Regenerative Medicine—Science Fiction Becomes Reality
From the Chairman

How can we find cures for blindness? This seemingly simple question is the one that we as an organization are called to answer. Schepens Eye Research Institute fights blindness by developing new technologies, therapies and knowledge to retain and restore vision. Through a continuum of discovery, the Institute works toward a future in which blindness is prevented, alleviated, and, ultimately, cured.

This continuum starts with fundamental scientific insights that open up new research areas and identify new approaches for solving old problems. The National Institutes of Health often fund such research, but not always. New ideas break conventions and often turn closely held beliefs on their head. In a world where funding decisions are made by scientific peers, it is often difficult to get support for truly new ideas. Visionary individuals, some of whom you will learn more about in the pages that follow, have joined the Institute to make visionary investments in ideas that are several steps ahead of the mainstream. Such investments leverage the enormous support we receive from the federal government to continue to produce rigorous, innovative, useful research into vision and vision disorders.

In the middle of the continuum are technologies, therapies and models that are ripe to make an impact on patients’ vision health today. Our scientists collaborate with private industry to develop new treatments and further refine existing ones. Through these partnerships, our researchers are continually reminded of urgent clinical needs, and our corporate partners reap the benefit of decades of federally funded research.

At the end of the continuum, the Institute turns its attention and expertise to defining the future of vision research. As keynote speakers, scientific consultants, study section members, visiting professors, and expert collaborators, our researchers set the course for new approaches to solving one of the major health challenges of our time. Those who trained at the Institute take the Institute’s visionary approach to research with them to leadership positions around the world, in both clinical and research organizations.

As an organization we continue to push forward aggressively in the fight against blindness, and our efforts ripple throughout the research and clinical communities, leading us all closer to answers. By stewarding and supporting this important work, private individuals like you make an enormous impact on blindness today, tomorrow and into the future.

Sincerely,

Kennett F. Burns
Chairman of the Board
Schepens Eye Research Institute
President and Chief Executive Officer, Cabot Corporation
Preserving the proud legacy of Dr. Charles Schepens’ many contributions and innovations is one of my greatest responsibilities as president of Schepens Eye Research Institute.

Maintaining a fresh awareness of clinical needs and priorities remains an important part of this legacy. Our faculty are key members of the Harvard Department of Ophthalmology and participate in clinical rounds and other activities that expose them to the reality faced by patients every day (see Q&A with Dr. Eli Peli on page 8 for an example). This approach allows us to ensure that our research addresses the lived experiences of those struggling with limited vision or blindness.

The other very real aspect of preserving the legacy is the challenge of maintaining the Institute’s position at the cutting edge of innovation and securing this position for the long term. At a time when federal research funding is shrinking, fixed costs are expanding, and state and federal compliance is requiring more and more infrastructure, supporting the research into cures for blindness presents greater challenges than ever before. However, our recent discoveries, some of which are featured in the cover story on regenerative medicine in this issue of Sightings, offer proof that even in this challenging research environment Dr. Schepens’ spirit of innovation continues to thrive.

Why is regenerative medicine so important? Improved health care has resulted in dramatic demographic changes in developed countries, causing an increase in the prevalence of diseases associated with aging. Many significant human diseases arising from the loss or dysfunction of specific cell types in the body, such as Parkinson’s disease, diabetes and cancer, are becoming increasingly common. Similarly, the greatest challenges in eye health are coming from the diseases of the aging eye, e.g., macular degeneration, glaucoma, and diabetic retinopathy.

Stem cell research and regenerative medicine offer unique opportunities to prevent and treat these blinding eye diseases, as well as new ways to explore fundamental questions of biology applicable to other areas of health care, such as cancer. The current optimism over potential stem cell therapies is driven by new insights into genetics and developmental biology, enabling us to harness stem cells’ regenerative and curative properties. With Schepens Eye Research Institute’s stem cell work already in clinical trials, we are determined to bring the benefit of this new technology to the aid of patients and their families.

Visionary research infused with an acute awareness of clinical needs – this is how the Institute continues to carry the Schepens’ legacy forward to maintain its place at the forefront of research, making a real difference in the lives of those struggling with limited vision.

