

CATALYST FOR A CURE RESEARCHERS REPORT RESULTS

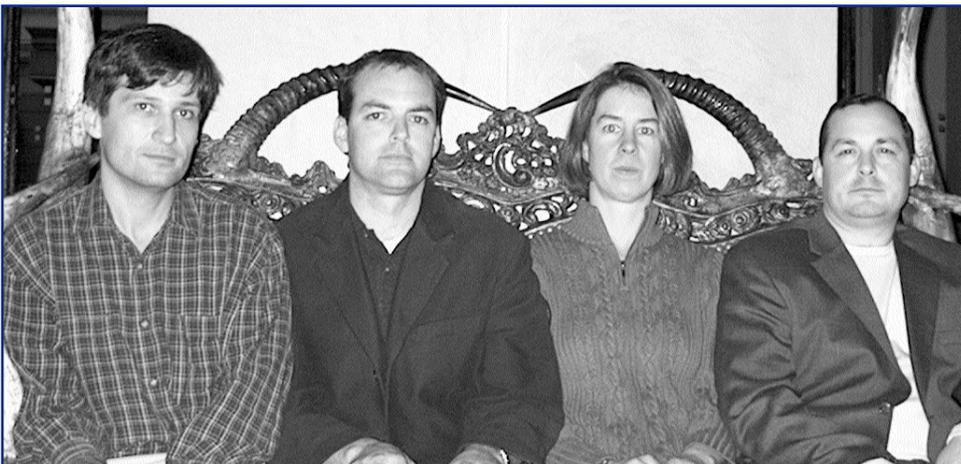
Catalyst For a Cure researchers met in San Francisco this past December to report on the results of their second year of investigations. The four scientists reported the establishment of a glaucoma model that will enable tracking the genetic changes that occur as glaucoma progresses. They also developed techniques for isolating genetic material for analysis. The researchers have created core capabilities at each research site to identify the genes responsible for the progression of glaucoma. The CFC team verified their process for using gene chip technology to isolate and identify genes that may play a key role in glaucoma.

The researchers explained the capabilities they have developed to study retinal nerve cells as glaucoma develops. By comparing changes in cells over time they will identify genes associated with the changes. Those genes are then possible targets for intervention. By blocking a particular gene's action and seeing the effect on the nerve cells, it is possible to test whether that gene is active in glaucoma. Once suspect genes are linked to the development of glaucoma they can be blocked to see if progression is halted. If glaucoma can be eliminated in the model, the next step is development of drugs that can block the gene in humans. Clinical trials

would then determine if the drug can stop the progression of glaucoma.

The Catalyst For a Cure research program is unique because it combines the expertise of four different research institutes to work on finding a cure for glaucoma. Each institute brings its particular expertise to the project. The result is that the glaucoma research benefits from a greater capability than any single investigator could bring. The team of investigators has made excellent progress as they work together to target and test genes that could protect the retinal neurons from damage due to glaucoma.

A joint \$1.5 million, three-year grant from the Glaucoma Research Foundation and the Steven and Michele Kirsch Foundation created the Catalyst For a Cure research program. Four experts in the fields of neurology, molecular biology, retinal physiology and genetics were selected to bring fresh new ideas to glaucoma research. David Calkins, PhD, Vanderbilt University School of Medicine, provides the background in retina; Phil Horner, PhD, University of Washington, brings his neurology experience; Monica Vetter, PhD, University of Utah, is the molecular biologist; and Nick Marsh-Armstrong, PhD, Kennedy Krieger Institute, contributes his genetics expertise to the team.



**Catalyst For a Cure
research investigators at
the 2nd Annual Meeting**

From left to right:
Nick Marsh-Armstrong, PhD
Phil Horner, PhD
Monica Vetter, PhD
David Calkins, PhD

BOARD OF DIRECTORS

Dennis E. Singleton, Chairman
Thomas M. Brunner, President & CEO
C. Seth Cunningham, Vice Chairman
John Hetherington, MD, Vice Chairman
Andrew G. Iwach, MD, Secretary
Deirdre Porter, Treasurer
F.T. Barr
J. Bronwyn Bateman, MD
June Behrendt
James D. Brandt, MD
Pamela Colbert
Timothy J. Dwyer
H. Dunbar Hoskins, Jr., MD
Michael L. Penn, Sr.
Robert L. Stamper, MD
George E. Thomas
Martin B. Wax, MD
Robert N. Shaffer, MD, Chairman Emeritus

Rita Loskill, Executive Director

Glaucoma is also available online at
www.glaucoma.org.

