

REPORT

Better Health Through Research

Winter 2006

NGR Grantee Announces Potential New Treatment for the Most Common Form of Glaucoma

Dr. Paul Kaufman's Research Yields Remarkable Results

At the University of Wisconsin-Madison, Dr. Paul Kaufman and his team are studying a new drug that could have a dramatic effect on people with glaucoma, thanks to a grant from National Glaucoma Research and people like you.

The drug – known as alagebrium – has been shown to chemically “break” abnormal crosslinks between proteins, restoring normal functioning to organs and tissues that have lost flexibility or functioning. By breaking the bonds that cause tissues, organs, and vessels to stiffen and lose function over time, alagebrium has demonstrated the ability to reverse a number of age-related conditions.

In the case of people with primary open angle glaucoma, the most common form of the disease, results from Dr. Kaufman’s study indicate that the use of alagebrium can substantially decrease pressure within the eye, and help restore the eye to normal functioning.

Primary open angle glaucoma can cause pressure within the eye (or intraocular pressure) to increase to the point that it damages the nerve at the back of the eye that conveys visual information to the brain. This can lead first to loss of peripheral vision—the things you see “out of the corner of your eye” while looking straight ahead. If not treated, it can also lead to total blindness.

Pressure in the eye increases because of blockage in the drainage system for the fluid produced in the front part of the eye. Dr. Kaufman believes that this blockage occurs, in large part, because of the accumulation of crosslinked proteins in the drainage system.

According to Dr. Kaufman, blockage may also happen because of increased stiffness in the ciliary muscle. This tiny muscle within the eye controls the shape of the lens, which focuses incoming light on the light-sensitive cells at the back of the eye. Contraction of the ciliary muscle also helps open the drainage system – but the ciliary muscle may become stiff because of accumulation of the same cross-linked proteins that clog the drainage system.

This cross-linking, caused by a chemical reaction in the blood between sugar molecules and proteins, fat molecules and DNA, occurs at an

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President's Corner

A Special "Thank You" to Our Donors

In the next 15 years, the number of Americans with glaucoma is expected to increase 50%, from 2.2 million to 3.3 million people. Not only that, but in half of all cases, the problem goes undetected until significant damage has already been done.

Medications and surgery can help slow the progression of the disease, but there is no cure... yet. Thanks to you, however, there is hope — not only for a cure, but for new treatments that may help restore eye health to countless people.

At National Glaucoma Research, we simply could not be more grateful for your support. I think I can speak for us all when I say that your vision of a world in which no one suffers from glaucoma fuels our research, and inspires us on a daily basis.

With your help, we will continue investing in innovative research that will one day find a cure for glaucoma. And when that day comes, you can be very, very proud of the part you played in making it possible.

Brian K. Regan, Ph.D.
President

P.S. Visit National Glaucoma Research's website, www.ahaf.org, to learn more about important information regarding risk factors for glaucoma and healthy choices that may help you minimize the risk of glaucoma.

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E-mail

As part of NGR's efforts to reap the many benefits offered by electronic communication, we are requesting that you provide us with your e-mail address. NGR will be pleased to add you to our list of e-mail recipients, allowing us to send you more timely updates on our researchers and their progress, as well as the latest educational information and practical advice regarding glaucoma. Space is available on the enclosed response form for your e-mail address. Thanks for your cooperation and watch for e-mails from us!

Research In Brief

Currently, National Glaucoma Research is funding 16 biomedical researchers, each of whom offers hope for a deeper understanding of the causes of glaucoma, as well as new treatments. We are highlighting five of these important projects from around the world to let you know how your contributions are working to improve the quality of life for the millions who live with eye disease.

- Glaucoma is a chronic disease in which the neurons, called retinal ganglion cells, undergo degeneration. Another trait of developing glaucoma is an increase of pressure within the eyes. *Raymond Chuen-Chung Chang, Ph.D. at The University of Hong Kong* is utilizing a novel approach to use the body's immunity to protect neurons in the eyes. Dr. Chang's study aims to define which factors or what conditions for the activation of immune cells can lead these cells to elicit protective effects against glaucoma — and hopefully pave the way for therapeutic interventions against loss of vision.
- A common surgical form of reducing eye pressure is known as laser trabecular ablation, or LTA, which can often have damaging side effects. *Dr. Deepak Edward of the University of Illinois*, is seeking to improve this technique by studying the use of an ultrafast Titanium Sapphire laser, which has been found to overcome the problems of the slower procedure. By looking at changes in the treated eye over a period of up to two months, Dr. Edward hopes to better understand the interplay between mechanical effects of the laser and the biologic response that might occur during the healing process.
- The eye depends on a clear nutritive fluid called aqueous humor in order to survive — a substance which can be lacking in people with glaucoma. *Haiyan Gong, M.D., Ph.D. at the Boston University School of Medicine* is hoping to increase aqueous humor outflow, which can lead to the development of novel therapeutic agents for the treatment of the elevated pressure associated with glaucoma.
- Many researchers believe that glaucoma has major genetic components, and though several genes have been identified, so far these only account for 5% of glaucoma cases. Studying twins, *David Mackey, M.D. of the Royal Victorian Eye & Ear Hospital in Melbourne, Australia*, will attempt to discover where twins consistently have similar DNA markers. Discovering the genes that cause glaucoma will enable other family members to be tested and predict who is at high risk or low risk of developing glaucoma, allowing for better early screening and potential new treatments.
- At *Marshfield Clinic Research Foundation in Wisconsin*, *Catherine McCarty, Ph.D.* is working on a study that may change treatment for patients with glaucoma and ocular hypertension using beta blockers — a common class of medication used to lower intraocular pressure. Interestingly, this same class of medications is used orally to treat high blood pressure, and genetics have been shown to play a role in how a person responds to this medication. Dr. McCarty believes that genetics is also associated with how a person responds to a prescription for medication to lower intraocular pressure.

