The Window of the Eye
Making a Clear Copy

The Schepens Eye Research Institute
We are coming to the end of a disruptive but exhilarating interval in the life of The Schepens Eye Research Institute. Ten years ago, the Institute embarked on an ambitious plan to redefine and reinvigorate its research programs. During the first six years of this decade, new programs were initiated in inflammation, immunity, and transplantation; in angiogenesis and its regulation; and in retinal degeneration, regeneration, and repair. Existing programs in biophysical optics, in the ocular surface and its diseases, and in macular degeneration causation and diagnosis were strengthened and extended. A Strategic Plan, which was developed in 1998 by the faculty, the administration, and the Board of Trustees, described an even more ambitious agenda for future research development. However, implemenation of this plan was stymied by the lack of additional space for growth. Faced with this dilemma, the Institute moved to enhance its physical facilities. In early 2000, the Institute bought out the long-term lease of Boston Biomedical Research Institute, which occupied approximately 40% of the 20 Staniford Street laboratory building. This made it possible to contemplate the creation of new laboratories (approximately 35,000 square feet), and to consider the renovation of the tired, cramped, and inefficient laboratories occupied at the time by Schepens scientists working in the 20 Staniford Street building. Plans were developed to reach these goals, and these plans were advanced and expanded when the Davis Company purchased Charles River Plaza, where the Institute had leased space to create the Starr Center for Scientific Communication and to house laboratories and offices in approximately 45,000 square feet of space. Charles River Plaza is being redeveloped by the Davis Company, not only to increase commercial space, but to create a six-story, 400,000-square-foot building that will contain new research laboratories for scientists of Massachusetts General Hospital.

The disruption referred to above is being caused now by the extensive renovation and building program that is transforming the Institute’s administration and laboratory buildings at 20 Staniford Street and its laboratories and offices in leased space at Charles River Plaza. The total cost of this program is $38 million, and it will come to completion in the summer of 2004. The exhilaration referred to above arises from the knowledge that virtually every laboratory and administrative office at The Schepens will have been renovated and improved by the summer of 2004. Our scientists will then be able to carry out their important work in state-of-the-art laboratories, second to none in sophistication and efficiency.

Many individuals and organizations have played essential roles in conceptualizing, planning, obtaining the resources, and implementing this successful renovation and construction program. We are grateful to the federal government for construction grants, to our architects and real estate consultants, and to philanthropic individuals and foundations. In particular, I want to express my deep appreciation to members of our Board of Trustees and Corporation who have contributed generously to this effort, giving of their time, their expertise, and their resources to bring it to fruition.

With a physical plant of high quality to match that of our researchers, we can look forward to decades of growth and achievement at The Schepens Eye Research Institute, decades in which discoveries made at the bench will be translated into clinical benefit. Finding the causes and cures of eye disease and eliminating blindness are the ultimate goals of our aggregate efforts. 

Sincerely,

J. H. Walton, Jr.
T
he Schepens Eye Research Institute takes stock of itself once each year, in conjunction with the annual meeting of the Corporation. The past year has been one of significant change for the Institute in which financial pressures have arisen in part from a difficult economy that is resistant to recovery, and from wars in the Middle East that sap resources and our national resolve. These financial pressures have weighed heavily on all not-for-profit organizations, including The Schepens, whose success depends upon private philanthropy. During the current fiscal year, the Institute is operating with budget constraints that are challenging the scientists and the administration to work even harder to maintain our momentum in discovery research. I am pleased to report that The Schepens community is responding to this challenge, and research productivity continues to climb.

Elsewhere in this annual report there is much good news to report. Chairman of the Board Jay Walton describes the striking progress that has been made in our extensive construction and renovation program, transforming our physical plant into a state-of-the-art facility. A group of Schepens scientists reports on their courageous goal of creating an artificial cornea with the hope that it will make it possible to restore sight to thousands of individuals with corneal blindness. The appointment of Schepens Senior Scientist Dr. Eli Peli as the first Moakley Scholar for Aging Eye Research, coincidental with his promotion to the rank of professor of ophthalmology at Harvard Medical School, indicates that our research programs are having success at developing new and novel strategies to improve the sight of individuals already afflicted with vision loss.

I would like to highlight two research developments of the past year which offer hope that new treatments for retinal blindness may not be far away. Senior scientist Dr. Mara Lorenzi, Levin Scholar in Diabetic Retinopathy, and director of the Diabetic Retinopathy Research Center at The Schepens, received a grant from the National Eye Institute to conduct a clinical research project that may reveal a new and simple treatment for diabetic retinopathy. Dr. Lorenzi’s prior research has pointed out that tiny retinal capillaries are the first to be damaged in this dreaded complication of diabetes. She will now test whether drugs such as aspirin and non-steroidal anti-inflammatory agents can promote blood flow in these small vessels — and thereby stop the complication in its tracks. Since diabetic retinopathy is the leading cause of blindness in adults under the age of 60, a treatment that could prevent or even delay this complication would save the sight of many, many patients.

Assistant Scientist Dr. Dong Feng Chen, a member of the Minda de Gunzburg Retinal Transplantation Research Center at the Institute, has just reported in the prestigious international journal Nature Neuroscience that she has discovered the identities of two genes that block transplanted retinal tissue from reestablishing connections with the recipient retina. Using special mice with mutations in these two genes, Dr. Chen and her colleagues have transplanted retinal tissue into the back of the eye and discovered that the transplanted cells were able to integrate robustly with the host retina. Not only does this discovery point to astroglial cells as the main culprits in preventing retinal graft integration after transplantation, but it may very well lead to treatment strategies that would silence these two genes in eyes of normal individuals as a way of promoting acceptance and integration of retinal transplants.

