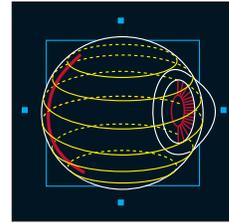


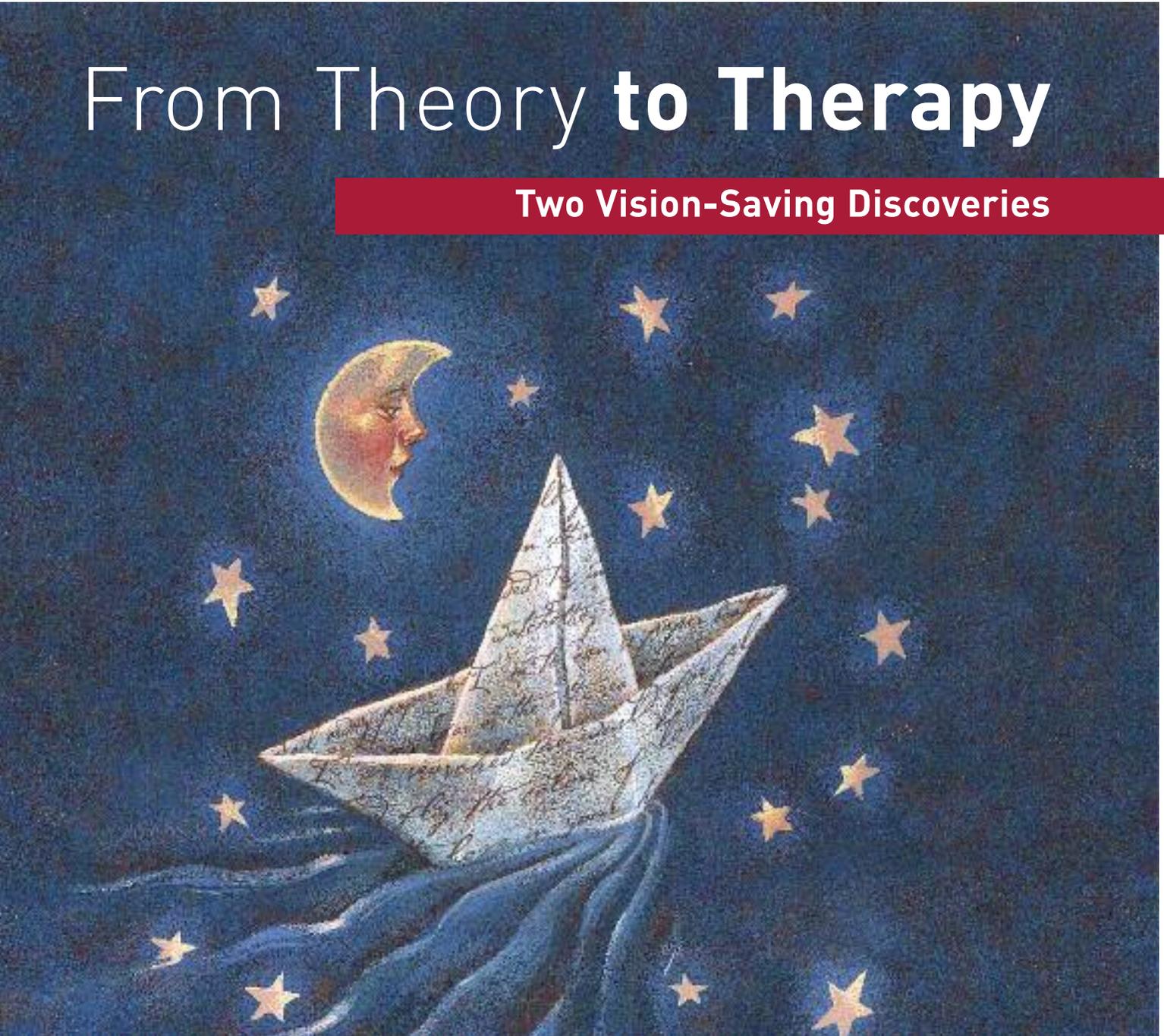
# Sightings



Schepens  
Eye Research  
Institute

## From Theory **to** Therapy

Two Vision-Saving Discoveries



Autumn 2009



An affiliate of  
Harvard Medical School

# From the President

**As many of you know I have been part of the Schepens Eye Research Institute community for many years as a Board member and now as President and Chief Operating Officer. As a Trustee I knew that Schepens scientists were leaders in eye research, working in multiple scientific disciplines to uncover the complex causes of eye disease and restore vision.**

