Expanding the frontiers of vision science
On the cover:
The evolution of sight restoration

Eyal Margalit, M.D., Ph.D., University of Nebraska Medical Center, shown on the cover examining a patient’s retina with an indirect ophthalmoscope, leads a research team that is developing a retinal prosthetic device. The Intelligent Retina Implant System (IRIS) is similar to other experimental visual prostheses: a camera mounted on a pair of eye glasses captures images which wirelessly transmit processed signals to an implantable module that stimulates retinal neurons. The IRIS, however, will have features that set it apart from existing devices. Instead of 16 electrodes to stimulate photoreceptors in the eye, the IRIS will use 3,200 to create much higher resolution images. It also will be capable of compensating for changes in retinal structure resulting from retinal degeneration. This will allow the patient to make adjustments that optimize the visual image after implantation surgery.

RPB also supports other artificial retina projects, including improvements to devices already in human testing. A Thumbtack Photovoltaic Retinal Prosthesis will incorporate self-powered, light-to-current transducers within the eye, with all interface circuitry outside the eye. Another lab has confirmed the suitability of a potential biochemical agent for a neurotransmitter-based retinal prosthesis, which may more closely mimic natural visual stimulation than prostheses using electrical stimulation.

Pictured at right: In order to study the way the visual system develops and integrates with the brain, structures within the eye are stained to determine the effects of enzymes, called kinases, involved in communication within the cell. See page 15.
Letter from the president

For 50 years, Research to Prevent Blindness has facilitated an extraordinary catalog of health-related, quality-of-life improvements associated with our vision research. How do we measure progress? Well, when a study of retinal surgical procedures concluded that there has been a significant increase in the use of vitrectomy and intravitreal injection to treat retinal detachment and macular degeneration, we know that both trends were initiated by our earlier investments in vitreo-retinal surgery. RPB support was critical in developing vitrectomy, and we have applied our resources to every aspect of the evolution of the anti-VEGF drugs used in intravitreal injections to treat wet macular degeneration. In fact, last year, in a first step toward creating a best surgical standard of practice for administering intravitreal injections, one of our researchers analyzed the variety of techniques currently in use by ophthalmologists.

Nevertheless, despite our successes, for the 39 million people worldwide who are blind and the 245 million with low vision, new treatments cannot be developed soon enough.

As we enter our second half-century of service, RPB researchers are continuing to expand the frontiers of vision science. (You will find a report on the ophthalmological uses of nanotechnology in this issue.) The flexibility of our unrestricted support to clinical and basic investigators allows them to invent and build equipment, to examine the effectiveness and side effects of surgical tools or drugs, to determine the optimum timing for use of a drug, and even to explore ways that the medical care system can improve preventive eye care.

Recently, we increased the dollar amounts of several grant categories to meet the growing demands of conducting research. We also created a new, basic science award. And we will continue to refine our programs in order to further catalyze the eye research community. The best is yet to come.

Diane S. Swift, President
Advances In Eye Research

RPB’s unrestricted grants allow scientists to literally go where no scientists have gone before: to advance eye research using new technologies, to test concepts, to develop potential treatments.

In a dramatic example of how this dynamic can help patients, the photo on this page shows Szilárd Kiss, M.D., Weill Cornell Medical College, standing “within” an image of a patient’s retina. That image is generated by the CAVE (Computer-Assisted Virtual Environment), an advanced technology that allows data to be viewed and manipulated in a fully immersive, interactive, 3D, virtual reality environment. Within the CAVE, wearing special glasses, scientists gain a better understanding of relationships between retinal structures with the goal of advancing therapeutic intervention in a variety of retinal disorders.

“With RPB’s unrestricted department grant, I have been able to carry out my research endeavors with the CAVE,” says Kiss. “One of my patients had scar tissue growing over his retina. Inside the CAVE I was able to isolate where the ridge of the scar tissue was located, which was not obvious from two-dimensional images. This allowed me to surgically remove the tissue from the retina.”

For a complete bibliography of the 1,094 published studies supported by RPB in 2010, go to www.rpbusa.org/rpb/research/search/.
Retinal diseases, including Age-Related Macular Degeneration (AMD)
RPB scientists have found a way to use chemicals, rather than genes, to reprogram adult human skin cells back to their pluripotent state, from which point they are able to change into all other cell types, including retinal photoreceptor cells. The chemical process reduces concerns associated with adenovirus delivery of genetic material. It also brings medical science closer to the possibility of creating healthy cells from a patient’s own cells to replace those that have succumbed to disease or injury.

In separate research, an RPB study shows that a person’s own pluripotent stem cells can be induced to become angioblasts (an early form of blood-vessel-forming cell). These can be used to repair the patient’s injured blood vessels in cases of retinal branch vein occlusion and diabetic retinopathy.

An RPB researcher has started a Phase I/II clinic trial exploring the combined use of proton beam irradiation therapy (used in some cancer treatments) and anti-VEGF therapy as a potentially permanent cure for wet AMD. Earlier results show that this combination is safe and may dramatically reduce the need for almost monthly retreatment with anti-VEGF injections.

Scientists have demonstrated that sustained topical therapy with dorzolamide hydrochloride, 2%, improves visual acuity and reduces cystic macular lesions in patients with retinitis pigmentosa (RP) and Usher syndrome (which causes RP and deafness).

Glaucoma
A non-invasive test known as PERGLA, in which electrodes are placed on the patient’s forehead, temples, and lower eyelids, was able to detect destruction of retinal ganglion cells early enough to allow intraocular pressure-correcting surgery in patients with glaucoma.

Investigators from two RPB-supported institutions have identified a new RPB grants are issued to U.S. medical schools, but funds can be applied to international research efforts to battle blindness. In one example, Mary A. O’Hara, M.D., F.A.C.S., University of California, Davis, School of Medicine works with doctors from undeveloped nations to assist in surgeries to prevent blindness. From these initial contacts, Dr. O’Hara continues to teach, exchange ideas and collaborate on research projects. RPB’s Unrestricted Grant to U.C. Davis helps cover the cost of telemedicine communication for these research collaborations.
candidate gene for the most common form of glaucoma, primary open angle glaucoma (POAG), opening the door to potential gene therapies. The gene may have a role in regulating intraocular pressure.