The next year promises to be at least as eventful as the past. We are recruiting a new Director of Research. We eagerly look forward to the prospect of our next scientific leader and the opportunities that this appointment will bring to further enhance our unrelenting attack on blindness and its causes.

Sincerely,

J. Wayne Streilein, M.D.
That is how it is with the human eye. The eye, often described as the window to the soul, has its own window — the cornea. When this thin layer of transparent, clear tissue is damaged or clouded by disease or injury, light cannot enter and therefore vision is impossible, even if the rest of the eye is healthy. And of course, without vision, the soul (and the brain) remains uninformed of the visual richness in the outside world.

In recent years, corneal transplantation has been a miracle cure for many of the diseases that ravage the human cornea and render it opaque. Among the common corneal blinding diseases are Fuch’s dystrophy, which causes a loss of the innermost layer of cells of the cornea; infections that cause inflammation of the cornea and threaten to erode its integrity; and degeneration of the middle layer of the cornea (the stroma) that produces vision-degrading cloudiness. For people nearly or totally blinded by these diseases, corneal transplantation can restore their “clear window on the world.”

The most successful of human organ transplants, nearly forty thousand Americans undergo this procedure each year. There are several reasons why human donor corneas transplant easily. First, they lack blood vessels that would otherwise transport immune cells to the graft (transplant) site and destroy the “foreign tissue.” Secondly, the eye itself is “immune privileged,” which means it has the inherent property of suppressing immunity and inflammation as a way of preventing vision loss. Together, these forces help to promote the acceptance of cornea transplants.

THE CASE FOR AN ARTIFICIAL CORNEA

Despite the undeniable success of cornea transplant surgery, vision loss caused by corneal disease still exists. And several factors contribute to this situation.

First, there are still many people for whom donor tissue does not work, either because immune privilege fails in the eye in need of the transplant, because blood vessels grow into the donor cornea and promote its rejection, or because the underlying original disease continues to damage the new, transplanted cornea tissue. “Patients for whom transplants are impossible are left literally in the dark,” says Dimitri Azar, M.D., professor at Harvard Medical School, associate scientist at The Schepens Eye Research Institute, and director of the cornea service at Massachusetts Eye and Ear Infirmary.

Second, the supply of healthy donor tissue is decreasing while at the same time the demand for corneal transplants increases. Even today, corneal tissue taken from donors after death has a shelf life measured in days to a week or so. Thereafter, the quality of the corneal tissue declines, rendering it unsuitable for transplantation. Thus, long-term storage of corneas for grafting is not an option.

Dimitri Azar, M.D.

Several forces create the increasing demand for donor corneas. As the baby-boomer generation ages, the number of individuals who need cornea transplants increases. Moreover, more than a million Americans a year are opting for LASIK (laser surgery to correct near and farsightedness). Refractive surgery of this type reshapes the cornea to improve vision, which renders the cornea much thinner. This makes surgically corrected corneas unsuitable for future transplantation. The supply of donor corneas in other countries is
even more questionable, given the many cultural and religious taboos and barriers against tissue transplantation. Thus, a growing disparity exists between the number of patients who need corneal transplantation, and the number of corneas available for this sight-restoring surgery.

“An artificial cornea would eliminate many of these issues,” says Azar, who is one of the busiest corneal transplant surgeons at the Massachusetts Eye and Ear Infirmary.

Clinicians are not the only ones seeking an alternative source of corneas. Scientists studying the cornea rarely have sufficient tissue for their research because healthy tissue is used for transplantation. And, the U.S. Department of Defense is looking for a way to use corneal tissue — as a living bandage — to save the vision of soldiers injured on the battlefield.

Scientists at The Schepens Eye Research Institute, therefore, have undertaken the daunting task of creating an artificial cornea out of living tissue. The hope is to design a cornea to withstand the destructive potential of the immune system, to avoid obsolescence, to resist underlying pathology, and to provide a ready future supply for the demand. According to its creators, the artificial cornea will also be available for the military to use as an organic bandage to preserve the eyes of injured combatants. Three Schepens scientists are heading up this research effort: senior scientist Nancy Joyce, Ph.D.; senior scientist James Zieske, Ph.D.; and adjunct assistant scientist Jeffrey Ruberti, Sc.D., who is also an associate consultant at Cambridge Polymer Group.

**HISTORY**

For nearly 50 years, scientists and clinicians have searched for a way to make an artificial cornea. Most have worked in plastic and other nonorganic materials. In fact, a plastic device designed by Marshall Doane, Ph.D., emeritus senior scientist at The Schepens, and tested and used as a last resort for vision-impaired patients by Claes Dohlman, M.D., a professor at Harvard Medical School, an adjunct senior scientist at The Schepens, and a corneal surgeon at MEEI, is probably the closest the medical world has come to an artificial cornea. It is a plastic plug attached to the patient’s own corneal tissue which allows light to penetrate through the otherwise opaque corneal surface to land on the retina.

The thrust in recent years has been to find a way to make an artificial cornea with living cells and tissues. While a number of laboratories have taken up this gauntlet, Schepens researchers believe their work is unique and will ultimately lead to a viable, usable cornea substitute.

