas of glaucoma.

Fostering new lines of scientific research is an expensive, but valuable venture. Contributions from individuals, like you, make it possible for TGF to provide the crucial seed funding that can uncover new treatment options, and eventually, cures for glaucoma. Your continued support is vital to ensure The Glaucoma Foundation's ability to answer the call of promising research.

One way to bolster our important work is by making a contribution to **The Joseph M. & Geraldine C. La Motta Endowment Fund for Glaucoma Research**. A gift to this Fund will help sustain The Foundation's efforts to promote and fund exciting research projects that can lead to sight-saving advancements and improve the quality of life for patients today and generations in the future.

*For further information on
The Endowment Fund for Glaucoma Research
or other ways to champion the work
of The Foundation, please visit
www.glaucomafoundation.org
or call us at (212) 285-0080.*

TGF would like to thank CIBC World Markets Children's
Miracle Day program for its recent
generous support of our molecular genetics research.

Miracle Day is an annual event during which CIBC World
Market's designates these fees and commissions to
charities with programs that benefit children.

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