Now that I spend every day working with our researchers, I have developed a much greater understanding and appreciation for the real progress they have made—from scientific theories on the causes of visual dysfunction to potential breakthrough therapies that have progressed to either clinical trials or the pre-clinical stage. This is a complex and painstaking process with each step of the way being equally critical. From theory to therapy describes the continuum of discovery taking place in each of our labs. Ideas are born, tested and developed at Schepens all the way through to clinical trials in patients. Partnering with pharmaceutical and biotherapy companies allows discoveries to advance to that final step—being commercially available to those in need.

To illustrate the continuum—from theory to therapy—we have chosen the stories of two compelling observations; one that led one of our scientists from his discoveries using stem cells and animals to now treating patients, and another that led our clinician scientist from treating his human patient back to his Schepens lab to answer new questions.

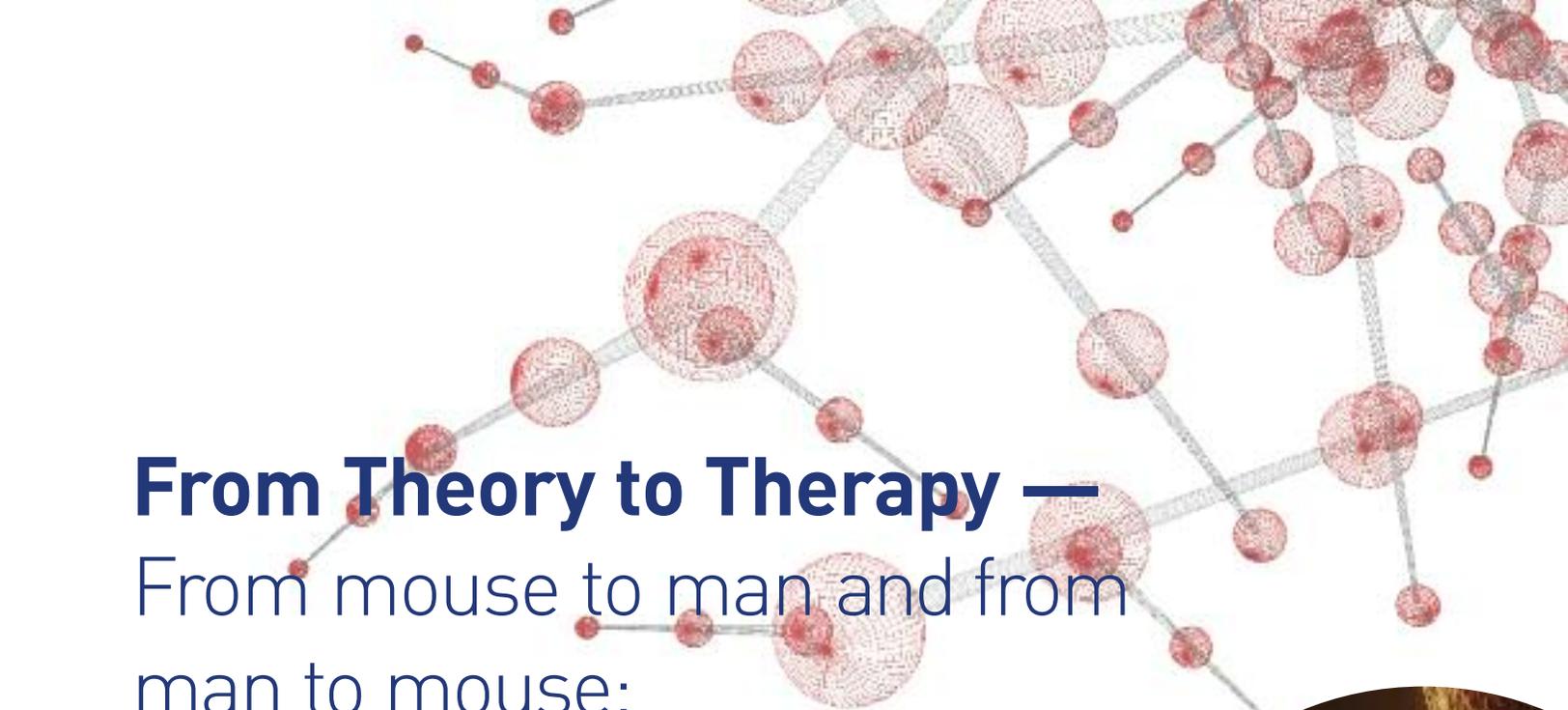


I sincerely hope this issue will give you a revealing picture of the journey from theory to therapy. It is also important to appreciate just how costly it is to advance research from the laboratory to the clinic. Financial support is essential to keep the theories moving through the research pipeline to ultimately making treatments a reality for so many sufferers currently without answers.

Sincerely,

A handwritten signature in cursive script that reads "Kenneth M. Fischer".

**Kenneth M. Fischer**  
President and COO  
Schepens Eye Research Institute



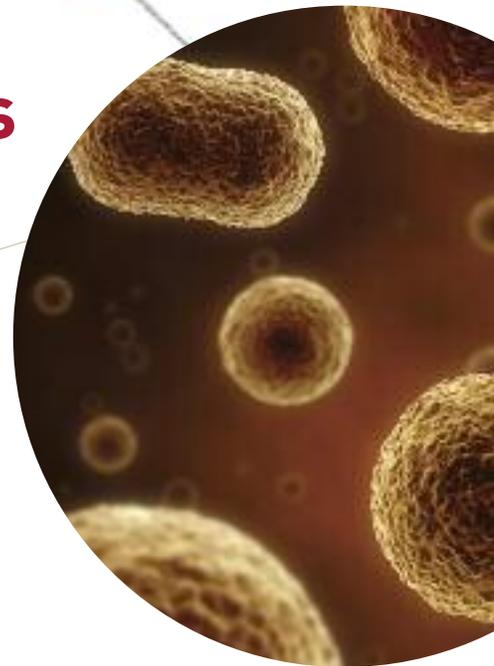
# From Theory to Therapy — From mouse to man and from man to mouse: **Two Vision-Saving Discoveries**

**Imagination is truly the key to any discovery,  
and science to cure blindness is no exception.  
It is the constant reexamination of the facts  