Sincerely,

Michael S. Gilmore, PhD
President, CEO and DeWalt and Marie Ankeny Director of Research
Regenerative Medicine—
Science Fiction Becomes Reality

Growing new organs, new limbs, new eyes? It sounds like the stuff of science fiction. Today, fiction is becoming reality.

With regard to the eye, Schepens Eye Research Institute plays an essential role in tapping the potential of this new scientific possibility. Known as regenerative medicine, this approach promises to save the sight and the lives of millions worldwide.

“Regenerative medicine is really the future,” says Charles de Gunzburg, a long-time trustee and supporter of the Institute who was its first partner in exploring this futuristic field. “It started as a dream of Dr. Charles Schepens to find ways to transplant whole retinas and optic nerves. It has evolved into a mission to transplant and stimulate stem cells and the body’s own resources to regrow and repair itself,” adds de Gunzburg, who several years later, at the request of Dr. Wayne Streilein, established the Minda de Gunzburg Center for Retinal Transplantation in memory of his mother.

“The ultimate aim of this new field is to prolong life and improve its quality,” says Assistant Scientist Dr. Kameran Lashkari, whose research with adult stem cells holds great promise for those who suffer from retinal diseases. “The eye is a perfect place to begin.”

Associate Scientist Dr. Michael Young, whose regenerative research has already improved vision in mice, agrees. “Because the eye has been studied so intensely and is so accessible, it will be one of the first organs to reap the benefits of this new approach,” he says.

“And what we learn about the eye, which is an excellent model of the central nervous system (CNS), will quickly translate to other parts of the body, improving treatments for such diseases as Parkinson’s and multiple sclerosis, among many others,” says Dr. Dong Feng Chen, an associate scientist at the Institute, who has already successfully regrown optic nerves in mice.

These three scientists and others, supported by benefactors like Mr. de Gunzburg, are reawakening the regenerative capacity of the human eye. “We are committed to exploring the full range of regenerative possibilities,” says Dr. Michael Gilmore, president and CEO of Schepens Eye Research Institute.

While many parts of the body (such as skin and liver) continue to grow and regenerate after birth, some of the most critical tissues do not, such as the spinal cord, the brain and the eye. Hence, if they are damaged after birth, retinal cells (which capture light and images) and the optic nerve (which transmits images to the brain) cannot replace themselves. Schepens Eye Research Institute’s regenerative medicine researchers are learning why our initial regenerative abilities shut down, and how to reactivate or circumvent the shutdown—helping us to retain and restore vision.
Regenerative Medicine: Solving the Mystery

From Babies to Boomers—

In his search to restore the vision of tiny premature babies with retinopathy of prematurity, Dr. Lashkari came upon a way to help all victims of retinal diseases, which are becoming epidemic as baby boomers age.

In premature babies, the blood vessel network in the eye is not fully formed, and remains unformed as the baby is given life-saving oxygen after birth.

The condition often resolves after the baby is taken off oxygen or with laser surgery, but in a small number of cases, the tiny retinas form scar tissue and totally detach. During reattachment surgery, surgeons remove the bits of scar tissue and discard them.

“The hope is that our collaboration will deliver this new therapy for blinding disease of the retina within a few years.”

Dr. Kameran Lashkari
Dr. Lashkari and his research team put that scar tissue to use, believing it might still contain “progenitor” cells that could develop into healthy retinal cells. Progenitor cells are like stem cells but are more mature and more restricted in what they can become, while stem cells can transform into many different types of tissue. The team found the cells they were looking for. When they tested them in lab cultures, these progenitor cells turned into retina-like tissue. And, when injected into the damaged eyes of chicks and mice, they reacted in the same way.

“We are now evaluating the ability of these newly minted retina cells to communicate with the optic nerve and the brain to help the animal see better,” says Dr. Lashkari.

If results are positive, human trials could follow soon, according to Dr. Lashkari. “The hope is that this discovery will deliver a new therapy for blinding disease of the retina within a few years.”

Funding for this research has been provided primarily through the generosity of the Canary Charitable Foundations through Mr. de Gunzburg.