**WHERE TO BEGIN?**

Joyce, Ruberti, and Zieske have been working on the development of their artificial cornea for several years. In order to make a perfect copy, the team first needed to understand what nature had in mind when it designed the original. “Those of us who spend entire careers studying the cornea are constantly astounded by its remarkable qualities — some would say it is the most exquisitely organized connective tissue in the body,” says Ruberti.

The cornea is the thin clear tissue that covers the surface of the eye in the area of the iris. To be effective, it must be strong and flexible, able to withstand the everyday trauma of blinking, eye rubbing, and dirt clearing. It must also be perfectly clear to capture the light transmitted from the outside world. And, it must be perfectly shaped to direct the light reflected from the object.

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being viewed to a single point on the retina, which then sends a clear image to the brain.

The cornea has three layers, each with its own purpose and each essential to the cornea’s smooth functioning. The first layer is the epithelium, the outer layer which is in contact with the tear film and the eyelids as they blink. Five to seven cell layers thick, the epithelium is the “skin” of the cornea and protects the inner layers from trauma, bacteria, caustic chemicals, and other invaders. The epithelium continually replicates and grows, sloughing off cells in its top layer with nearly every blink. The middle and thickest layer of the cornea is known as the stroma, which is made up of hundreds of thin layers of collagen fibrils (ropes of collagen) and cells known as keratocytes, which also generate the fibrils. The precise directional organization of these fibrils within each layer and the plywood-like stacking of these layers are responsible for the cornea’s clarity, transparency, flexibility, and strength.

The innermost layer of the cornea is the endothelium, which is a single cell layer at the back of the cornea, bordering the stroma on one side and the aqueous humor on the other side. The endothelium’s purpose is to help the stroma maintain transparency and to keep the cornea thin and nourished. It does so by pumping excess water out of the stroma and at the same time allowing nutrition from the aqueous humor to pass through. Unlike other types of cells, the corneal endothelium does not grow and replicate itself. Once these cells are destroyed by injury, they and their function are lost forever. Corneal endothelial cells are irreplaceable.

**PROGRESS**

The research team is designing and building their artificial cornea layer by layer. “We are working on each layer separately to stimulate its growth and development. Then we plan to put them all three layers together in a very thin ‘Dagwood’ sandwich,” says Joyce. “We believe, with the right conditions, these layers should work together to form corneal tissue and to function as a cornea.”

The epithelium has been the easiest tissue to create, according to Zieske, who has been able to stimulate the growth of epithelium cells in culture, and has published several studies on his success. “The biggest challenges,” he adds, “have been with the stroma, which has a very intricate design, and with the endothelium, which, in the human eye, does not replicate itself.” Both of these challenges are being met with innovation by the three scientists and their laboratories.
Joyce and her laboratory are the first in the world to stimulate corneal endothelial cells to grow and replicate in culture. “As we began to look at these cells, we realized that they had not yet left the cell reproduction cycle. After reviewing the literature, we developed a cocktail of growth factors and other chemicals, which we then combined with the endothelial cells in culture. This helped to push the cells back into the growth cycle and the cells started to divide,” she says, adding that the cells from younger subjects divided many more times than those of older subjects, but they all divided. Among the chemicals she combined were epidermal growth factor, nerve growth factor, and bovine pituitary extract, which contains several other growth factors.

Joyce and her group have also been able to arrest the replication of the corneal cells so that they line up in the one layer necessary to mimic the human corneal endothelium. Having too many endothelium cells can be as damaging to vision as too few, so getting the cells to form a single, flat, organized layer is very important.

With a handle on the top and bottom layers of the cornea, the team is now focusing its major efforts on the stroma, which they all agree is the linchpin that will give structure to their creation.

According to Ruberti, who is considered the middleman in the research effort, the stroma, too, has yet to be replicated in any laboratory. Most scientists, he says, have tried to re-create a stroma by putting stromal cells in a collagen gel. And, while these concoctions of random cells and collagen have sometimes appeared similar to a stroma, they do not have the strength and clarity of living corneal tissue.

Ruberti, who is a bioengineer and works at Cambridge Polymer Group, has found a unique way to build a stroma. Through trial and error, he and his colleague, Dr. Gavin Braithwaite, have found that taking pure collagen and dripping it on a warm disk spinning at very high RPMs causes the collagen to lay down and self-assemble into oriented fibrils that mimic the normal healthy stroma. They subsequently lay down multiple layers changing the fibril orientation direction each time. They have been able to demonstrate the concept in principle, by generating two fibril layers that cross each other at 90 degrees. “A stroma has 500 layers. This is a beginning,” Ruberti says.

Zieske, too, is working on the development of a stroma and has found that stromal cells treated with vitamin C and placed on a layer of fibrils and stromal cells (such as Ruberti’s initial layer) will begin to grow in patterns that mimic a normal stroma. Succeeding layers “learn” from the first and so on, in a process called “contact guidance.”

The two stroma-building techniques are being studied simultaneously. “We believe that a combination of these techniques will end up giving us a viable stroma,” says Zieske.

CHALLENGES

After the scientific team has put the corneal sandwich together, the next challenge will be to ensure that the three-layered living window has the right curvature, one that matches the curve of the human eye. “We are not yet sure how we will make that happen, or whether it is absolutely necessary,” says Joyce. “It really depends on how large a piece of tissue is needed to be an effective replacement for a cornea,” she says. At present, most corneal transplants only need to replace the tiny central portion of a damaged cornea. This is usually sufficient to restore vision.