along with creative leaps of thought that give  
birth to innovation in every field.**

Likewise, it is what has brought Schepens scientists to the brink of restoring hope and vision to millions with retinal diseases such as retinitis pigmentosa and age-related macular degeneration (AMD).

“The imaginative insight can come at any point along the discovery continuum,” says Michael Young, PhD, an Associate Scientist who heads the Minda de Gunzburg Center for Ocular Regeneration at Schepens. It can begin as an idea in the lab and end in the clinic as a therapy,” he says.

“Or, the spark can come from an observation in the clinic that leads us back to the lab for answers,” says Kameran Lashkari, MD, a Schepens clinician/scientist who is focused on the study of AMD and other retinal diseases in his laboratory, while also maintaining a busy practice as a vitreoretinal surgeon.



**“Science does not know its debt to imagination.”**

—Ralph Waldo Emerson



Drs. Young and Lashkari are both in the process of discovering new therapies. While their paths from insight to application are different, their goal—improving the lives of patients with blinding disease—is the same.

### **From the Lab to the Clinic**

“I can say most concretely that being able to see the stars again would be a wonderful thing,” says former professional photographer and sailor Ryck Lent, whose ability to see starry nights was stolen 25 years ago, with the onset of retinitis pigmentosa (RP). Lent has been a frequent participant in low vision studies at the Institute and hopes some day his vision will be restored.

Diagnosed with RP in 1980 at the age of 30, Lent responded to the news by leaving his job, sailing the US east coast for two years and going back to graduate school. He has transformed his career and daily life to accommodate the disease.

Today Lent no longer drives, uses a white cane to navigate while walking, and works as an IT professional online where he can manipulate visual input.