Dr. Young’s research has already shown that these transplants can become retina cells, migrate to where they are needed in the damaged eye, and wire themselves into the optic nerve. Most importantly, he and his team have proven that mice with these newly transformed retina cells have improved vision.

To do this, Dr. Young first took retinal and brain stem cells from “green mice”—mice bred with flourescent green tissues—and transplanted them in mice of normal color with damaged retinas. He then tracked and watched the green tissue as it grew and was transformed. To learn whether the new green retinas improved vision, he placed the mice with transplants and control mice (without the transplants) in dark cages and flashed a series of increasingly lower-level light stimuli at both groups over a period of time. Mice are photophobic and stop their normal activity when they detect light. The mice with the stem-cell-derived green retinas responded at the very lowest levels, while the others did not.

Dr. Young and his team are now investigating the same phenomenon in pigs, whose eyes are larger and more like human eyes. He also has created and is now using a more organized way of delivering the stem cells. He grows the stem cells in groups on tiny scaffolds, made of biodegradable polymers, and implants the whole sheet of cells in damaged eyes.

Collaborating with scientists at Reneuron, one of the Institute’s corporate partners, Dr. Young is finding ways to begin testing what he has learned in human beings. “Our challenge, as we initiate...
human studies,” he says, “will be to grow enough cells so we have an ‘immortalized’ supply and do not need to keep going back to the source.”

Dr. Young is currently the director of the Minda de Gunzburg Center for Retinal Transplantation.

Turning on the Inside Switch—
Learning to turn on the switches that have shut down the eye’s ability to regenerate is the essence of Dr. Chen’s work.

“This aspect of regenerative medicine is very powerful,” she says. “Harnessing the body’s own capacity for regrowth can avoid negative side effects like rejection, which often accompany tissue transplants.”

Chen has already switched on several dormant triggers responsible for regenerating the optic nerve. In studies using mice, she has found and turned on a gene, and found and eliminated a physical scar, both of which are impediments to optic nerve regeneration. She also believes that the myelin sheath surrounding the nerve may be a third inhibitor of regeneration and is now studying that possibility.

To add one more piece of the optic nerve puzzle, Dr. Chen is investigating regeneration at the cellular level. Her target is the ganglion cells of the retina from which optic nerve cells grow. In late stage glaucoma, ganglion cells are often destroyed, leaving no foundation from which to regenerate optic nerves.

“We are identifying the ‘progenitor’ cells or stem cells sitting in the adult retina that could become ganglion cells and developing ways to stimulate that transformation,” says Chen, who adds that she and her team have already had success. “What we really want to do is to skip the transplantation step and tap the cell’s and the body’s original ability to recreate itself.”

The Gift of Hope
“Schepens scientists have already made enormous progress in this fledgling, fascinating field,” says Mr. de Gunzburg. “I was already a believer, but in the past few years, my commitment has grown even greater. It is an amazing feeling to support the dedicated people at Schepens Eye Research Institute who have fantastic dreams which, when realized, could change so many lives.”

“What we really want to do is to skip the transplantation step and tap the cell’s and the body’s original ability to recreate itself.” Dr. Dong Feng Chen
Question: Two questions. First, how early and often should we have eye exams? Second, you were recently in Central America to promote eye health. Can you tell us why?

Answer: Regular eye exams are absolutely essential for the health of your eyes. While several organizations have guidelines, I follow the recommendations of the American Optometric Association. According to those recommendations, if you have no risk factors for vision loss, children should have an eye exam by six months, at age 3, before first grade and every two years until age 18. They also suggest eye exams every two to three years until age 40, every two years between 40 and 60, and annually after age 60.

If, on the other hand, you have risk factors, consult your doctor on how early and often to get checkups. Risk factors for infants and young children include low birth weight, rubella during pregnancy, a family history of eye disease or severe far- or near-sightedness. Difficulty reading in a school-age child can also be a sign of a vision problem.

This brings me to my trip to Central America. Most of us in the US have access to good eye care. This is not true in many countries, particularly in the third world. So, every few years, my daughter, Dana, and I spend a week as volunteers, testing and caring for children and adults in poor countries.

The experience has been wonderful, first because I travel with Dana, who speaks better Spanish than I and connects instantly with children. And, second, because I never forget the expressions of children who put on glasses and see clearly for the first time.