Cataract
Among infants who undergo surgery to treat congenital cataract, surgical lens replacement appears to cause more complications while achieving the same benefit as treatment with contact lenses, according to an RPB-supported report.

Cornea
With support from RPB, researchers have found a gene that is likely responsible for Fuchs’ corneal dystrophy, an inheritable genetic disorder and leading cause of corneal transplant operations. Armed with the new information, they hope to find a way to prevent or slow Fuchs’ progression.

Studies show that topically applied Lucentis and Avastin are highly effective in suppressing corneal neovascularization (CN), the formation of microvascular networks, a leading cause of blindness worldwide. CN is a common pathologic response to infection, trauma and chemical exposure, and significantly raises the risk of rejection for corneal transplants performed to treat corneal scars.

Dry Eye
Why is dry eye worse in cold, windy weather? Scientists have found that colder outside temperatures drive down temperatures on the eye surface and eyelid. The meibum (the oily substance in the outermost layer of the tear film) becomes too thick and too stiff to spread evenly and protect the eye. The cold also can affect over-the-counter and prescription eye lubricants. One solution: during winter, use protective eye wear.

Diabetic Eye Disease
It is known that good blood sugar control helps retard the progression of diabetic retinopathy. RPB scientists recently reported that damage to tiny blood vessels in the eye, initiated by high blood sugar, continues for a while even after normal blood sugar has been restored. They have further found that specific supplements block the mechanism that causes this lingering effect, suggesting a new approach to minimizing chronic eye damage from diabetes.

In addition to disorders of the retina and lens, diabetics can also experience persistent corneal surface defects. Researchers report use of a topically applied antimicrobial agent that may become a mainstream therapy for healing postsurgical and corneal epithelial defects and for preventing corneal infection associated with these defects in patients with diabetes.

Investigators have found that nicotine, in the presence of high blood sugar, promotes cataract progression, raising a red flag for diabetics who smoke or use nicotine patches.

Infectious Eye Diseases
An RPB-supported study suggests that people who have frequent recurrences of corneal disease should use oral antiviral medications following infection with the herpes simplex virus. This may reduce risk of recurring inflammation or infection of the cornea or eyelid.

Tests on the Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) show it is an improvement over rigid contact lenses that are the gold standard for patients with severe dry eye. The PROSE creates a fluid filled reservoir over the cornea, providing immediate relief from irritation and photosensitivity for patients with Sjogrens Syndrome, Stevens-Johnson Syndrome, post-LASIK problems and chronic graft-versus-host disease.
**Myopia**

In a pilot clinical trial, subjects treated with red-blocking lenses showed significant slowing in the development of progressive myopia. This follows earlier RPB-supported research indicating that exposure to red light activates myopia genes.

**Night Blindness**

An RPB investigator reports that clinical vitamin A deficiency still occurs in countries that have fairly well established vitamin A supplementation programs, such as Bangladesh. Further, among children who did not receive vitamin A, the lack of a home garden (to provide additional sources of vitamin A) was associated with a three-fold increased risk of night blindness. Promoting home gardens in developing countries may help prevent nutritional blindness in children.

**Ocular Albinism**

Research indicates that the severe visual defects in those with albinism may be treated with L-DOPA, a naturally occurring dietary supplement found in certain foods and herbs (and currently used to treat Parkinson’s disease).

**Ocular Tumors and Cancer**

Once malignant eye melanoma spreads to the liver, which happens in 40 percent of cases, it forms small islands that have the potential to grow and develop new blood vessels, ultimately leading to death. Despite progress in the diagnosis and treatment of the primary melanoma, the death rate has remained unchanged for the past 25 years. RPB scientists have found that the drug KCN1 may be used to block this blood vessel growth.

While most eventually shrink, eyelid capillary hemangiomias are non-cancerous tumors typically found at birth. They grow during the first decade. If they involve the eyelids, and if not treated early, they can cover the eye and cause loss of vision (amblyopia) and can lead to irreversible blindness. An RPB lab is the first to use topical timolol in the successful treatment of these tumors.

Scientists have identified how a protein called galectin-3 promotes angiogenesis (blood vessel growth), and may be on the verge of developing new treatments for conditions caused by excessive angiogenesis, including corneal graft failure, AMD and proliferative diabetic retinopathy.

Right: blood vessel formation that resulted from normal galectin-3 function. Far right: reduced blood vessel formation when galectin-3 was depleted.
“We find that these nanoparticles are analogous to aspirin,” says James F. McGinnis, Ph.D., Dean A. McGee Eye Institute. “They don’t prevent the primary defect, but they do prevent the symptoms. So the downstream effects, including blindness, should be preventable.”

Nanotechnology
Looking for big things from tiny particles

An important part of RPB’s mission has been steady support for the development of advanced technological equipment. Today, RPB researchers are creating devices and drug delivery systems the size of atoms to explore a broad frontier of treatments for eye disorders. As a point of reference, one inch equals 25.4 million nanometers. The diameter of an atom ranges from .1 to .5 nanometers.

Nanotherapy
Researchers have tested small-molecule therapies that might restore visual function to individuals blind from retinitis pigmentosa and AMD. Early results indicate that these new chemicals appear to restore light-dependent function to the blind retina.

Cerium oxide nanoparticles (nanoceria) have been used to prevent damage to photoreceptor cells caused by oxidative stress and vision loss due to hereditary defects. While remaining in the retina for extended periods of time, the nanoceria both prevent and treat blood vessel-related lesions that develop from AMD, diabetic retinopathy, retinitis pigmentosa and retinopathy of prematurity.

Drug Delivery
In order to minimize the need for monthly injections directly into the eye to treat AMD, scientists are testing microneedle-delivered, sustained-release drug formulations using nanoparticles.
Sensors
RPB glaucoma researchers have developed a nano-fabricated pressure sensor to directly measure the outflow resistance of aqueous humor (fluid) in the eye. They believe that such a tool could be used to identify patients at highest risk of developing glaucoma due to rising intraocular pressure and to help monitor response to treatment.

Gene Therapy
While gene therapy delivered by adenoviruses has partially restored sight in several patients with a form of retinitis pigmentosa, concerns remain about the use of viruses to deliver corrective genetic material. Recently, a team of RPB researchers used DNA nanoparticles as a non-viral gene carrier to replace genes in mature photoreceptor cells. The particles proved more efficient than conventional viral delivery methods at enabling the cells to express the new DNA.