Like all RP patients he is slowly losing photoreceptor cells called rods and cones, which are responsible for capturing light and color and details in the retina. The first to go are the rods, located mostly in the periphery of the retina, which explains why stars lose their sparkle. Then cones, too, die. Thus, people with retinitis pigmentosa (RP) first experience defective dark adaptation (“night blindness”), then constriction of the visual field (“tunnel vision”) and eventually loss of central vision.

While his central vision is still fairly good, Lent understands that it, too, will eventually deteriorate.

Helping patients with RP to see the light again has been Young’s mission for the past ten years. Today he is on the verge of using stem cells in clinical trials to repair human retinas damaged by this sight-stealing disease. But his journey began far from the clinic.

Young’s insight came in the form of encouragement and inspiration from one of his mentors, Dr. Rusty Gage, who believed that the retina might be a place where stem cells could flourish and integrate to repair damaged tissue.

“We were skeptical,” says Young, “that is until we witnessed it for ourselves.” Young put his mentor’s theory to the test almost immediately. His first subjects were rats, into whose eyes he injected brain stem cells. He watched in awe as they transformed into retina-like cells.

Further proof came when he transplanted retina stem cells, which not only morphed into retina cells in mouse eyes, but also wired themselves into the optic nerve and appeared to make the mice more light sensitive.





**RP patient Ryck Lent (left) learns firsthand from Dr. Michael Young that stem cells might someday restore his vision.**

Encouraged by positive findings, Young and his team performed the same kinds of studies in pigs who have larger, more human-like eyes, and had similar results. Young was especially gratified by the results with small pigs bred with retinitis pigmentosa.

Nearly a decade after his laboratory insight, Young is now preparing for clinical trials, which he hopes will begin within about three years. To facilitate that critical step, he has enlisted the help of two new collaborators. The first is Reneuron, a company in England with experience developing “immortalized” stem cells – genetically altered stem cells that reproduce indefinitely. “With just a few cells, we can reproduce enough tissue for thousands of patients,” he says. Reneuron is currently engaged in clinical trials using such immortalized cells to heal the brains of stroke patients.

The second new partner is Harvard Center for Human Cell Therapy (CHCT), which has agreed to begin growing and storing the human retina

stem cell tissue for clinical trials. The CHCT helps scientists within the Harvard affiliate community more rapidly translate novel cell therapy protocols from the laboratory to the clinic. The CHCT Steering committee selects promising discoveries from many applicants and CHCT then provides assistance from the technical level to the submission of Clinical Protocols and Investigational New Drug applications.

Over the next three years, Young and his research team will refine their pig studies and make certain that the therapy will be safe for human beings.

“We are not expecting miracles in these first trials,” he says. “Our initial goal will be to regrow some of the rods in the retinas of patients with RP to increase their light perception. Our hope is that the potential of this kind of therapy will improve as we continue to refine our techniques.” Lent’s hope is that the continued success of this research may someday give him another glimpse of the stars in the night sky he loves so much.



AMD patient, Marion Morse (left), feels she owes the vision she has to Dr. Kameran Lashkari.

### From the Clinic to the Lab and Back Again

Two years ago at the age of 89, Marion Morse of Dartmouth stopped driving. “I was having visual distortion and decided then that I shouldn’t be on the road anymore.”

Although driving was the first sign of diminished vision for Morse, she was also gradually losing her ability to see the details of the birds she so loved to watch, and to read without intensive magnification. Age-related macular degeneration (AMD) was slowly destroying her macula, the tiny center of the retina that allows people to see fine details in order to recognize faces, read a book or watch TV.

When she sought Dr. Lashkari’s help, he told her that wet AMD was gradually taking her central vision in both eyes. Initially, with the help of Lucentis, a drug that blocks abnormal blood vessel

growth in the retina, he was able to maintain her vision fairly well. But, when she suffered a hemorrhage behind the macula, emergency surgery to clear the blood and injections of the clot-busting drug TPA were necessary. After surgery, Morse regained her ability to read in both eyes and today is continuing Lucentis treatment in hopes of preserving the precious sight she still has.

