

50 YEARS OF RESEARCH TO PREVENT BLINDNESS





Research to Prevent Blindness

645 Madison Avenue, New York, NY 10022-1010 Jules Stein, M.D., Founder (1896-1981)

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"...the problem of blindness must be met before darkness sets in."

-from RPB's first annual report, 1960

A Time for Reflection

The founding of Research to Prevent Blindness (RPB) a half-century ago ushered in what can be termed the golden age of eye research. A partial list of RPB's significant accomplishments may be found on succeeding pages.

I was privileged to become RPB's Chief Executive Officer when its grants program was first being formulated, and have served RPB in a voluntary capacity as Chairman of its Board of Trustees since 2003. As RPB marks its 50th Anniversary, it continues to stimulate an aggressive research effort to eradicate all blinding disorders, but the challenges are significant! Due to our aging population, a cluster of serious eye diseases threatens to reach epidemic proportions within the next few years.

RPB is an absolutely unique public foundation. Since its establishment, it has been associated with virtually every advance in eye research and patient care. It has attained an enviable record of efficiency, economy and accomplishment. It is distinctive in the manner in which it seeks to support talented scientists with innovative ideas and often contrarian concepts. It has the smallest professional staff (never more than ten employees during its entire existence) and enjoys the lowest historic fund-raising expense ratio (less than two percent) among all major nonprofit foundations in this country.

RPB's founder, Dr. Jules Stein, an ophthalmologist, created an endowment and a special fund to match gifts up to \$1,000,000 from others. While the endowment allows for the stability and continuity of RPB's long-range research effort, tax deductible gifts from the public sector make the difference between a marginally successful program and a dynamic one. Historically, RPB has an outstanding record of converting contributed dollars into solid scientific achievements.

I hope that you will share this Report with others, and we welcome your support of our efforts to preserve vision and restore sight.

David F. Weeks, Chairman

Creating a Golden Age of Eye Research A Partial List of RPB's Achievements

In 1960, RPB opened a new and exciting era of ophthalmic research, spurring more scientific advances in a short span of time than in all the previous recorded years in history. As the result of its comprehensive efforts, RPB has been identified with virtually every major advance in the treatment of diseases that diminish or destroy sight. Today, RPB researchers are closer than ever to determining the causes of blinding eye diseases, which are still largely unknown to science.

Creating the Environment to Stimulate Eye Research

- Soon after launch, RPB initiated the first and only exhaustive survey of eye research in the U.S. It exposed a severe lack of laboratory space and shortage of scientific personnel. RPB followed that study with a landmark national public opinion poll indicating that Americans feared blindness more than any physical affliction except cancer.
- Before RPB, Ophthalmology was relegated to subdivision status, under departments of Surgery in most medical schools. This made funding

more difficult to obtain. By limiting its support to departments of Ophthalmology, RPB encouraged medical schools to upgrade Ophthalmology to departmental status. With the consequent infusion of basic scientists (stimulated by RPB) into these new departments, the entire thrust of eye research was enhanced and invigorated.

• In 1961, RPB launched a unique laboratory construction campaign that led to the development of eye institutes in every section of the country.



RPB's first major endeavor was sponsorship of a comprehensive national survey which found that only 15 ophthalmologists and 37 basic scientists were engaged in vision research in the entire country. The one year survey report (left), comprised of 171 pages, recommended the creation of eye departments at U.S. medical schools and the creation of a National Eye Institute within the National Institutes of Health.

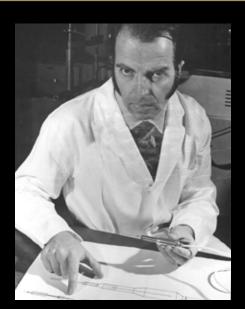
- A few years later, RPB initiated and spearheaded a movement that created the National Eye Institute (NEI) within the National Institutes of Health. The effort succeeded despite stiff political opposition. RPB then became a major influence in stimulating interest and support on the Institute's behalf.
- To this day, RPB's grants provide innovative scientists the seed money to help attract major grants from the NEI and other sources.