©2004 by the Glaucoma Research Foundation. All rights reserved. No part of this publication may be reproduced without permission from the publisher. Glaucoma articles are intended to help readers understand glaucoma. Every effort is made to assure the accuracy of this information. This information is not a substitute for the advice and recommendations of health professionals. Always consult a health professional prior to any decision regarding your eyes or other health concerns.

ISSN # 1072-7906

Remember Us In Your Will
800-826-6693
415-986-3162
donate@glaucoma.org

LETTER FROM OUR PRESIDENT & CEO



Dear Friends,

Thank you for the incredible response to the Catalyst For a Cure collaborative research program. Your generous donations have confirmed our commitment to this unique approach to finding a cure for glaucoma.

It is a pleasure to report that the Board of Directors of the Glaucoma Research Foundation voted at our January board meeting that the work of the Catalyst For a Cure team must continue. Our board and our Catalyst For a Cure partner, the Steven and Michele Kirsch Foundation, each approved an additional \$100,000 to support the CFC researchers through the end of this year. These donations will assure successful completion of the first phase of the investigation.

Based on the outstanding progress of the researchers and the response of our supporters, we are committed to the next three-year phase of the Catalyst For a Cure program. The program will not end this December; it will continue into the next exciting phase of identifying possible means to protect retinal nerve cells. There is much to do and we are convinced of the future success of this program.

Our feature article in this issue of Glaucoma features a brief summary of the Catalyst For a Cure second year report. Thank you again for your confidence and for your donations to Catalyst For a Cure.

Sincerely,

A handwritten signature in blue ink that reads "Thomas M. Brunner". The signature is fluid and cursive, with a long horizontal stroke at the end.

Thomas M. Brunner
President & CEO

Glaucoma Research Foundation Pilot Project Grants - Fiscal Year 2004

Providing seed money for promising pilot research projects was one of the major goals of the Glaucoma Research Foundation when it was established in 1978, and it remains a critical focus today. GRF continues to actively and aggressively support new, high-impact research that has breakthrough potential.

"In its 25 years, GRF has been an exciting catalyst for new scientific inquiry and has made progress in glaucoma research possible. The most unique and important meetings I have ever participated in were GRF sponsored Catalyst Meetings, where scientists from many fields came together - the atmosphere was bubbling with excitement and new ideas. As former Chair of the Scientific Advisory Board, I have been impressed by the huge impact that GRF funding has had, allowing new and exciting concepts to be fully explored by some of the brightest minds in the field."

David E. Epstein, MD
Professor & Chairman Dept. of Ophthalmology
Duke University Medical Center Durham, North Carolina



Brad Fortune, OD, PhD, Discoveries in Sight / Devers Eye Institute, Portland, OR

Project: Effects of Acutely Elevated Intra-Ocular Pressure (IOP) on Retinal Structure and Function in Pigmented Rat

Grant: \$31,000

Dr. Fortune plans to identify the level of IOP that causes temporary, and then permanent loss of function among the different cell types within the retina. In particular, he is interested in the effects of a relatively short-term pressure elevation or 'spike'. He will compare changes in the functional status of different retinal cell types with their microscopic appearance to determine the relationship between structural and functional damage. The results should help focus experimental rodent models of glaucoma more acutely so that they are most relevant to human glaucoma. As well, the results may contribute to improvements in existing diagnostic techniques.

Paul R. Lichter, MD, University of Michigan/ W.K. Kellogg Eye Center

Project: Pedigree Collection in 500 Patients from the Collaborative Initial Glaucoma Treatment Study (CIGTS)

Grant: \$36,000

Dr. Lichter proposes to use a 60-minute telephone interview of CIGTS subjects more than 8 years after they were first diagnosed to obtain family history information that will be both more accurate and more complete. This information will then be used to determine whether borderline associations are in fact significant and likely to be real, to identify other associations that were undetectable with an inaccurate data set, and to determine whether there are any associations with mode of inheritance. If associations with family history are identified, it will have practical implications since the questionnaire format he proposes to use is one that could be applied in the context of a clinical practice. Although it is common practice to ask briefly about family history of glaucoma, the results of this study will determine whether there is a basis for making much more effective use of family history information in evaluating risks among newly diagnosed glaucoma patients in clinical settings.