Each year, Lashkari treats hundreds of patients like Morse, with varying degrees of success. With no cure available for AMD, finding new ways to detect the disease early, prevent further damage or slow its progression has become one of his major research goals. While it is known that there is a connection between inflammation in the retina and AMD, he had a hypothesis that there might be a connection between systemic inflammation and the development of AMD.

Lashkari began to wonder if some of the chemical substances called cytokines produced by the body when inflammation is present might be associated with development or progression of AMD and potentially could be traced in the patient's blood. If so, a simple blood test might make it possible to identify AMD through a "biomarker" before any signs of clinical diseases were visible to an ophthalmologist.

He and his lab team, headed by research associate Fanny Mo, tested the blood of groups of patients with AMD in several stages and a group of control subjects without AMD. They found that several

factors or molecules associated with inflammation were elevated in the blood of the AMD patients and not in the control group. The next step was to determine if these factors were present in the eyes of people proven to have AMD.

One of the molecules he identified in his patients' blood was also elevated in donor eyes of people with AMD, supporting Dr. Lashkari's belief that the molecule might predict the onset of early AMD. He also found that patients with more severe dry AMD had greater amounts of this marker in their blood than those with milder disease.

**"The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them." —William Lawrence Bragg**

To test his theory further, Lashkari has now taken his discovery to his research laboratory where he can more closely investigate the molecule, its relationship with AMD, and its potential as a way to both identify those at risk of AMD and later as a possible target for drugs.

"In the laboratory, we can more freely manipulate the levels of the molecule and the way they impact the eye," he says, adding that he and his team will be breeding special mice that over- or under-produce or lack the receptor for the molecule. "If it turns out that inhibiting the molecule slows experimental AMD, we can then focus on producing a drug or antibody to neutralize the molecule." says Lashkari.

Once established in animal studies, the new therapy would then be evaluated in human clinical trials.

Grateful for the care she has already received and the vision she still has, Morse says of this new treatment possibility, "If Dr. Lashkari has another treatment and says it will help me, I will do whatever he recommends."

### Two of many

These research projects are but two of the many underway at the Institute, that, with the help and support of friends and donors, could soon change the lives of patients with RP, AMD, glaucoma, diabetic retinopathy, and others.

### The Continuum of Discovery

Schepens Eye Research Institute is a place where ideas become realities. Both Young's and Lashkari's inspiration happened in an environment that nurtured and supported their journeys along a continuum of discovery. The Institute's world-class faculty, state-of-the-art facilities, cutting-edge technologies, and clinical expertise conspired to help transform these insights into discoveries that will improve lives.

These are but a few of the many projects nurtured and supported by the Institute. And, with the help of friends and supporters, Schepens will help guide each on the path to help restore vision to millions suffering from blinding diseases.



# Aspirin and Diabetic Retinopathy

**Question:** Because I have diabetes, I worry about my vision. Can taking aspirin help, and why?

**Answer:** We know that taking aspirin when there is already some sign of diabetic retinopathy will do no harm, and we have reasons to suspect that aspirin may help prevent retinopathy. In fact, it was the members of my laboratory here at Schepens Eye Research Institute who first revealed why and how it might protect the retina.



Diabetic retinopathy (DR) wreaks havoc by blocking the flow of blood and oxygen carried by tiny blood vessels to the retina, the thin tissue covering the back of the eye that captures images and light and transmits them to the brain. Because the retina is starved for nutrients, it reacts by forming new and fragile abnormal blood vessels that leak and further injure delicate retinal tissue. If left unchecked, DR can cause blindness.

Physicians have long known that increased glucose (sugar) levels in the blood of people with diabetes can damage blood vessels and cause clots made of platelets, small cell fragments specialized in forming plugs. They often prescribe aspirin, an anti-platelet agent, to help prevent the formation of those clots.



In our research we learned that it is not only the heart blood vessels that form these clots with increased frequency in diabetes. The tiny capillaries that feed the retina, too, have literally thousands of tiny, even microscopic blood clots, numbering four times the amount found in people without diabetes. These clots—formed mostly by platelets—reduce the flow of blood and thus nourishment to the retina, and ultimately trigger the growth of the destructive and leaky new blood vessels.