Researchers used gold nanoparticles to deliver gene therapy to treat abnormal corneal blood vessel growth and to prevent scarring.

Imaging
Vision researchers are uncovering fundamental information about the action of rhodopsin, the pigment in photoreceptor cells that initiates the eye’s reaction to light. To do this, they have utilized single molecule force spectroscopy (see illustration below) to probe the smallest details of the visual system currently unavailable. Mutations in rhodopsin lead to inherited retinal disorders such as retinitis pigmentosa and stationary congenital night blindness.

RPB scientists have created a nano knife, above, capable of surgically paring down nerve endings, demonstrating the possibility of creating a new family of micro-scale instrumentation that can extend surgical procedures down to individual cells and beyond. Figure A shows the unassembled nano knife against a penny for scale.

Single Molecule Force Spectroscopy
*In this method, rhodopsin is mechanically unfolded by pulling on one end of the pigment molecule using an atomically sharp probe. By pulling apart rhodopsin, researchers learn about the nature of chemical bonds that stabilize its structure and allow its function. This novel method will provide key insights into how mutations in the pigment molecule lead to inherited retinal disorders.*
RPB Ad Hoc Committees convene each spring and fall to conduct initial reviews of all RPB grant applications. The Committees are comprised of selected ophthalmology department heads whose recommendations are forwarded to the RPB Scientific Advisory Panel for further evaluation. Membership on the Ad Hoc Committee changes from meeting to meeting. This year’s participants were:

Gary W. Abrams, M.D.
Wayne State University School of Medicine

Stephen P. Christiansen, M.D.
Boston University School of Medicine

Roy S. Chuck, M.D., Ph.D.
Albert Einstein College of Medicine of Yeshiva University

Donald J. D’Amico, M.D.
Weill Medical College of Cornell University

Jack M. Dodick, M.D.
New York University School of Medicine

Michael A. Kass, M.D.
Washington University in Saint Louis School of Medicine

Paul L. Kaufman, M.D.
University of Wisconsin-Madison School of Medicine

Naresh Mandava, M.D.
University of Colorado HSC at Fitzsimons

Peter J. McDonnell, III, M.D.
The Johns Hopkins University School of Medicine

Joseph M. Miller, M.D., M.P.H.
University of Arizona College of Medicine

Joan M. O’Brien, M.D.
University of Pennsylvania School of Medicine

P. Andrew Pearson, M.D.
University of Kentucky College of Medicine

Gregory L. Skuta, M.D.
University of Oklahoma Health Sciences Center

David J. Wilson, M.D.
Oregon Health & Science University School of Medicine
2010 RPB Scientific Advisory Panel

The Scientific Advisory Panel includes distinguished scientists representing a broad range of scientific disciplines and interests. Their recommendations are presented to the RPB Board of Trustees for final approval.

HAROLD F. SPALTER, M.D.  
Chair, RPB Scientific Advisory Panel  
Emeritus Professor of Clinical Ophthalmology  
Columbia University College of Physicians & Surgeons

ROBERT FOLBERG, M.D.  
Founding Dean, Oakland University  
William Beaumont School of Medicine  
Professor, Departments of Biomedical Sciences, Pathology and Ophthalmology

ANTHONY MOORE, MA, FRCS, FRCOPHTH, FME DSCI  
Duke-Elder Professor of Ophthalmology  
Institute of Ophthalmology  
Division of Inherited Eye Disease  
University College of London

ROBERT EUGENE ANDERSON, M.D., Ph.D.  
Professor, Departments of Cell Biology & Ophthalmology  
Director of Research, Dean A. McGee Eye Institute  
University of Oklahoma Health Sciences Center

EVE J. HIGGINBOTHAM, S.M., M.D.  
Senior Vice President & Executive Dean for Health Sciences  
Howard University

KRZYSZTOF PALCZEW SKI, Ph.D.  
Professor & Chair, Department of Pharmacology  
Case Western Reserve University

JOHN E. DOWLING, Ph.D.  
Gordon and Llura Gund Professor of Neurosciences  
Department of Molecular and Cellular Biology  
Harvard University

HAIG H. KAZAZIAN, Jr., M.D.  
Professor, Institute of Genetic Medicine  
The Johns Hopkins University School of Medicine

STEPHENV J. RYAN, M.D.  
President, Doheny Eye Institute  
Beardsley Distinguished Professor of Ophthalmology  
Keck School of Medicine of the University of Southern California

HAIG H. KAZAZIAN, Jr., M.D.  
Professor, Institute of Genetic Medicine  
The Johns Hopkins University School of Medicine

RODERICK R. McINNES, CM, M.D., Ph.D., FRSC  
Director, Lady Davis Research Institute  
Jewish General Hospital  
Alva Chair in Human Genetics  
Professor of Biochemistry  
McGill University

SHEILA K. WEST, Ph.D.  
Professor, Departments of Epidemiology & Ophthalmology, Vice Chair for Research  
Wilmer Eye Institute, The Johns Hopkins School of Medicine

Pictured on page 10, left to right: Drs. Spalter, Ryan, Moore, Folberg, Dowling and Palczewski listen while a colleague provides an in-depth review of a grant application before they add comments.
Before Dr. Elisseff received her RPB award she created biomaterials for musculoskeletal reconstruction. Now, she is applying her knowledge to an eye concern with global health relevance: developing a novel bio-adhesive to treat corneal injuries. “RPB recognizes the importance of biomedical engineering to vision issues,” says Peter J. McDonnell, M.D., Chair, Department of Ophthalmology, The Johns Hopkins University School of Medicine. “No researchers with Dr. Elisseff’s specific skill set have ever tackled this particular problem.”

“It’s really hard to get funding with no strings attached to pursue more high risk ventures. The Stein Professorship gives me the freedom to explore new research.”

Jennifer H. Elisseff, Ph.D.
The Jules and Doris Stein RPB Professorships

The Jules and Doris Stein Professorship, RPB’s premier award, fosters translational research by recruiting outstanding basic scientists to conduct clinically relevant research in a department of ophthalmology. In 2010, it provided up to $500,000 across five years, a possible additional $150,000 in matching funds to equip lab space, and a potential $200,000 two-year extension.