Another challenge will be making the artificial cornea rejection-proof. “In some ways the burden on the artificial cornea will be greater. It not only has to replace what we have today, it has to be better,” says Azar, who hopes (continued on page 14)
We think slower reading may be due, in part, to changes in the visual system that occur with age. These changes may make it more difficult for older people to take in and identify visual information even when their eyes are healthy and their vision excellent. This would result in less efficient “sampling” of the visual world, and more difficulty processing the visual signal once it has been sampled.

Before investigating our theory, we took a look at what we already know about the visual processes involved in reading.

THE YOUNGER READER

In order to see detailed information, we must move our eyes around the visual scene and sample small chunks of the information available. This is because of the anatomy of the eye, which can only process fine details in the fovea, the tiny center of the retina that is packed with photoreceptors. We move our eyes so that the information we are interested in falls on the fovea. When we read, we move our eyes across a line of type in steps of about seven letters each. Between these steps (known as saccades) we pause, or fixate, for about 250 milliseconds. It is during these fixations that we sample and process the information in the text. It is also during these fixations that the visual system is planning the next one or two saccades needed to successfully gather the next bits of information.

THE OLDER READER

From the results of recent studies, we knew that when older people read, they make smaller saccades than younger people, and they tend to make longer fixations. This means that they can process fewer letters with each fixation and, therefore, require more eye movements to read the same amount of text. It also means that it takes longer to process the information that is available on each fixation. This would, of course, mean slower reading.

VISUAL CROWDING

This finding led us to ask, “Why do older people make these smaller eye movements when they read?” One possibility is that older people might be more susceptible to “visual crowding.” Visual crowding occurs when a visual object (such as a letter) is surrounded by other similar objects. As a result, these objects are harder to identify. For instance, one letter by itself is easy to identify, but surrounded by other letters (as is the case when reading words), it is much more difficult to identify.

While visual crowding is an issue for young and old alike, we theorized that it is more of a problem for older people and may be responsible for the smaller saccades and, ultimately, the slower reading for older people.

TESTING THE THEORY

To test the theory we asked volunteers of all ages with good vision to identify

(continued on page 14)
Peter A.D. Rubin, M.D., FACS, is a graduate of Princeton University and Yale Medical School. He completed his residency in ophthalmology at Manhattan Eye, Ear, and Throat Hospital, followed by a fellowship in orbital oncology and oculoplastics at Massachusetts Eye and Ear Infirmary and Harvard Medical School. Rubin, now the director of eye plastics, orbital and cosmetic surgery at Massachusetts Eye and Ear Infirmary and Harvard Medical School.

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Q: A friend of mine had an eye surgeon, not a plastic surgeon, remove wrinkles around her eyes. Can you tell me about this kind of surgeon?

A: It sounds like your friend went to an ophthalmologist specializing in eye plastics, orbital and cosmetic surgery. Those of us who trained in this field after our ophthalmic education treat a broad range of problems in and around the eye, ranging from the forehead to the mid-cheek. We often use our skills to improve the appearance of this area as it ages, but just as frequently, our goal is to reconstruct it when disfigured by disease or trauma.

While most plastic surgeons work their magic on all parts of the body, we focus solely and intensely on one small yet critical part of the face — the human eye. Our training intimately acquaints us with both the structure of surrounding tissues, muscles, and bones, and the functioning of the eye itself. Always aware of the eye as a complicated, delicate organ, we can offer safe and comprehensive solutions to patients with aesthetic or reconstructive needs.

Here are some of the conditions that call upon our knowledge, skill, and art.

**EYELIDS**
Malpositioned eyelids can block vision or cause constant pain. By removing extra skin and fatty tissue, or by repositioning the elevator muscle of the upper eyelid, we can correct droopy eyelids that impair vision (ptosis). We also perform other procedures to correct rotational problems affecting the eyelid margin, causing it to turn in or out (entropion or ectropion) and potentially causing lashes or skin to damage the eye's surface.

**ORBITAL DISEASES**
Disorders of the eye's orbit (socket), caused by thyroid diseases such as Grave's disease, can force the eye to protrude and prevent it from closing properly, misalign the eyes causing double vision, or, in rare cases, compress the optic nerve and result in loss of visual function. Eye plastics experts can reconstruct the eye socket and allow the eyeball to move back to a normal position.

**TRAUMA, TUMORS**
Trauma to the eye is usually in the form of lacerations to the eyelids or tear ducts or in the form of fractures to the orbit of the eye. Orbital fractures can cause pain, double vision, and, if large enough, disfiguring inward sinking of the eye. Again our skills can repair cuts and fuse bones so that the eye is positioned correctly and can move smoothly.

Tumors, both benign and malignant, may involve many different parts of the eyelids and orbit. As plastics experts, our job is to remove tumors and reconstruct the defect to maximize the patient's appearance and function.

**LOST EYES**
Eyes that no longer function because of injury or disease can be very painful and unattractive. We can surgically remove the nonfunctioning eye, place an artificial implant, and prepare the patient for fitting of a custom prosthetic eye to restore a quite normal appearance.

**TEARING**
Constant tearing because of blocked tear ducts, which normally drain tears, not only can be a nuisance, but is also potentially sight threatening. To relieve (continued on page 14)
Dr. Peli is the perfect choice for the first Moakley Scholar in Aging Eye Research,” according to J. Wayne Streilein, M.D., president of The Schepens Eye Research Institute. A recently appointed professor of ophthalmology at Harvard Medical School, Peli has dedicated his career to improving the vision and quality of life of people suffering from low vision.