Because a low dose of aspirin (85 mg per day) has been successful in protecting the cardiovascular system, my research team and I believe that it may also help protect the retinal vessels in people with diabetes. However, before we can recommend or prescribe aspirin as a standard therapy specifically for diabetic retinopathy, we must complete several tests and a clinical trial to confirm our beliefs.

In any case, it is very important not to begin an aspirin regimen on your own. Every person with diabetes is different and should be treated individually. Be sure to seek your physician's advice before starting this or any other therapy.

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Mara Lorenzi, MD, is a senior scientist and the George Frances Levin Scholar in Diabetic Retinopathy. She is also a professor of ophthalmology at Harvard Medical School and a clinical associate in medicine at Massachusetts General Hospital. The focus of her research is understanding how increased blood sugar levels can damage blood vessels in the eye and lead to diabetic retinopathy, and how to prevent or slow that process. ●



Barbara and Ken Burnes (left);  
Dr. Michael Gilmore, Ken Fischer  
and Ken Burnes touring the  
Gilmore lab (right).



## Champions of Vision Research

**For those of you who do not recognize his name, Kennett (Ken) Burnes is Chairman of the Schepens Board of Directors. In 2000, while President and CEO of Cabot Corporation, Ken was introduced to the Institute by his friend and former Schepens Chairman, J.H. Walton, Jr. For nearly a decade now, Ken has been a man on a mission—to help Schepens succeed in its quest to fight blindness by discovering new treatments through research. Even though eye disease has never touched him personally, he is committed to promoting Schepens’ sight-saving research to help those affected by vision loss.**

Ken considers himself honored to be Chairman of the Board at Schepens. “Whenever I meet with the scientists and administration, I am more convinced that the future of treatment, and even cures, for every eye disease from macular degeneration to glaucoma or dry eye will come from Schepens. Through my service as Chairman and my financial support I can also play a small role in improving the lives of people touched by vision loss. That is what makes my contributions and involvement so meaningful.”

Well aware that funding is critical to research progress and concerned about the fundraising challenges associated with the recent downturn in the economy, Ken stood up and made an important personal decision to significantly increase his support. Recognizing that this was not a time to slow the forward motion of scientific breakthroughs



at the Institute, Ken and his wife Barbara have generously made a six-figure “challenge” gift to stimulate research at the Institute. The challenge Ken offered to the Schepens community was for each of them to double their previous year’s Annual Fund support. This has prompted many donors to recommit themselves to supporting research, but more help is needed.

While larger organizations and universities have significant financial reserves to carry them through economic hard times, smaller Institutes such as Schepens are forced to search for scarce new sources of funding and have greater dependence on those who have traditionally provided support. Although even a substantial six-figure gift to a large university may not make any noticeable difference, Ken knew his gift to Schepens would have tremendous impact in sustaining research programs, supporting scientists, and enabling pursuit of new ideas.

The turmoil in the financial market has affected us all and is causing many to re-examine their charitable giving. But the Institute is indeed on the verge of helping those afflicted with eye disease and those who will feel its impact themselves or through a loved one as the population ages. It can happen to any one of us, so please be extra generous this year. From everyone at Schepens Eye Research Institute, thank you for your ongoing friendship and your past generosity.

*Please contact Melanie Saunders at 617-912-2564 to find out how you can make a difference for today, tomorrow, and for our children’s future.*

## Ask the Expert • Peter Bex, PhD

**Question:** My son was diagnosed with amblyopia two years ago, but the corrective patch is making the surrounding area feel “itchy,” and his classmates are teasing him. Is there any promising treatment to strengthen his weak eye without the patch?

**Answer:** Your son is not alone. Amblyopia is the leading cause of visual impairment in children. Around three percent of children under age six have this condition. Often referred to as lazy eye, it is characterized by decreased visual acuity in one eye that cannot be corrected with glasses and frequent visual distortions and can cause a child to lose three or more lines on a reading chart during an eye examination.