This August, we spent a week in Nicaragua as part of a special program designed to establish a national system to ensure eye exams and follow-up
care for children to prevent vision-related learning problems. Volunteer Optometric Service to Humanity (VOSH), the group we usually work with, and the Lions Clubs joined forces with UNICEF for this project.

The project began in spring 2006 when some of our VOSH colleagues spent a week training elementary school teachers in the basics of visual screening. The teachers then screened more than 8500 children and identified 250 who failed the screening. When Dana and I and a dozen other volunteers arrived last summer, we evaluated the kids who had failed and another group who had not yet been screened. Our purpose was to assess the skills of the teachers and provide needed follow-up care, including glasses to both groups.

The final piece of the project will be to train local optometrists and ophthalmologists to follow up with the children and their teachers. This will make the system self-sufficient and sustainable, improving the lives of hundreds of kids, a goal we have already achieved in Costa Rica.

A pioneer in vision rehabilitation, Dr. Eli Peli is a Senior Scientist and the Moakley Scholar in Aging Eye Research at Schepens Eye Research Institute and a Professor of Ophthalmology at Harvard Medical School. He is also an Adjunct Professor of Optometry and Visual Sciences at the New England College of Optometry. Since 1983, Dr. Peli has been Director of the Vision Rehabilitation Service at Boston’s New England Medical Center Hospital.
Ask the Expert • Patricia A. D’Amore, Ph.D.

Question: I have “wet” age-related macular degeneration (AMD) and have been hearing about new drugs for this disease. Can you comment on whether they work and how?

Answer: Three new drugs have recently become available for “wet” macular degeneration. This form of macular degeneration, unlike the “dry” variety, is characterized by the growth of small blood vessels known as capillaries under the retina, particularly its tiny center, the macula. The macula is responsible for central vision and activities that require visual acuity such as reading, driving and face recognition. These fragile new blood vessels leak fluid, which collects under the macula, damaging vision. All three new drugs work by blocking the action of a growth factor called VEGF (vascular endothelial growth factor), which has been proven by scientists to stimulate vessel growth (angiogenesis) and their tendency to leak.

Macugen was the first “anti-angiogenic” therapy for AMD and was approved by the FDA in 2004. Although some success has been reported, it has not been as effective as ophthalmologists hoped.

Shortly thereafter, eye doctors began treating patients with Avastin, a drug produced by Genentech that was the first anti-angiogenic therapy approved for treating colorectal cancer. Ophthalmologists reasoned that if Avastin could block blood vessel growth in tumors, it might also affect angiogenesis in “wet” AMD. Extensive testing in what is known as “off label use” has yielded outstanding results.

Lucentis™ is the latest in this series of drugs. Created specifically for the treatment of “wet” AMD, it is very similar in structure and action to Avastin. In a large, two-year study, this drug stopped vision loss in more than 90 percent of patients studied and restored vision in 33 percent.

Scientists are now comparing the efficacy of Lucentis and Avastin, since Avastin is much less expensive.

Side effects are also a concern. For instance, my laboratory has strong evidence that VEGF in the adult is also necessary for the health and integrity of normal blood vessels. The side effects that have been seen in patients taking systemic Avastin support this idea. So, although anti-VEGF therapies are important and effective, further study is needed to assess long-term effects.

AMD is the leading cause of legal blindness in Americans 55 and older and its numbers will jump from nine to 18 million by 2020. Thus, research into these and other medications to prevent and halt its escalation is of vital interest to us all.

Dr. Patricia A. D’Amore is a Senior Scientist, the Ankeny Scholar of Retinal Molecular Biology, and the Associate Director of Research at Schepens Eye Research Institute, Professor of Ophthalmology and Pathology at Harvard Medical School, and Research Associate in Surgery at Boston’s Children’s Hospital. Her research focuses on blood vessel growth (angiogenesis) with an emphasis on the retina. Work conducted in her laboratory, and in collaboration with investigators at Massachusetts Eye and Ear Infirmary, has formed the basis for new drug therapies for “wet” macular degeneration.
Champions of Vision Research

“On the road again, I just can’t wait to get on the road again.” Typically those famous lyrics conjure thoughts of Willie Nelson crooning the song that helped shape his successful music career. However, to Mark Harter, this is a new mantra. For Mark, driving trucks isn’t just a job, it is a way of life, and has been the life he has wanted to lead for as long as he can remember.