David A. Antonetti, Ph.D.
The Regents of the University of Michigan School of Medicine
Using small-molecule inhibitors to restore and maintain normal blood vessel function in diseases of the retina.

Jennifer H. Elisseeff, Ph.D. (pictured at left)
The Johns Hopkins University School of Medicine

Paulo A. Ferreira, Ph.D. (Stein Professorship extension)
Duke University School of Medicine
Understanding genetic and molecular bases of retinal neurons.

The RPB Walt and Lilly Disney Award For Amblyopia Research

The RPB Walt and Lilly Disney Award for Amblyopia Research was created through a pledge from The Walt and Lilly Disney Foundation and provides funds to respected ophthalmic scientists for research into improved detection, treatment or cures for amblyopia.

Amblyopia affects two to four percent of U.S. children and is the leading cause of childhood vision loss. It can be extremely difficult to detect due to the age of the patient, who may not be able to communicate the nature of his or her vision problem.

Jeffrey Louis Goldberg, M.D., Ph.D. (pictured below)
The University of Miami School of Medicine

“Relatively little is known about the structure and function of the human brain in amblyopia. As a developmental neurobiologist and practicing ophthalmologist, I am seeking to understand what changes can be detected in the visual pathways of the human amblyopic brain. We are using high-resolution and diffusion tensor MRI to study the amblyopic brain in children, in both successfully and unsuccessfully treated adults, and in matched controls.”

Jeffrey Louis Goldberg, M.D., Ph.D.
The Lew R. Wasserman Merit Award provides $60,000 to a mid-career scientist, creating a continuum of financial resources to build on earlier work and maintain a research career.

**Lloyd Paul Aiello, M.D., Ph.D.**
Harvard Medical School
*Developing an approach to predict who will respond to diabetic eye disease therapy, and when to initiate and terminate therapy.*

**John D. Ash, Ph.D.**
University of Oklahoma Health Sciences Center
*Restoring mitochondrial activity through new gene expression as a means of preventing or delaying retinal degeneration.*

**Michael P. Fautsch, Ph.D.**
Mayo Medical School
*Determining whether reducing intracranial pressure over a significant period alters optic nerve health.*

**Krystel R. Huxlin, Ph.D.**
University of Rochester School of Medicine & Dentistry
*Laying the scientific groundwork for developing more efficient and successful retraining strategies to induce visual recovery in cortically blind patients.*

**Peter Kazuo Kaiser, M.D.** (pictured below)
Cleveland Clinic Lerner College of Medicine of Case Western Reserve University
*“It has always been assumed that diabetic retinopathy (DR) followed a linear progression, beginning with a dropout of blood vessels caused by restricted blood supply (nonproliferative DR), followed by faulty and excessive blood vessel growth in the late, potentially blinding stage (proliferative DR). Our research shows that, instead, there is oscillation. This poses a paradigm shift crucial to the proper understanding and treatment of DR. There are critical periods during early retinopathy where the vessels are actually trying to reverse the lack of blood supply, but eventually fail, leading to pathologic blood vessel growth. Just before that happens, therapies that promote healthy blood vessel growth may be able to prevent DR progression. Treatments delivered at the wrong time may be harmful.”*

Peter Kazuo Kaiser, M.D.
In 2010, RPB Career Development Awards provided $200,000 across four years to outstanding young clinical and basic scientists conducting research in departments of ophthalmology. The award is a valuable recruiting tool for department chairs.

Zubair M. Ahmed, Ph.D.
University of Cincinnati College of Medicine
*Understanding the genetic and molecular basis of normal vision and hearing; translating this knowledge into molecular therapies for loss of vision and hearing associated with Usher syndrome.*

Benjamin J. Frankfort, M.D., Ph.D.
Baylor College of Medicine
*Understanding the earliest stages of visual disturbance in glaucoma to allow early diagnosis and management.*

Tonia S. Rex, Ph.D.
University of Tennessee Health Science Center
*Using gene therapy with erythropoietin to develop treatments for currently incurable blinding diseases.*

Rebecca M. Sappington, Ph.D.
Vanderbilt University School of Medicine
*Uncovering the cellular signals that drive microglia (immune system cells) to the ganglion cell layer in glaucoma.*

Akrit Sodhi, M.D., Ph.D.
The Johns Hopkins University School of Medicine
*Identifying novel targets for the treatment of retinal vascular diseases.*

Kwoon Y. Wong, Ph.D.
The Regents of the University of Michigan School of Medicine
*Identifying novel targets for the treatment of retinal vascular diseases.*

Hilary E. Beggs, Ph.D., Career Development Award 2005
University of California, San Francisco, School of Medicine

"Accurate visual perception of the world requires precise mapping of neuronal projections from the eye to the brain during development of the visual system. Errors in correct wiring of these projections can result in compromised vision and lead to sight-threatening diseases in children such as amblyopia and optokinetic nystagmus. Our findings indicate that a key signaling protein responsible for transmitting environmental cues is required for proper patterning of retinal ganglion cell projection to the brain."
RPB Senior Scientific Investigator Awards

RPB Senior Scientific Investigator Awards provide $75,000 to extend the productivity of seasoned vision scientists who can play a crucial role in training the next generation of vision scientists.

**Neil M. Bressler, M.D.**
The Johns Hopkins University School of Medicine
* Evaluating a new home device for detecting the onset of choroidal neovascularization in age-related macular degeneration.

**Thomas A. Ferguson, Ph.D.** *(pictured below)*
Washington University in Saint Louis School of Medicine

**Lin Gan, Ph.D.**
University of Rochester School of Medicine & Dentistry
*Identifying retinal ganglion cell (RGC) survival or death factor regulators; applying these discoveries to stem cell programmed RGC regeneration.*

**Ching-Hwa Sung, Ph.D.**
Weill Medical College of Cornell University
*Employing state-of-the-art technologies to understand the basic cell biology of both normal and diseased photoreceptors, and identifying candidate drug(s) that may slow or prevent photoreceptor death.*

**Kang Zhang, M.D., Ph.D.**
University of California, San Diego, School of Medicine
*Employing small molecule driven, stem cell based therapies (using human induced pluripotent stem cells) to treat geographic atrophy from dry age-related macular degeneration.*

“Many current theories for the development of age-related macular degeneration suggest that inflammation in response to age-related changes in the eye is a key element. Often overlooked, however, is the immune privileged status of the eye* and how certain mechanisms, which control intraocular inflammation and abnormal blood vessel growth, impact the development of this disease. In fact, little is known about the effect of aging on immune privilege. Our studies are exploring the effect of aging on immune privilege and how immune privilege can be modulated to treat this disease.”