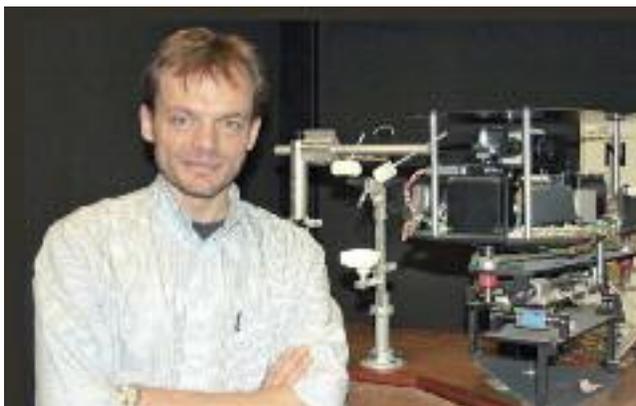
Experts suspect that amblyopia is caused by any situation that consistently prevents clear vision in one eye and not the other, such as in strabismus, where one eye is turned in or out. Because in normal vision the eyes work together and transmit images to the brain in stereo, amblyopia confuses the brain, which then suppresses vision in the troubled eye. If not treated, vision may never reach normal levels in the “lazy” eye.

As you know, preferred treatment for many years has been patching or putting eye drops in the dominant eye to make the amblyopic eye work harder. Unfortunately, 25-50 percent of the time, this treatment doesn’t work because it is difficult to monitor the compliance of children, who often experience skin irritation from the patch and harassment from their peers. And drops can impede a child’s sight in an emergency



situation. Moreover, even when these treatments provide good vision in each eye, they rarely restore the stereo cooperation of normal vision.

There is some hope for an alternative treatment, however. My laboratory is now creating a computer-based stereo video system that uses a game format, which we believe will be more effective and more appealing to kids. It consists of a pair of video glasses attached to a computer and controlled by computer software that can display the same or different images to each eye. Because



**Dr. Peter Bex is an Associate Scientist at Schepens Eye Research Institute and Associate Professor of Ophthalmology at Harvard Medical School. His research uses behavioral assessment of visual function to increase understanding of visual processing in people with vision loss from diseases such as macular degeneration, glaucoma and amblyopia. The ultimate goal is to help people maximize the vision they still have. ●**

competition between the two eyes is causing the amblyopia, if we artificially correct the image given to the lazy eye, we believe that the brain will correct the visual distortion. Over time, the two eyes will begin to work together.

This system will also make it easier to measure the amount of distortion in the lazy eye, monitor compliance with treatment and assess the progress of therapy. Each day, there will be a computer record of the child's participation in treatment and visual status. The natural offshoot of this will be to create age-appropriate computer games that will keep kids engaged in the process without feeling burdened by it.

While we have designed, created and are now testing a prototype of the system, we are now searching for a computer software company who can help make this innovative treatment available for any child who needs it. ●

## *Charitable Giving Through your IRA Opportunities for Current & Future Gifts*

**Individual Retirement Accounts (IRAs) offer tax-efficient opportunities for supporting Schepens Eye Research Institute—either through a current gift or a deferred gift payable at death. The benefits of a current gift from your IRA are only available for a limited time, as the law that makes them possible expires December 31, 2009. However, the benefits of making a future gift from your IRA are available in 2009 and beyond. In fact, the tax benefits of such deferred gifts extend beyond IRA's to include other retirement accounts such as 401(k)s and 403(b)s.**

### **Gifts in 2009**

Recent legislation allows a person over age 70½ to make up to \$100,000 of charitable gifts directly from an IRA to the Schepens Eye Research Institute, as long as the gift is made in calendar year 2009. Although the donor will not be able to claim a charitable income tax deduction for the gift, the

continued on page 14

donor will benefit by not having to report the IRA distribution as taxable income. Such a gift is an excellent option for anyone who wanted to use IRA funds for charitable giving but did not want to take a taxable distribution from their IRA.

For certain donors, a gift from their IRA in 2009 has particular appeal. The biggest winners under this new law are folks over age 70½ who take the standard deduction. If such donors made a gift by writing a check they wouldn't receive any tax break because they do not itemize their deductions. By making a gift through their IRA, they avoid the income taxes that would be due if they took that same distribution for themselves.

Also benefiting from this law are individuals who live in states that provide no tax benefits for charitable gifts. Connecticut, Indiana, Michigan, New Jersey, Ohio, Massachusetts and West Virginia do not allow itemized deductions. Eligible donors in these states may save state income taxes by making a charitable gift to Schepens from their IRA instead of from their checking account.