"Glaucoma Research Foundation - Pilot Project Grants - Fiscal Year 2004" continued on page 4



Luca Scorrano, MD, PhD, Venetian Institute of Molecular Medicine, Padova, Italy

Project: Role of OPA1 and of mitochondrial remodeling in retinal ganglion cell death

Grant: \$35,000

Dr. Scorrano intends to study the role of OPA1 in the life and the death of the retinal ganglion cells. Some proteins, called dynamins, control the shape of mitochondria, and when they are damaged serious diseases leading to blindness ensue. In particular, one of these proteins, called OPA1, is affected in a condition that shares with glaucoma the death of the retinal ganglion cells. Dr. Scorrano wants to explore if OPA1 is crucial in the maintenance of the life of RGCs and if it can be a target of drugs that interfere with the death of these cells and ultimately can stop the path to blindness.

Cheryl Hann, MS, Mayo Clinic, Rochester, MN

Project: Are Focal Adhesions Present in Schlemm's Canal Endothelial Cells?

Grant: \$28,000

Ms. Hann's research will examine proteins composing focal adhesions and their relationship to Schlemm's canal cytoskeleton. It is her belief that the type and number of focal adhesions change under the increasing pressures found in glaucoma. These changes may retard the formation of fluid vacuoles and fluid passage between Schlemm's canal cells. Focal adhesion signaling pathways could then be targeted for drug development.



Daniel Y. Ts'o, PhD, SUNY Upstate Medical University, Syracuse, NY

Project: Ganglion cell contribution to noninvasive retinal functional imaging

Grant: \$35,000

Dr. Ts'o's lab is working on a new technique to help detect and treat glaucoma. The promise of their project is the development of a reliable, objective instrument for monitoring the activity of the retina, in health and disease, simply by taking pictures of its response to patterns of light. Glaucoma is one disease that may greatly benefit from such an instrument. It would facilitate the early detection and characterization of glaucoma in patients and help in the monitoring of the progress of the disease and its treatment. This project aims to target this new technique specifically to the monitoring of the health and activity of the ganglion cells of the retina, the cells that are most affected by glaucoma. Dr. Ts'o's lab plans to isolate the responses of the retinal ganglion cells and optimize the instrument for its detection and measurement. These developments are designed to make this new technology most useful for the diagnosis and treatment of glaucoma.

Do You Qualify For a Free Referral?

EyeCare America offers multiple eye care programs for which individuals may qualify. Callers will be automatically screened to determine the program that provides the most appropriate eye care services. Eligible seniors who have not seen an ophthalmologist in three or more years may be able to receive a referral for **eye care at no out-of-pocket cost for up to one year**. Callers who have not had an eye exam in the past 12 months and are at increased risk for glaucoma may be eligible to receive a referral for a glaucoma eye exam.

To determine if you, a family member, or friend qualify for a Glaucoma EyeCare Program (GEP) referral, call **1-800-391-EYES (3937) toll-free** or read more about the program at www.eyecareamerica.org.

WE KNOW WHO YOU ARE!

Half of those with glaucoma in the United States are sitting at home without being monitored or treated for their disease. What explains this failure to recognize and to treat the second leading cause of blindness in the world? Certainly, groups like the Glaucoma Research Foundation and other charitable groups have tried to get the message out, through media like this newsletter, and by screening for glaucoma in vans, senior centers, and health fairs throughout the country.

But, in every city in the U.S., as well as in other countries of the developed world, population studies that examine persons at random in the population have determined that the failure to identify those with glaucoma comprises more than half of the 33 million people with open-angle glaucoma worldwide.