**Thomas A. Ferguson, Ph.D.**

*Certain sites in the body tolerate the introduction of foreign matter without immune system rejection.
Sybil B. Harrington Endowment

Since 1994, the Sybil B. Harrington Endowment has generated funds for several RPB grant awards and has enabled RPB to create an additional Senior Scientific Investigator Award for work focused on age-related macular degeneration. This year’s recipient is Artur V. Cideciyan, Ph.D., University of Pennsylvania School of Medicine. Dr. Cideciyan develops state-of-the-art, non-invasive methods to understand abnormalities in retinal structure and the resulting loss of vision experienced by patients with hereditary retinal degenerations. He then applies this knowledge to evaluate the efficacy of novel treatment approaches.

“Throughout my career, I have divided my time between clinical research studies with patients and basic research. Our new studies should allow a better understanding of the pathophysiology in human retinal diseases caused by mutations in the CRB1 gene, and provide a solid foundation for expanding recent gene therapy successes,” says Cideciyan.
RPB Special Scholar Awards

RPB Special Scholar Awards recognize promising young scientists of exceptional merit and are given in honor of former Trustees and others who have made generous contributions of time, energy and financial resources in support of eye research.

**Abigail S. Hackam, Ph.D.**
Ernest & Elizabeth Althouse Scholar Award
University of Miami School of Medicine
*Defining a connection between the innate immune system and cell survival in retinal disease.*

**Qingxian Lu, Ph.D.**
William & Mary Greve Scholar Award
University of Louisville School of Medicine
*Determining if anti-inflammatory medication can be helpful in delaying the onset of retinitis pigmentosa.*

**Geunyoung Yoon, Ph.D., Dolly Green Special Scholar Award 2007**, University of Rochester School of Medicine

“Patients with keratoconus [a degenerative corneal disease causing a cone-shaped protrusion of the central cornea] have greatly degraded visual performance due to extremely large amounts of irregular astigmatism. Theoretically, accurate correction should benefit them substantially. However, best corrected visual acuity after successful correction is often worse than that predicted by optical theory. We are investigating whether the neural system can be re-adapted to fully translate improved retinal image quality into visual performance.”
RPB Physician-Scientist Awards

RPB Physician-Scientist Awards provide $60,000 each to nationally recognized M.D.s who bring to the laboratory a practical understanding of patients’ needs while their research efforts yield new knowledge in treating patients.

Ula V. Jurkunas, M.D., Harvard Medical School,
Examining how oxidative stress causes molecular and cellular damage in the susceptible Fuchs’ dystrophy endothelium.

Srinivas Sadda, M.D.
Keck School of Medicine of the University of Southern California
Applying advanced quantitative image analysis approaches to imaging data from eyes of patients with AMD in order to define characteristics that are predictive of response to therapy or risk for disease progression.

Cynthia A. Toth, M.D. (pictured below)
Duke University School of Medicine

“Currently, retinal disease in infants is recorded in a manner that provides little information about the macula. In older children and adults, optical coherence tomography (OCT) is used to detail macular disease processes such as edema or atrophy. This has not been possible in young children who cannot cooperate for imaging. Thus, during the period when the complex visual pathway between the retina and brain is rapidly developing, it is not easy to evaluate macular disease. I recently developed a method to record OCT macular images in awake, premature newborns using a handheld imaging head, and discovered that macular edema [swelling] was common in infants with retinopathy of prematurity (ROP) or other systemic diseases such as liver failure. My study will be important in monitoring new therapies for ROP.”

Cynthia A. Toth, M.D.

RPB International Research Scholar Awards

In 2010, RPB’s International Research Scholar Program provided two travel grants that enabled foreign researchers to travel to the U.S. for collaborations with U.S. researchers.

XianPing Fu, Ph.D.
Harvard Medical School
Developing driving and crash warning systems using computer vision and driving safety research, including eye and head tracking.

Rosana M. Gerometta, M.D.
Mount Sinai School of Medicine
Measuring simultaneous current and fluid movement around the lens surface.
RPB Medical Student Eye Research Fellowships

RPB Medical Student Eye Research Fellowships, of $30,000 each, enable students to take a year off from their usual course of studies to pursue a laboratory research project within a department of ophthalmology.

Ferhina S. Ali (pictured below)
The Johns Hopkins University School of Medicine

Nika Bagheri
Cleveland Clinic Lerner College of Medicine of Case Western Reserve University
Understanding the overall role of microglia in the pathology of age-related macular degeneration (AMD).

Joey Yen-Cheng Hsia
Case Western Reserve University School of Medicine
Elucidating the role of the host response in Acanthamoeba keratitis.

Janelle Marshall
University of California, Irvine, College of Medicine
Understanding interactions between AMD-associated haplogroups to Benzo(e)Pyrene, a toxic component of cigarette smoke.

Grant H. Moore
University of California, San Diego, School of Medicine
Comparing inter-eye differences in retinal structure in healthy and glaucoma patients of African descent to those of European descent.

Wenlan Zhang
Duke University School of Medicine
Testing the hypothesis that dysregulation of the complement cascade (an immune system pathway) will exacerbate AMD.

“The developing world is currently facing what the World Health Organization has identified as the ‘double burden’ of disease, continuing to combat areas of infectious disease and maternal and child health, but also the health crises that arise from chronic disease. One of these areas is diabetes and in turn, diabetic retinopathy. Developing nations are ill-equipped to deal with diabetic retinopathy from a screening or intervention standpoint. With support from Research to Prevent Blindness, I am working on a pilot program that implements diabetic retinopathy treatment and screening in the Chittagong region of Bangladesh.”

Ferhina S. Ali
RPB has been focusing its public education efforts on communicating research findings that may help people make lifestyle choices to reduce risk for developing a serious eye disorder. As part of RPB’s move to digital distribution of educational materials, we launched an expanded version of the “Guide to Eye Health” fact sheet on our Web site in 2010. Following are the most current updates to that section, which can be found at www.rpbusa.org/rpb/eye_info/page_4/.