Peli’s principal research interests are in the area of low-vision rehabilitation. Trained as an engineer and an optometrist, he is developing and testing new devices to help those with low vision to function better in their daily lives. For instance, he is developing and testing spectacle-mounted telescopes and other devices that help visually impaired people continue driving safely, new television monitors with improved visibility, head-mounted cameras, and display systems to improve mobility and facial recognition and to help with night blindness.

Peli is the author of over 90 scientific studies and holds five US patents. He is also the author of the book "Driving with Confidence, A Practical Guide to Driving with Low Vision."

Senator Edward M. Kennedy and Congressman Michael Capuano joined The Schepens Eye Research Institute in honoring the memory of a champion of eye research, the late Congressman Joseph Moakley, on April 14, 2003. At the event, world-class, low-vision expert Eli Peli, M.Sc., O.D., senior scientist at The Schepens, was named the first Moakley Scholar in Aging Eye Research, and a portrait of the late congressman was unveiled and dedicated.

Dr. Eli Peli

“Dr. Peli is the perfect choice for the first Moakley Scholar in Aging Eye Research,” according to J. Wayne Streilein, M.D., president of The Schepens Eye Research Institute. A recently appointed professor of ophthalmology at Harvard Medical School, Peli has dedicated his career to improving the vision and quality of life of people suffering from low vision.

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The Schepens Eye Research Institute decided to commission the portrait of the late Congressman Moakley and create an endowed chair in his name because of his tireless efforts to obtain federal funding for innovative multidisciplinary eye research.

“Congressman Moakley was a true hero to those of us who are searching for the causes, treatments, and cures for blinding eye diseases,” says Streilein. “He worked relentlessly to make sure that funding for cutting-edge, sight-saving research was not only sustained, but enhanced, even when the odds were stacked against it. Together with Senator Kennedy, he inspired others in the Massachusetts congressional delegation to join this mission, and his inspiration has sustained their dedicated efforts and commitments up to the present.”

According to Donald Korb, O.D., who was Moakley’s optometrist for 30 years and helped him overcome a complex eye condition with special contact lenses, the congressman took up the eye research gauntlet in the early 1980s. In 1998, when an opportunity to promote multidisciplinary research emerged at The Schepens Eye Research Institute, Korb, who in the interim was named a trustee of The Schepens, asked for Moakley’s help. Between 1998 and 2000, Moakley, in his search for additional sources of funding, was able to encourage the Department of Defense (DOD) to create a low-vision research initiative. Through TATRC (Telemedicine and Advanced Technology Research Center), the DOD funded a Low-Vision Research Initiative that enabled Schepens scientists to launch a multidisciplinary research program that evolved into the Institute’s Center for Research on the Aging Eye.

Since then, funding from that Moakley-motivated initiative has totaled $4 million and has stimulated research on macular degeneration, glaucoma, and other diseases common to the aging eye. Moreover, a strong relationship has grown between The Schepens and TATRC, evolving into a Center of Excellence in Military Low Vision Research.
**ODD NAME ... EXTRAORDINARY SUPPORT**

There is nothing odd about the generosity bestowed upon The Schepens Eye Research Institute by the Odd Fellows of Massachusetts.

The Odd Fellows, founded in 1819 as a fraternal organization dedicated to improving and elevating the character of man, has continued to strengthen and develop their original charge to the changing needs of society. Each year, the incoming grandmaster of the Odd Fellows and the president of the Rebekahs (the Odd Fellow’s sister organization) choose a charity for which to raise money.

In 2002, Dick Whelan, the immediate past grandmaster of the Odd Fellows of Massachusetts, and Judy Vaghini, immediate past president of the Rebekahs (the Odd Fellow’s sister organization) choose a charity for which to raise money.

During their successful year as leaders of the fraternal organization, they set a precedent by not only choosing to support the Institute’s sight-saving research, but also by having both branches of the organization raise money and awareness for the same cause. For Dick and Judy, agreeing on eye disease was the easy part. Finding an organization — with strong affiliations in and out of the laboratory, a successful history, vision for the future, and excellent stewards of donated funds — was the difficult task.

Dick explained that both he and Judy have a history of eye disease in their families (retinitis pigmentosa in his and diabetic retinopathy in hers). Therefore, they arrived at the joint conclusion that they would be a stronger force evoking a greater impact if they pooled their resources to raise money for eye research.

Upon a reference from an Odd Fellow member, Dick searched the Institute’s website for more information and was impressed by the nature of our research, longevity, and affiliation with Harvard.

In selecting the Institute as the recipient of their fundraising efforts, the Odd Fellows honored their mantra “to raise the dignity of man” through their joint quest to alleviate blinding disorders and working toward the discovery of cures for eye diseases, such as those that robbed their family members of the gift of sight.

The Odd Fellows and Rebekahs have been in the forefront of organizations helping to make this world a better place in which to live. Odd Fellowship is a family fraternity with activities and programs for every member of the family. Today, there are 42 active chapters in Massachusetts, all of which actively raised money for the Institute during Dick and Judy’s tenures.

Compassion, comradery, and a commitment to improving the lives of those less fortunate embody the essence of the Odd Fellow Organization and their members, making them an “odd” but inspiring asset to the community.

**LIONS ROAR**

The aptly named organization has proven to be the king of the jungle in regards to battling eye disease. The Massachusetts Lions have continuously set a high standard of giving and remain the leader of philanthropic support to the Institute with cumulative support exceeding $4 million over the span of 52 years.