Tragically, a motorcycle accident in August 2005 rendered him legally blind. Mark cannot say much about the accident; he has no memories of it. He knows only what has been recounted by witnesses and medical responders. His life changed when he awoke from a three-week coma with no vision in his right eye due to optic nerve damage and 20/400 in his left because of trauma to the macula (the part of the retina that provides central vision).

During his rehabilitation, Mark learned how to read Braille and how to use adaptive technology at the Bosma Vocational Rehabilitation Center for the Blind and Visually Impaired in Indianapolis. Also, his support network of family and friends helped research potential cures to restore his vision. That search led him to Schepens Eye Research Institute, where he learned more about the successful re-growth of the optic nerve demonstrated by researchers in the Institute’s regenerative medicine group.

Inspired by the Institute’s research that might one day restore his sight, Mark gathered his friends, including Craig Zwiener, CEO of Truck.Net, and Pat Fagan, a copywriter for Keller Crescent Advertising Agency, to combine efforts and raise money for eye research while simultaneously giving back to the truck-driving community at large through education and prevention.

Through this collaborative effort, “Eyes on the Road” (www.eyesontheroad.org) was created to serve as a resource to truck drivers and industry professionals with various tips about protecting their vision as well as that of their family members.

continued: next page
“Eyes on the Road” officially launched on the Midnight Trucking Network on Sirius Satellite Radio with hosts Eric Harley and Gary McNamara on December 5, 2006.

Mark has a knack for encouraging others to join the fight against blindness and to help the Institute restore vision for those who have lost sight to disease, whether from injury or age-related causes. He is also quick to remind people not to feel sorry for him, but instead to think positively and use their energy and resources to help him make a difference for everyone with vision loss.

“One of the most important lessons I learned through this experience is to cherish the sight you have and do everything in your power to protect it, including routine eye exams,” said Mark. “It is definitely something I appreciated more once it was taken from me.”

Mark longs for the day that he is again driving an 18 wheeler, shifting through the gears. Until then, he will keep his “eyes on the road” to raise money for vision research, and to educate the driving community about ways to protect sight.

For more information on the Eyes on the Road program or to make a charitable contribution to benefit our vision research, contact Melanie Saunders at 617.912.2564 or melanie.saunders@schepens.harvard.edu. You can also make an on-line donation by visiting www.eyesontheroad.org.
Charitable Remainder Trust’s tax and financial benefits were tailor-made to their circumstances. By structuring their gifts in this manner, the Lincolns were able to reduce taxes on their capital gains, generate lifetime income, and take a significant charitable income tax deduction. Most importantly, their favorite causes would receive a larger gift upon their deaths than they could currently afford to make.

While charity was always high on Dallas and Nancy’s list of priorities, eye research had not been among the causes they supported. That changed in January 2004, when their 43-year-old son, Kent, was involved in a snowmobile accident that rendered him totally blind in both eyes. Since the accident, Kent has been through years of rehabilitation and has endured considerable financial loss, ultimately selling his home to pay off his debts.

Furthermore, Kent’s relationship with his 8-year-old son, Chase, has changed drastically since the accident, and both are now in counseling.

“The Lincolns spent a great deal of time trying to learn about Kent’s injury and the possibility of a cure. Eventually, one of Kent’s doctors made them aware of Schepens Institute, and in particular, Dr. Dong Feng Chen’s research in optic nerve regeneration. This was their first ray of hope when all else was telling them there was no chance Kent would ever see again.

In July, Dallas and Nancy made Schepens Eye Research Institute the sole beneficiary of their Charitable Remainder Trust. Since they no longer need the income that the trust provides, they also decided to relinquish their lifetime interest so that the Institute could use the principal to support Dr. Chen’s work this year.

The Lincolns know that their gift alone will not lead to a cure for blindness, but they hope that it will serve as a call to action for others. According to Dallas, “It is our wish that this act will encourage others to do something similar, and the compounding of contributions will provide enough support for Schepens Institute researchers to enable them to give the gift of sight that we all take so much for granted.”