A growing body of evidence suggests that eating foods rich in a variety of vitamins and minerals (high quantities of fruits, vegetables, whole grains, and lean protein such as beans, fish, eggs, and low quantities of salt and fat) may help postpone nuclear cataract, the most common type of cataract in the United States.

The use of medications that increase sensitivity to the sun, combined with exposure to sunlight, appears to be associated with risk of age-related cataract. Medications in the study included diuretics, antidepressants, antibiotics and the pain reliever naproxen sodium. The mechanism for this interaction is unclear.

Use of oral contraceptives for five or more years has been associated with a 25 percent increased risk of developing primary open angle glaucoma (the most prevalent form of the disease).

Pre-term infants born following assisted reproductive technology have a higher risk of developing retinopathy of prematurity, suggesting a need to closely monitor pre-term infants born using this method.

Julie A. Mares, Ph.D., University of Wisconsin (pictured advising a shopper on eye-healthy food choices), led a team of researchers who reported that a combination of healthy diet, physical activity and not smoking is associated with 71 percent lower odds of developing age-related macular degeneration (AMD). Their findings suggest that following a combination of healthy practices may be more important in reducing AMD risk than emphasizing a single healthy activity. They also comment that risk for AMD is passed to subsequent generations not only through genes but also possibly through the lifestyle habits we model and encourage.
RPB’s National Network of Eye Research

RPB’s Unrestricted Grant support is available to vibrant departments of ophthalmology across the United States with a demonstrated commitment to clinical, basic and translational research. The flexible grants can be used to amplify restricted grant work from other sources, to promote collaborations with other research departments or other schools, and to explore highly innovative ideas. The list on page 23 includes U.S. medical institutions that received new departmental grants, or new awards for individual investigators, in 2010.

RPB-Supported Research Reported During 2010

Hundreds of RPB-supported vision scientists throughout the U.S. are investigating the areas of basic and clinical research graphed below. Basic research refers to fundamental laboratory research such as molecular biology, genetics, biochemistry, immunology and pharmacology. Clinical investigation refers to research applied to the human condition.