In 1925, the Lions were challenged by Helen Keller to become the Knights of the Blind. They have surpassed their original charge and continue to raise the bar for other fraternal organizations.

To find out more about how your fraternal organization can help the Institute, contact Melanie Saunders at (617) 912-2564.

In 2002, Dick Whelan, the immediate past grandmaster of the Odd Fellows of Massachusetts, and Judy Vaghini, immediate past president of the Rebekahs, combined forces to maximize their fundraising efforts for a non-profit organization that matched both of their philanthropic interests. The Institute was that fortunate beneficiary, receiving $10,000 from the Odd Fellows to aid the progress of vision research.
Florence Cohen’s teenage years were filled with wide-ranging health problems that affected her digestive tract as well as her eyes. The mystery of her condition was solved when, at the age of 19, she was diagnosed with Crohn’s disease, a chronic disorder that causes inflammation of the digestive tract. Her affliction was so severe that at the age of 26 she underwent an ostomy procedure that removed most of her gastrointestinal tract. Though her life would be forever altered, she was grateful to be alive, to be a productive member of society, and to experience the joys of motherhood.

Florence was saddened to learn, however, that the procedure that improved the condition of her life rendered those in third-world countries pariahs. Unfortunately, most ostomates in these countries lack the resources for supplies to help them keep clean. As a result, they are often confined to institutions and are effectively shut off from mainstream society. Florence was so moved by the plight of these people that she became active in Friends of Ostomates Worldwide, an organization that provides supplies and materials to needy ostomates so that they may live their lives with dignity.

Over the years, Florence also experienced serious eye problems that were linked to her Crohn’s disease. In her high school years she suffered from corneal ulcerations that not only impaired her vision but also caused her great pain and discomfort. As part of the treatment, her eyes were often covered with bandages for extended time periods. The experience left her with a sense of what it must be like to be blind. “The thought of going blind is frightening,” says Florence. “It would be heartbreaking not being able to see the faces of the people you love.”

Though Florence’s corneal ulcerations eventually subsided, she developed a retinal hole in her adult years that severely limited her vision in one eye. This condition brought back the painful memories of her adolescence and led to Florence’s interest in The Schepens Eye Research Institute’s mission to eliminate blinding diseases.

Like many of her contemporaries, Florence owned stocks that had appreciated significantly since the time she acquired them. Unfortunately, these stocks did not provide Florence with much income. Then Florence’s financial advisor suggested a way that she could generate higher income from her stocks while providing much needed funding for the future of her favorite charities.

Florence established a charitable trust and funded it with some of her appreciated stocks. The trust provides her with an annual income during her life that is significantly higher than the dividends paid by her stocks. Furthermore, it allows Florence to provide a future gift to The Schepens that will support our research initiatives in the battle against blindness. In addition, every time Florence transfers stock to this trust, she receives an income tax deduction.

Last year, Florence had an opportunity to tour some of the Institute’s laboratories with her fellow William Wolff Society members. She was fascinated by the groundbreaking research that The Schepens is doing — both to find cures to blinding diseases, and to improve the lives of those who are afflicted with low vision. When asked about what motivated her to create a charitable trust to support the Institute’s future research, Florence replied, “Somewhere down the line, your children or grandchildren may benefit from this research.”

We are grateful for Florence Cohen’s foresight as well as that of her fellow William Wolff Society members. Their support will allow us to continue and expand our research activities so that future generations may be given the gift of sight.

To learn more about increasing your income and supporting our research with a life-income gift, please contact George Constant at (617) 912-2572, (877) 724-3736 (toll-free), or at constant@vision.eri.harvard.edu.
At the symposium, Dr. Streilein will make additional presentations to loyal Palm Beach supporters, and then provide an update on stem cell transplantation research, led by Dr. Michael Young of The Schepens. Dr. Young was the featured speaker at the last Schepens symposium, held at the Harriet Himmel Gilman Theater last February. His research uses stem cells derived from the central nervous system, and neuroretinal transplantation in animal models of retinal degeneration.

Seating at the event is limited and reservations are being accepted on a first-come, first-serve basis. Tickets for the luncheon are $85 each. Reservations for the luncheon are available by calling The Schepens Eye Research Institute at 1-888-997-6364 (toll-free).
that patients will some day be able to donate their own healthy cells to be grown and fashioned into new corneas, and these “artificial corneas” can then be reimplanted as a way of ensuring compatibility.

**THE PROMISE**
If progress continues at the pace it is going, The Schepens Eye Research team believes that the scientific and medical community and, most importantly, the vision-impaired community will see an artificial cornea within the next two to five years. *With its creation, the window will be opened.*

**A PIECE OF THE PUZZLE**
The results of our visual crowding research suggest that one of the reasons older adults make smaller saccades when they read is because they need to fixate closer to each of the letters in order to identify them accurately. The longer time they spend fixating may also be due to visual crowding. While changes in visual crowding are not the only reason older people may read more slowly, it is an important piece of the puzzle that is the aging visual system.

**MAKE A DIFFERENCE**
In our combined roles as ophthalmologists, plastic surgeons, and to some extent, artists, we believe we make a real difference for patients — sometimes restoring sight, but always restoring quality of life.

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**THE Window of the Eye**
*continued from page 7*

**Ask a Schepens Scientist**
*continued from page 8*

a series of target letters flashed on a screen, both singly and surrounded by other letters.