New Treatment


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accelerated rate during aging and is thought to play a role in many aging-related diseases, including atherosclerosis, diabetes, arthritis, and Alzheimer's disease.

Because alagebrium breaks the abnormal bonds between proteins, it is being investigated as a treatment for diseases including hypertension. In fact, clinical trials using human patients have shown that it improves heart function and reduces hypertension. In animal models, alagebrium is being evaluated as a treatment for macular degeneration, Alzheimer's disease, and arthritis, among other diseases.

Dr. Kaufman — with the help of his associate

researcher Julie Kiland — will administer alagebrium in animal models and examine the effects on intraocular pressure, eye fluid drainage, and ciliary muscle function, with the hopes that all will improve significantly. They will also examine how long the effects of alagebrium last.

Investigations like Dr. Kaufman's are the direct result of your support, and offer the 2.2 million Americans with glaucoma significant hope for the future. With your help, since the program's inception, NGR has awarded more than \$11.6 million to support basic research into the causes and potential treatments of this disease. 

Non-Compliance a Major Treatment Issue

Study Finds that 47% of Glaucoma Patients Take Drugs Improperly


A recent study published in **Ophthalmology**, the clinical journal of the American Academy of Ophthalmology, shows that as many as 47% of patients receiving glaucoma therapy do not comply with their doctor's prescribed medicine regimen.

"Cost of medications, multiple medications, confusing instructions all contribute to a patient's non-compliance to their therapy," said Alan L. Robin, M.D., author of the study and an Academy member. Dr. Robin believes that non-adherence to their prescribed treatment is probably what causes many glaucoma patients to go blind.

As examples, Dr. Robin refers to a 2003 Harris poll that found:

- One-third of patients surveyed took their medications less often than directed
- One-quarter delayed refilling prescriptions
- One-fifth failed to fill prescriptions
- One-fifth stopped taking a medication sooner than prescribed

"Non-compliance is a bigger problem than we imagined, and glaucoma therapy is only the tip of the iceberg," added Dr. Robin. "It becomes a life-and-death situation for doctors to educate and motivate their patients on their therapy and with glaucoma; this may lead to visual disability and blindness."

If you or a loved one is on glaucoma medication and have any questions or concerns about your prescription therapy, please contact your eye doctor immediately. 

Adapted from the following source: American Academy of Ophthalmology

Advancements in Research


Scientists Discover Enzyme that Contributes to Glaucoma

At its worst, glaucoma causes blindness by killing retinal ganglion cells – the cells that make up the optic nerve. Today, scientists at the Massachusetts Eye and Ear Infirmary (MEEI) are a step further in their understanding why retinal ganglion cells die – and a major leap closer to developing more effective treatments for glaucoma.

In findings posted on the **Proceedings of the National Academy of Sciences** website in August, 2005, scientists revealed the discovery of an enzyme, calcineurin, that contributes to retinal ganglion cell death in animal models. Better yet, they have successfully used a drug to inhibit the death of these cells.

"In glaucoma," Cynthia L. Grosskreutz, M.D., Ph.D., the senior author of the study and co-director of the Glaucoma Service at MEEI says, "we know that the disease progresses because the retinal ganglion cells die. Our goal is to figure out what mechanisms govern this cell death and to develop a strategy for protecting the cells from the things that cause them to die."

"We use animal models of glaucoma to identify calcineurin as a contributor to retinal ganglion cell death in experimental glaucoma" she adds. "We were able to use the drug FK506 to inhibit calcineurin and observe significant protection of the optic nerve and retinal ganglion cells."

"Better understanding of how and why the retinal cells die can help us develop better treatments for this disease, which affects more than 66 million people worldwide and is the leading cause of irreversible blindness," Grosskreutz said. 

Adapted from the following source: Massachusetts Eye and Ear Infirmary

PLANNED GIVING UPDATE

Leaving a Lasting Legacy

Many of our most faithful donors want to do more than simply make an occasional gift to National Glaucoma Research — they want to play a major role in finding a cure! One of the most effective ways to do that is by leaving a **bequest to National Glaucoma Research in your will**, which will allow us to continue our vital investigations on behalf of those with glaucoma.

Another wonderful way to help advance our research — and receive current income — is through a **charitable gift annuity**.

A charitable gift annuity is an agreement between you and National Glaucoma Research in which you transfer cash or appreciated assets. In return, you (or a person of your choice) will receive guaranteed fixed income for as long as you live – as well as significant tax savings. The income that you receive depends on your age and the amount of the annuity.

Have questions? Would you like more information on planned giving? Please contact Gayle Handiboe, Manager of Development, at gandiboe@ahaf.org or call 1-800-437-2423. And thank you for thinking of National Glaucoma Research!