50 Year Alliance

The scope of the RPB network was evident at the May 1, 2010 celebration of RPB’s 50th anniversary, held in Fort Lauderdale. RPB-supported researchers and department chairs from across five decades gathered to reconnect and reminisce. Pictured, left to right: Dr. Paul Sieving, Director of the National Eye Institute (NEI); Diane S. Swift, RPB President; and David F. Weeks, RPB Chairman. “The NEI and RPB have been partners in the nation’s vision research, going back 40 years to the founding of the NEI, in which RPB played a critical role,” says Dr. Sieving. “There is a symbiosis between our organizations. RPB grants frequently are used to lay the scientific foundation in applying for NEI grants as well as to extend existing work funded by the NEI.”
<table>
<thead>
<tr>
<th>State</th>
<th>RPB Grantee Institutions</th>
<th>Total Grants 2010</th>
<th>Total Support Including 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALABAMA</td>
<td>University of Alabama at Birmingham School of Medicine</td>
<td>$100,000</td>
<td>$3,535,000</td>
</tr>
<tr>
<td>ARIZONA</td>
<td>University of Arizona College of Medicine</td>
<td>100,000</td>
<td>1,845,000</td>
</tr>
<tr>
<td>CALIFORNIA</td>
<td>University of California, Davis, School of Medicine</td>
<td>100,000</td>
<td>3,173,900</td>
</tr>
<tr>
<td></td>
<td>David Geffen School of Medicine at UCLA</td>
<td>100,000</td>
<td>7,990,750</td>
</tr>
<tr>
<td></td>
<td>University of California, Irvine, College of Medicine</td>
<td>30,000</td>
<td>565,000</td>
</tr>
<tr>
<td></td>
<td>University of California, San Diego, School of Medicine</td>
<td>205,000</td>
<td>2,965,000</td>
</tr>
<tr>
<td></td>
<td>University of California, San Francisco, School of Medicine</td>
<td>100,000</td>
<td>5,889,256</td>
</tr>
<tr>
<td></td>
<td>Keck School of Medicine of the University of Southern California</td>
<td>160,000</td>
<td>4,393,500</td>
</tr>
<tr>
<td>FLORIDA</td>
<td>University of Florida College of Medicine</td>
<td>160,000</td>
<td>3,385,600</td>
</tr>
<tr>
<td></td>
<td>University of Miami Miller School of Medicine</td>
<td>275,000</td>
<td>3,945,200</td>
</tr>
<tr>
<td>GEORGIA</td>
<td>Emory University School of Medicine</td>
<td>100,000</td>
<td>3,387,100</td>
</tr>
<tr>
<td>ILLINOIS</td>
<td>Northwestern University Feinberg School of Medicine</td>
<td>100,000</td>
<td>2,295,000</td>
</tr>
<tr>
<td></td>
<td>University of Illinois at Chicago</td>
<td>100,000</td>
<td>3,706,712</td>
</tr>
<tr>
<td>IOWA</td>
<td>University of Iowa Carver College of Medicine</td>
<td>100,000</td>
<td>3,627,425</td>
</tr>
<tr>
<td>KENTUCKY</td>
<td>University of Kentucky College of Medicine</td>
<td>100,000</td>
<td>1,170,000</td>
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<tr>
<td></td>
<td>University of Louisville School of Medicine</td>
<td>220,000</td>
<td>3,389,800</td>
</tr>
<tr>
<td>LOUISIANA</td>
<td>Louisiana State University Health Sciences Center in New Orleans</td>
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<td>2,282,100</td>
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<tr>
<td>MARYLAND</td>
<td>The Johns Hopkins University School of Medicine</td>
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<td>7,735,140</td>
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<tr>
<td>MASSACHUSETTS</td>
<td>Harvard Medical School</td>
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<td></td>
<td>Tufts University School of Medicine</td>
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<tr>
<td>MICHIGAN</td>
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<tr>
<td></td>
<td>Wayne State University School of Medicine</td>
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</tr>
<tr>
<td>MINNESOTA</td>
<td>Mayo Medical School</td>
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<tr>
<td></td>
<td>University of Minnesota, Academic Health Center, Medical School</td>
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<td>2,828,701</td>
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<tr>
<td>MISSOURI</td>
<td>University of Missouri–Columbia School of Medicine</td>
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<td>1,912,300</td>
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<tr>
<td></td>
<td>Washington University in Saint Louis School of Medicine</td>
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<tr>
<td>NEBRASKA</td>
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<td>1,540,000</td>
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<tr>
<td>NEW JERSEY</td>
<td>University of Medicine &amp; Dentistry of New Jersey Medical School</td>
<td>100,000</td>
<td>2,067,000</td>
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<tr>
<td>NEW YORK</td>
<td>Albert Einstein College of Medicine of Yeshiva University</td>
<td>100,000</td>
<td>1,507,500</td>
</tr>
<tr>
<td></td>
<td>Columbia University College of Physicians &amp; Surgeons</td>
<td>100,000</td>
<td>4,393,167</td>
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<tr>
<td></td>
<td>Weill Medical College of Cornell University</td>
<td>75,000</td>
<td>4,223,700</td>
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<tr>
<td></td>
<td>Mount Sinai School of Medicine</td>
<td>102,500</td>
<td>3,748,200</td>
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<tr>
<td></td>
<td>University of Rochester School of Medicine &amp; Dentistry</td>
<td>235,000</td>
<td>2,435,250</td>
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<tr>
<td></td>
<td>SUNY at Buffalo School of Medicine &amp; Biomedical Sciences</td>
<td>100,000</td>
<td>580,000</td>
</tr>
<tr>
<td></td>
<td>SUNY Upstate Medical University</td>
<td>100,000</td>
<td>2,310,000</td>
</tr>
<tr>
<td>NORTH CAROLINA</td>
<td>Duke University School of Medicine</td>
<td>390,000</td>
<td>6,103,350</td>
</tr>
<tr>
<td></td>
<td>University of North Carolina at Chapel Hill School of Medicine</td>
<td>100,000</td>
<td>1,170,500</td>
</tr>
<tr>
<td>OHIO</td>
<td>Case Western Reserve University School of Medicine</td>
<td>130,000</td>
<td>2,942,500</td>
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<tr>
<td></td>
<td>Cleveland Clinic Lerner College of Medicine</td>
<td>190,000</td>
<td>1,610,000</td>
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<tr>
<td></td>
<td>University of Cincinnati College of Medicine</td>
<td>300,000*</td>
<td>1,396,750</td>
</tr>
<tr>
<td>OKLAHOMA</td>
<td>University of Oklahoma Health Sciences Center</td>
<td>160,000</td>
<td>4,111,600</td>
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<tr>
<td>OREGON</td>
<td>Oregon Health &amp; Science University School of Medicine</td>
<td>100,000</td>
<td>3,962,150</td>
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<tr>
<td>PENNSYLVANIA</td>
<td>University of Pennsylvania School of Medicine</td>
<td>175,000</td>
<td>5,288,500</td>
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<tr>
<td></td>
<td>University of Pittsburgh School of Medicine</td>
<td>100,000</td>
<td>3,568,372</td>
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<tr>
<td>SOUTH CAROLINA</td>
<td>Medical University of South Carolina</td>
<td>100,000</td>
<td>2,077,500</td>
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<tr>
<td>TENNESSEE</td>
<td>University of Tennessee Health Science Center</td>
<td>300,000*</td>
<td>2,235,000</td>
</tr>
<tr>
<td></td>
<td>Vanderbilt University School of Medicine</td>
<td>300,000*</td>
<td>2,250,500</td>
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<tr>
<td>TEXAS</td>
<td>Baylor College of Medicine</td>
<td>300,000*</td>
<td>4,004,060</td>
</tr>
<tr>
<td></td>
<td>The University of Texas Southwestern Medical Center at Dallas</td>
<td>100,000</td>
<td>3,546,000</td>
</tr>
<tr>
<td>UTAH</td>
<td>University of Utah Health Sciences Center</td>
<td>100,000</td>
<td>4,665,300</td>
</tr>
<tr>
<td>WASHINGTON</td>
<td>University of Washington School of Medicine</td>
<td>100,000</td>
<td>3,062,638</td>
</tr>
<tr>
<td>WISCONSIN</td>
<td>Medical College of Wisconsin</td>
<td>100,000</td>
<td>3,764,215</td>
</tr>
</tbody>
</table>

* Includes a four-year $200,000 Research to Prevent Blindness Career Development Award, payable at the rate of $50,000 per year.

# Includes a five-year $500,000 Jules and Doris Stein Research to Prevent Blindness Professorship payable at $100,000 per year and a $150,000 Stein Professorship Laboratory renovation grant.
RESEARCH TO PREVENT BLINDNESS, INC. (RPB)
RESEARCH TO PREVENT BLINDNESS ENDOWMENT FUND (RPBEF)
COMBINED STATEMENT OF FINANCIAL POSITION
DECEMBER 31, 2010

<table>
<thead>
<tr>
<th>ASSETS</th>
<th>RPB</th>
<th>RPBEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and cash equivalents</td>
<td>$1,195,424</td>
<td>$5,438,899</td>
</tr>
<tr>
<td>Investments, at market value</td>
<td>16,071,190</td>
<td>238,380,506</td>
</tr>
<tr>
<td>*Amounts due from RPB</td>
<td>77,490</td>
<td>0</td>
</tr>
<tr>
<td>Interest receivable</td>
<td>456,340</td>
<td>1,719,221</td>
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<tr>
<td>Contributions receivable</td>
<td>98,845</td>
<td>0</td>
</tr>
<tr>
<td>Due from investment managers—net</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Prepaid expenses and refundable deposits</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Net fixed assets</td>
<td>24,321</td>
<td>0</td>
</tr>
<tr>
<td>Other assets</td>
<td>6,000</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td><strong>17,929,610</strong></td>
<td><strong>245,538,626</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LIABILITIES</th>
<th>RPB</th>
<th>RPBEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accounts payable and accrued expenses</td>
<td>36,870</td>
<td>30,608</td>
</tr>
<tr>
<td>Due to investment managers—net</td>
<td>392,892</td>
<td>4,697,138</td>
</tr>
<tr>
<td>Grants payable</td>
<td>0</td>
<td>4,573,078</td>
</tr>
<tr>
<td>*Amounts due to RPBEF</td>
<td>0</td>
<td>77,490</td>
</tr>
<tr>
<td><strong>Total current liabilities</strong></td>
<td><strong>429,762</strong></td>
<td><strong>9,378,314</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NET ASSETS</th>
<th>RPB</th>
<th>RPBEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrestricted net assets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrestricted—general operating</td>
<td>7,447,951</td>
<td>136,686,543</td>
</tr>
<tr>
<td>Unrestricted—designated</td>
<td>0</td>
<td>45,164,528</td>
</tr>
<tr>
<td><strong>Total unrestricted net assets</strong></td>
<td><strong>7,447,951</strong></td>
<td><strong>181,851,071</strong></td>
</tr>
<tr>
<td>Temporarily restricted net assets</td>
<td>2,694,916</td>
<td>8,327,430</td>
</tr>
<tr>
<td>Permanently restricted net assets</td>
<td>7,356,981</td>
<td>45,981,811</td>
</tr>
<tr>
<td><strong>Total net assets</strong></td>
<td><strong>17,499,848</strong></td>
<td><strong>236,160,312</strong></td>
</tr>
</tbody>
</table>