We consistently found that with the same viewing conditions, older adults have more trouble identifying the target letter when it was surrounded by other letters than do younger adults. That is, they are more susceptible to visual crowding. Important to our hypothesis, visual crowding was even greater in the older volunteers when the target letter was farther from the point of fixation, but still within the seven-letter span that younger adults are able to use when they read. We also learned that by giving older adults about twice as much time to view the target letter, their performance matched that of the younger adults.

**Clinically Speaking**
*continued from page 9*

this condition, we may now use an endoscope, a tiny camera inserted through the nasal passages, rather than through the skin, to allow us to see and bypass the blockage.

**COSMETICS**
The eye is a focal point for human connection. For that reason, many people want their eyes to look their best. The skin around the eye and on the eyelids is the thinnest in the body and the first to show age. As eye plastic surgeons, we can smooth forehead wrinkles, lift brows and upper cheek areas, address age-related changes of the eyelids, and, through techniques such as Botox® injections, which paralyzed tiny muscles, we can eliminate crow’s feet at the corner of the eyes.
In FY03 the Institute continued to build a solid financial infrastructure to support current research and to position itself to be able to take advantage of future growth opportunities. The accomplishments this year included increasing both our unrestricted and restricted endowments, continuing the investment in our physical plant, implementing an aggressive cost containment program, and ending the fiscal year with a $1.5 million surplus. These steps help solidify a financial strategy that will provide the Institute with a financial foundation that will support future growth.

A synopsis of the Institute’s financial picture for the fiscal year ending June 30, 2003, shows total assets of $64.6 million, which increased $8.1 million from the previous year. The increase is primarily due to an increase in cash of $3.8 million for the building fund, an increase of $0.9 million in our long-term investments, and an increase in our land, buildings and equipment of approximately $4.1 million, reflecting the ongoing construction during FY03. These additions are offset by the reduction of our pledge receivables of $0.8 million.

The increase in liabilities of $8.3 million is primarily due to an increase in construction advance of $9.9 million offset by a reduction of our deferred support and accounts payable obligations of $1.4 million.

Total equity (net assets) of $37.1 million decreased by $0.2 million. The decrease results primarily from the decrease in temporarily restricted assets for our building program and to meet certain donor restrictions of $1.7 million. This decrease is offset by additions to the unrestricted endowment of $0.7 million, and bequests used to fund operations of $0.7 million.

Total unrestricted revenue of $27.1 million increased $1.0 million over the last fiscal year primarily due to increased operating revenues of $2.8 million (mainly federal and non-federal grants and contracts) offset by deferred revenue released from donor restrictions of $1.8 million over FY02.

Total operating expenses were $25.6 million, an increase of $2.2 million primarily due to an increase in funded research programs.

In summary, FY03 follows FY02 in becoming a building block for the future of the Institute, supporting our research, programmatic, and building initiatives.

Robert L. Gable
Chair, Finance Committee
## Financials

### Statements of Financial Position

<table>
<thead>
<tr>
<th>June 30, 2003 and 2002</th>
<th>2003</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash in interest-bearing accounts</td>
<td>$ 5,967,672</td>
<td>$ 2,185,829</td>
</tr>
<tr>
<td>Funds held in trust by others</td>
<td>696,118</td>
<td>376,118</td>
</tr>
<tr>
<td>Trustee-held bond funds</td>
<td>3,405,947</td>
<td>3,379,726</td>
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<tr>
<td>Pledges receivable, net</td>
<td>989,956</td>
<td>1,828,205</td>
</tr>
<tr>
<td>Grants and contracts receivable</td>
<td>680,966</td>
<td>620,686</td>
</tr>
<tr>
<td>Prepaid expenses and other assets</td>
<td>137,996</td>
<td>410,990</td>
</tr>
<tr>
<td>Land, buildings and equipment, net of accumulated depreciation</td>
<td>24,494,299</td>
<td>20,420,760</td>
</tr>
<tr>
<td>Long-term investments at fair market value</td>
<td>28,272,507</td>
<td>27,351,989</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>64,645,461</td>
<td>56,574,303</td>
</tr>
</tbody>
</table>

| **Liabilities and Net Assets** |            |            |
| Accounts payable and other accrued expenses | 1,348,661  | 2,499,232  |
| Construction advance | 9,907,282  | —          |
| Accrued payroll | 631,002    | 605,064    |
| Deferred support | 1,788,212  | 2,008,884  |
| Annuity obligations | 100,000    | 100,000    |
| Unearned royalty income | —         | 89,000     |
| Long-term debt | 13,795,000 | 14,000,000 |
| **Total liabilities**       | 27,570,157 | 19,302,180 |

| **Commitments and contingencies** |            |            |
| Net assets:                        |            |            |
| Unrestricted                       | 6,609,677  | 5,817,251  |
| Board designated                   | 4,383,542  | 3,722,524  |
| Temporarily restricted             | 12,530,953 | 14,273,354 |
| Permanently restricted             | 13,551,132 | 13,458,994 |
| **Total net assets**               | $37,075,304 | $37,272,123 |
| **Total liabilities and net assets** | $64,645,461 | $56,574,303 |
### Statements of Activities