Scientific studies that try to look at the "why" of this failure of our diagnostic system have identified several reasons. First, open-angle glaucoma, the most common form of the disease in European-derived persons, is a silent disease that hides its effects from those affected until late in its progressive damage to vision. Second, studies show that mass screening is ineffective and costly as an approach to the recognition of those with the disease in a population. While vans can go out into neighborhoods to find some cases, the cost of identifying one case of glaucoma was estimated at several thousand dollars in a recent study in the Northeastern U.S.

Glaucoma clearly hides well. Doctors who have spent a lot of time trying to devise methods to find those with glaucoma had concluded that it takes much more than simply measuring the eye pressure to find the disease. In fact, in order to have an effective screening system, one must have highly trained personnel who are using at least 2 methods of eye examination, typically a form of optic disc evaluation (ophthalmoscopy) combined with a functional test of vision (a visual field test).

Until screening methods are made more effective, what can we do? Researchers at the Wilmer Institute, Johns Hopkins in Baltimore, have reasoned that we can already find a large number of these undiagnosed glaucoma sufferers. In fact, we can easily get their telephone numbers! This comes from the fact that open-angle glaucoma is a disease with a genetic tendency.

Among all adults in a population, glaucoma affects 2% of those whose families came from Europe, and 6% of those of African derivation. Hispanics also share a greater

proportion of glaucoma than those who are European-derived. While 2 in 100 have glaucoma generally, if you have a family member with glaucoma, your chance of developing the disease is 10 times higher.

How can we use this fact to find those who need glaucoma treatment? The simple answer is to ask the known glaucoma patients to "tell on their family". The statistics tell us that if someone with glaucoma has 3 living family members (parents or brothers and sisters), the chance that there is one of these persons with glaucoma is nearly one in three. Put another way, for every 8 persons with glaucoma, there is one member of their families who has glaucoma at this moment that is undiagnosed.

We all want the best for our families, and many glaucoma patients are asked by their doctors if there is someone in their family with glaucoma. So, we would think that all of the existing persons with glaucoma would have made sure that their family members had gone to the doctor and had a detailed examination. Right?

Unfortunately, studies show that those with glaucoma often don't tell their family to have eye exams that are detailed enough to determine if glaucoma is present. Or, they simply say nothing. The clinicians who study this question have determined that going to have glasses made or "having your pressure checked" misses more than half of those with glaucoma.

The best approach is to tell every adult relative (mother/father, brother/sister, adult children) to go to an eye doctor and to say: "my relative has glaucoma and I want a detailed exam of my optic nerve and a visual field test". This raises the consciousness of the examiner and makes sure that all the appropriate tests are done. If every existing patient with glaucoma would do this, we could find 100,000 undiagnosed cases of glaucoma and save 10,000 persons from going blind in their lifetime.

Don't you have some phone calls to make?



*Harry A. Quigley, MD,
the A. Edward Maumenee professor,
the Wilmer Eye Institute,
Johns Hopkins
University School of Medicine,
Baltimore*

YOUR SUPPORT DIRECTLY
CONTRIBUTES TO THE
CURE OF GLAUCOMA.
PLEASE JOIN OUR FIGHT.

GLAUCOMA RESEARCH FOUNDATION
MAY 2004

490 Post Street, Suite 1427
San Francisco, CA 94102



Return Service Requested

NONPROFIT
ORGANIZATION
US POSTAGE
PAID
Oakland, CA
PERMIT NO. 1397

IT'S NO SECRET GLAUCOMA RUNS IN FAMILIES!

**TELL YOUR LOVED ONES TO GET A DETAILED EYE EXAM
AND A VISUAL FIELD TEST ON A REGULAR BASIS.**

Join the Blanche Matthias Society!

Thank you to the following for remembering the Glaucoma Research Foundation in their wills:

M. Helen W. Davis Trust
Ernest and Virginia Esberg Trust
Jack F. Flowers and V. Fern Flowers Marital Trust
Eugene H. Gray and Stephanie S. Gray Irrevocable Trust
Estate of Luther Bain Haddick
The Parris Trust and the Estate of Virginia Lee Parris
Guardianship of the Person and Estate of Ms. Bert Sketchley
Estate of Joan H. Wickert

**Include the Glaucoma Research Foundation in your Will.
Call for a free brochure at 800-826-6693.**