| Total liabilities and net assets | $17,929,610 | $245,538,626 |

* Amounts due to RPB and from RPBEF are eliminated upon combination.
## RPB-RPBEF
### COMBINED STATEMENT OF ACTIVITIES
#### YEAR ENDED DECEMBER 31, 2010

<table>
<thead>
<tr>
<th>Net assets released from restrictions or designation</th>
<th>2010</th>
<th>2009</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total net assets released from restrictions or designation</td>
<td>$144,134,494</td>
<td>$45,164,528</td>
<td>$189,299,022</td>
</tr>
<tr>
<td>Total public support and revenue</td>
<td>$14,195,638</td>
<td>$3,222,184</td>
<td>$11,481,962</td>
</tr>
<tr>
<td>Realized gain and change in unrealized appreciation of investments</td>
<td>$14,195,638</td>
<td>$11,481,962</td>
<td>$11,418,640</td>
</tr>
<tr>
<td>Net assets, beginning of year</td>
<td>$129,430,348</td>
<td>$48,386,712</td>
<td>$177,817,060</td>
</tr>
<tr>
<td>Net assets, end of year</td>
<td>$129,430,348</td>
<td>$48,386,712</td>
<td>$177,817,060</td>
</tr>
</tbody>
</table>

A complete set of RPB’s combined financial statements has been reproduced, along with the report of independent accountants, as a separate document. A copy may be obtained by contacting RPB at 1-800-621-0026.
Investing in Research to Prevent Blindness

The leverage generated by an RPB grant is difficult to measure because it can take so many forms. An RPB-supported pilot trial can lead to major funding from the National Institutes of Health for a large-scale clinical trial. Using RPB’s unrestricted support, a department of ophthalmology can demonstrate enough success to attract new research faculty or even major donors. A discovery may lead to a patentable treatment that not only helps countless people but also creates significant revenue for an institution to conduct further research. A medical student, having received an RPB Fellowship, can choose to become a vision scientist after spending a year conducting supervised research. In fact, all of the previous scenarios can follow from that early career experience.

While it is difficult to quantify, for 50 years RPB’s leverage has been plain to see, as nearly every major development in eye research and treatment can be traced to RPB support.

Contributions to RPB from the public sector increase that leverage. One way to join our effort is to include in a will a bequest that assures the continuity of research. To make a bequest, this simple form may be followed:

I give and bequeath to Research to Prevent Blindness, Inc., the sum of $_____ or _____ percent of my residuary estate or the following described property, i.e., securities and other assets to be used in furtherance of RPB’s general purposes or for research related to a specific eye disease, e.g., macular degeneration, glaucoma, etc.

Contact RPB to discuss any number of options for supporting eye research, including: donating securities; creating endowment funds; making a tribute gift; or establishing a Charitable Remainder Trust that enables you to provide for yourself and/or your family, and to support eye research as well. Please be sure to consult your attorney or financial advisor regarding the final form of any lifetime or testamentary transfer.

All gifts and bequests are tax deductible. Research to Prevent Blindness, Inc. (RPB) is recognized by the U.S. Internal Revenue Service as a publicly supported tax-exempt organization under section 501(c)(3) of the Internal Revenue Code.
Several donors have developed fundraising initiatives to help RPB cure, prevent and treat blinding disorders. 2010 saw the launch of a Web site, Contacts4change.com, which sends one dollar to RPB for every pair of contact lenses ordered through the site. Neil Kalin, the site’s founder, says: “We are in this business to succeed, but we also wish to give something back. Most contact lens wearers don’t know much about blinding eye diseases as they usually affect older adults. Our pledge, beyond customer satisfaction, is to support research into finding cures.”

For six years now, Dr. Rebecca Schoonover has held Cocktails for a Cause (www.icare4eyes.com/specialty3.htm), an annual fundraiser supporting blindness research. She has donated thousands of dollars to RPB in loving memory of a colleague “who was an optometrist, friend, and mother whose passion for helping people will be continued through the advancement of vision research.”

In late 2010, RPB was contacted by Tauru Chau and Christi Bruchok (below), both legally blind, whose ambition is to ride a bicycle-built-for-two from the southern-most tip of South America to Alaska in 2012. As they travel, they will create small media events at local blindness service institutions, raising awareness about the need to support vision research through RPB, as well as appreciation for the abilities of those who have lost significant sight. Anyone interested in following their progress, or in seeing how they perceive the world, can do so through RPB at www.rpbusa.org/rpb/resources/page/ or at 2blind2ride.tauruandchristi.com.
RPB is committed to stimulate, sustain and intensify a concerted research assault, with the goal of developing more effective treatments, preventives and cures for all diseases of the visual system that damage and destroy sight. RPB mobilizes financial resources in support of eye research making available essential laboratory space, scientific personnel and advanced technological equipment in its mission, which seeks to preserve vision and restore sight.

A Record of Economy and Efficiency

RPB’s fund-raising cost ratio has been less than 2% for over fifty years of service. Its staff of nine is among the smallest of all major organizations in the voluntary health field.