<table>
<thead>
<tr>
<th>Years ended June 30, 2003 and 2002</th>
<th>2003</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Changes in unrestricted resources:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Operating revenues:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Federal grants and contracts</td>
<td>$17,478,860</td>
<td>$15,137,075</td>
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<tr>
<td>Contributions</td>
<td>1,023,919</td>
<td>1,076,026</td>
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<tr>
<td>Bequests</td>
<td>1,162,298</td>
<td>1,475,103</td>
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<tr>
<td>Non-federal grants and contracts</td>
<td>2,829,946</td>
<td>2,217,896</td>
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<tr>
<td>Income on long-term investments</td>
<td>211,428</td>
<td>226,392</td>
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<tr>
<td>License and royalty fees</td>
<td>629,023</td>
<td>440,553</td>
</tr>
<tr>
<td>Other</td>
<td>74,709</td>
<td>49,118</td>
</tr>
<tr>
<td><strong>Total operating revenues</strong></td>
<td>$23,410,183</td>
<td>$20,622,163</td>
</tr>
<tr>
<td><strong>Net assets released from restrictions:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contributions-satisfaction of program restrictions</td>
<td>2,504,123</td>
<td>4,621,576</td>
</tr>
<tr>
<td>Income on long-term investments-satisfaction of program restrictions</td>
<td>1,187,097</td>
<td>867,400</td>
</tr>
<tr>
<td><strong>Total resources released from restrictions</strong></td>
<td>$3,691,220</td>
<td>$5,488,976</td>
</tr>
<tr>
<td><strong>Total unrestricted revenues</strong></td>
<td>$27,101,403</td>
<td>$26,111,139</td>
</tr>
<tr>
<td><strong>Operating expenses:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>19,286,621</td>
<td>17,494,539</td>
</tr>
<tr>
<td>Management and general</td>
<td>5,443,357</td>
<td>6,097,774</td>
</tr>
<tr>
<td>Fundraising</td>
<td>903,830</td>
<td>1,116,568</td>
</tr>
<tr>
<td><strong>Total operating expenses</strong></td>
<td>$25,633,808</td>
<td>$24,708,881</td>
</tr>
<tr>
<td><strong>Unrestricted income (loss) from operations before gain on sale of land and building and net unrealized gains (losses) on investments:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gain on sale of land and building</td>
<td>—</td>
<td>440,090</td>
</tr>
<tr>
<td>Net unrealized (losses) gains on investments</td>
<td>(14,151)</td>
<td>(34,101)</td>
</tr>
<tr>
<td><strong>Increase in unrestricted net assets</strong></td>
<td>$1,453,444</td>
<td>$1,808,247</td>
</tr>
<tr>
<td><strong>Changes in temporarily restricted net assets:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contributions</td>
<td>634,420</td>
<td>2,510,235</td>
</tr>
<tr>
<td>Realized gains on sale of investments</td>
<td>2,175,518</td>
<td>1,304,120</td>
</tr>
<tr>
<td>Net unrealized losses on sale of investments</td>
<td>(1,560,242)</td>
<td>(1,960,215)</td>
</tr>
<tr>
<td>Income on long-term investments</td>
<td>699,123</td>
<td>827,943</td>
</tr>
<tr>
<td>Net assets released from temporary restrictions</td>
<td>(3,691,220)</td>
<td>(5,488,974)</td>
</tr>
<tr>
<td><strong>Decrease in temporarily restricted net assets</strong></td>
<td>(1,742,401)</td>
<td>(2,806,891)</td>
</tr>
<tr>
<td><strong>Changes in permanently restricted net assets:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gifts and bequests</td>
<td>92,138</td>
<td>1,808,297</td>
</tr>
<tr>
<td><strong>Increase in permanently restricted net assets</strong></td>
<td>92,138</td>
<td>1,808,297</td>
</tr>
<tr>
<td><strong>Increase (decrease) in net assets</strong></td>
<td>(196,819)</td>
<td>809,653</td>
</tr>
<tr>
<td><strong>Net assets at the beginning of the year</strong></td>
<td>$37,272,123</td>
<td>$36,462,470</td>
</tr>
<tr>
<td><strong>Net assets at the end of the year</strong></td>
<td>$37,075,304</td>
<td>$37,272,123</td>
</tr>
</tbody>
</table>
EMERITUS SENIOR SCIENTISTS
Adler, Alice J., Ph.D.
Cintron, Charles, Ph.D.
Doane, Marshall G., Ph.D.
Refojo, Miguel F., Sc.D.
Schepens, Charles L., M.D.

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Delori, François, Ph.D.
Elsner, Ann, Ph.D.
Gipson, Ilene K., Ph.D.
Joyce, Nancy, Ph.D.
Kazlauskas, Andrius, Ph.D.
Peli, Eliezer, O.D.
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Streilein, J. Wayne, M.D.
Sullivan, David A., Ph.D.
Webb, Robert H., Ph.D.
Zieske, James, Ph.D.

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Taylor, Andrew, Ph.D.

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Lashkari, Kameran, M.D.
Young, Michael, Ph.D.

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Ng, Tat Fong, Ph.D.
Rawe, Ian, Ph.D.
Rios, Jose, Ph.D.
Romeo, Giulio R., M.D.
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Ruberti, Jeffrey, Ph.D.

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Tolentino, Felipe I., M.D.

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Dohlman, Claes, H., M.D.
Hirose, Tatsu, M.D.
McMeel, J. Wallace, M.D.
Trempe, Clement L., M.D.
Weiter, John, M.D.

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Wing, Glenn L., M.D.

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Anthony R. Kalica, Ph.D.
Director of Research Administration & Resources

Frances Ng
Director of Human Resources
We are proud to announce the launch of our new website! To learn more about The Schepens Eye Research Institute’s world-class research, to access the best and most up-to-date information on eye diseases, and to learn more about research into their causes, cures, and preventions, visit us at www.theschepens.org.