Others who may also benefit from this law are donors over 70½ whose annual charitable deductions exceed 50% of their adjusted gross income (AGI) as well as taxpayers whose deductions and exemptions are phased out because their income exceeds certain thresholds.

### **Future Gifts – Bequests**

A planned gift or bequest through your will, trust or other estate planning vehicles can be a wonderful way to support the Institute's mission to eliminate blindness in future generations. Perhaps the most tax-effective way to remember Schepens Eye Research Institute in your estate plans is by naming Schepens Eye Research Institute as a beneficiary of your IRA or other retirement account.

Although, all bequests to the Institute avoid estate taxes, gifts of your retirement accounts at death, also avoid income taxes. When you leave a retirement account to a family member or other individual, that person will have to pay income taxes on the distributions they take from that account. Conversely, if Schepens receives your retirement account upon your death, we do not incur any income tax liability because we are a tax exempt organization. If you were planning on leaving assets to

Schepens in your will or trust, and naming family members as beneficiaries of your retirement accounts, you may be able to leave more after-tax money to your loved one by doing the reverse.

To leave all or a portion of your IRA or other retirement account to Schepens, all you have to do is fill out your retirement plan's beneficiary designation form naming Schepens Eye Research Institute as a beneficiary upon your death. If you're married and you want your spouse to be the primary beneficiary, you may name the Institute as a contingent beneficiary. In either case, you would be providing meaningful and significant support to our future research.

*To learn more about making a gift from your IRA in 2009 or naming Schepens Eye Research Institute as a beneficiary of your retirement accounts, please call the Development Office at (877) 724-3736 or send an email to: [george.constant@schepens.harvard.edu](mailto:george.constant@schepens.harvard.edu)*



## Save the date

For the Schepens Eye Research Institute's annual Florida symposia series on Macular Degeneration and other blinding diseases.

### Learn about:

- The Institute's pioneering research in regenerative medicine targeting AMD, other retinal diseases and optic nerve disorders
- The latest treatment options and new treatment combinations for macular degeneration
- Understanding and living with low vision

For more information, please contact Ann Marie Ware at [Annmarie.ware@schepens.harvard.edu](mailto:Annmarie.ware@schepens.harvard.edu), (617) 912-2573 or 1-877-724-3736.

### West Coast Venues

#### Ft. Myers

Friday, January 15, 2010  
Broadway Palm Dinner Theater  
1380 Colonial Blvd.

#### Naples

Saturday, January 16, 2010  
Naples Hilton Inn  
5111 Tamiami Trail North

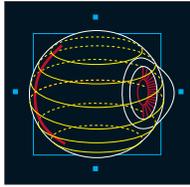
### East Coast Venues

#### Palm Beach

Thursday, February 11, 2010  
The Colony Hotel  
155 Hammon Ave

#### Boca Raton

Friday, February 12, 2010  
Boca Raton Marriott  
5150 Town Center Circle



**Schepens Eye Research Institute**

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## Vision of Beauty Luncheon

**Wednesday, December 2, 2009**

**The Mar-A-Lago Club**

**1100 South Ocean Boulevard, Palm Beach, Florida**

- Season kick-off event for Schepens Eye Research Institute
- Featuring a fashion presentation from Neiman Marcus Palm Beach
- With special guests of honor Olivia Newton-John & John Easterling
- Silent Auction featuring Judith Ripka Jewelry
- Raffle for a \$10,000 shopping spree at Neiman Marcus Palm Beach
- Tickets are on sale for \$250 each



### Vision of Beauty Committee Chairs

Grand Honorary Chair: Hermé de Wyman Miro

Honorary Chairs: Judith Murat Grubman and  
Kathryn Vecellio

Chairwomen: Colleen Bain, Sandra Krakoff, Kay Lyons,  
Anne Moran, Monika Preston, Nancy Raquet,  
Linda Salandra-Dweck, Laurie Silvers and Andrea Stark

**Kathryn Vecellio,  
Hermé de Wyman Miro,  
Beth Pine, and  
Judith Murat Grubman.**

**Please contact Ann Marie Ware to purchase tickets or for  
more information at 1-877-724-3736.**