To learn more about supplementing your income and supporting our research with a planned gift, please call the Development Office at 877.724.3736 or send an email to george.constant@schepens.harvard.edu.
Collings Foundation Private Showing

Schepens Eye Research Institute will host an event at the Collings Foundation estate in Stow, Massachusetts, on Saturday, June 9, 2007. The estate is home to an aircraft collection that spans over 80 years of powered flight including the Wright Vin Fiz (replica), UC-7, and an A-36 Apache, to name a few. For over twenty years the Collings Foundation has recovered and restored many of the true landmark aircraft that shaped world aviation history. Moreover, the estate contains a stunning collection of American classic cars from the Brass Era, the roaring 20s and celebrity cars such as a 1940 Cadillac Limousine V-16, owned by Al Capone.

Please join us for an evening’s journey through history as chronicled by this impressive collection of aircraft and classic automobiles. The evening begins with a cocktail reception followed by dinner and a tour of the entire collection.

Mark your calendars for this remarkable event, “Flight for Sight”, to raise money for vision research while viewing this private collection of vehicles and planes.

For more information or to purchase tickets, please contact Ann Marie Ware at 617.912.2573 or visit our website at www.schepens.harvard.edu.
2006 Vision of Beauty Luncheon Chairwomen: Michele Millard, Katie Vecellio, Andrea Stark and Judy Murat Grubman hosted more than 250 individuals for a program and fashion show at Mar-a-Lago in Palm Beach in November.

**Florida Initiatives**

The Schepens Eye Research Institute’s annual research symposia series will be held in Florida from February 21 through 24, 2007. Last year, this series drew nearly 2,000 year-round and seasonal Florida residents to Palm Beach, Boca Raton, Ft. Myers, and Naples to learn about advances in vision research. Once again we are partnering with Retina Consultants of Southwest Florida and Dr. David Snyder of Delray Eye Associates to present the latest on breakthroughs in eye disease research, targeting macular degeneration and optic nerve disorders, with an emphasis on new work in regenerative medicine. In addition to the presentation, each symposium will include a display of low vision aids presented by The Magnifying Center.

The Institute is grateful for the continuing support of the following clinicians: Retina Consultants of Southwest Florida: Dr. Glenn Wing, Dr. Tom Ghuman, Dr. Donald Fletcher, and Dr. David Snyder of Delray Eye Associates. In addition, we are particularly grateful for the generosity of The Daphne Seybolt Culpeper Foundation, The Magnifying Center, Mr. John Palmer, Ms. Victoria McCullough, Mr. and Mrs. Leo Vecellio, Jr.

*Seating is limited and advance registration is required. Please call toll free: 1.866.258.8505.*

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**Can You Benefit from the Pension Protection Act of 2006?**

*New law provides tax incentives for Charitable Gifts from IRAs – for a limited time.*

You may be able to if...

- You are 70 1/2 years of age or older
- You own an Individual Retirement Account (IRA)
- You want to support Schepens and its mission to eliminate blindness

The Pension Protection Act of 2006 allows individuals aged 70 1/2 or older to make gifts of up to $100,000 directly from an IRA to Schepens Institute, without incurring the tax liability that would normally occur from an IRA withdrawal. However, this provision expires after this calendar year so *this opportunity is only available for IRA gifts occurring in 2007.*

The new law may be most beneficial to those who...

- Do not itemize their deductions and wish to make a charitable gift below the standard deduction amount
- Are forced to reduce their itemized deductions because their Adjusted Gross Income is too high
- Make gifts that are capped by the ceiling of 50% of Adjusted Gross Income on charitable deductions
- Live in states that do not offer a state charitable deduction, such as Massachusetts
- Are required to take minimum withdrawals from their IRA but do not need the additional income

*For more information, please feel free to contact us at 617.912.2571.*

Please consult your tax advisor with regard to your specific circumstances.
Join us for a private tour of antique aircraft and automobiles at the Collings Estate
Stow, Massachusetts

June 9, 2007, 6:00-9:00 P.M.
(more details inside on page 14)