Shown here is an artist's sketch depicting the Congressional testimony of RPB's founder, Dr. Jules Stein, in support of the successful legislation, introduced by RPB, that led to the creation of the National Eye Institute.



RPB organized the first major Capital Gifts Campaign to construct a new research building at The Johns Hopkins University School of Medicine. The concept stimulated the creation of dozens of eye research institutes serving millions of patients across the country. Shown here are just four construction campaign projects financed by RPB. *Clockwise from top left:* The Casey Eye Institute at the Oregon Health & Science University; The Jules Stein Eye Institute at UCLA; The Lions Eye Institute at the University of Louisville; and the Cullen Eye Institute at the Baylor College of Medicine.



With pioneering funding from RPB in 1971, Robert Machemer, M.D., of the Bascom Palmer Eye Institute, University of Miami, developed the instrumentation to perform vitreoretinal surgery that today saves and restores the sight of thousands of Americans each year. Here, Dr. Machemer shows a diagram of his instrument.

With major grant support from RPB, David L. Guyton, M.D., at The Johns Hopkins School of Medicine, developed an automatic pediatric vision screener to catch amblyopia earlier in children, thereby increasing the opportunity for successful treatment. Amblyopia occurs in two to three percent of all children.

Photo: Keith Weller

Dramatic Improvements in Treatment

In the decade before RPB was founded, *cataract* patients were hospitalized for an extended period, with sand bags on both sides of their heads to immobilize them during recovery. After surgery, they were required to wear quarter-inch thick glasses, which were not only unattractive but distorted the world around them. The introduction of the intraocular lens brought with it great promise—and many surgical challenges. Scientists at several RPBsupported institutions collaborated to improve both the lens and operative procedures. Today, the cataract patient does not require hospitalization and can generally return home within a few hours after the procedure with greatly enhanced visual acuity. Current research supported by RPB seeks to delay the onset or prevent the formation of cataracts altogether.

During the same period, **retinal detachment** almost always led to blindness. Fewer than four percent of retinal detachment patients recovered their sight. Today, the treatment is more than ninety percent successful through the use of laser surgery and other improved procedures.

RPB's Pioneering Grant Support and Promise for the Future

(a partial list of sight-saving accomplishments)

- One of RPB's early grants provided support to explore the adaptation of the laser to treat vision disorders. At the time, the government did not encourage this research for security reasons. Since then, the laser has been used to save the sight of patients suffering from many eye diseases, including *glaucoma, cataract, myopia,* and retinal conditions such as *macular degeneration* and *diabetic retinopathy*.
- RPB awarded the first grant ever for the development of vitreoretinal surgical instrumentation. Support from other sources was unavailable because of the controversial nature of the procedure. Today, the surgery known as vitrectomy restores the sight of thousands of Americans each year.
- RPB supported the initial basic research that led to today's anti-VEGF treatments for patients with **wet macular degeneration** and **diabetic retinopathy**.



- RPB has awarded continuous, critical support for gene therapy treatments that have so far reversed a form of retinitis pigmentosa (RP) in a dozen patients and corrected color blindness in laboratory experiments. Gene therapies are in development for many other eye diseases.
- RPB continues to support numerous, promising developments in *stem cell therapies* to restore sight by replacing or regrowing retinal photoreceptor cells.
- RPB's grant support has invigorated scientific efforts to correct **amblyopia**—the leading cause of vision loss among children in this country.

Scientific advances supported by RPB have saved patients and the government billions of dollars in Medicare costs. But, more important, they have saved the sight and/or preserved the vision of millions worldwide.

Albert Maguire, M.D., University of Pennsylvania School of Medicine, prepares an eight-year-old patient for gene therapy surgery that restored the child's sight, lost to a form of retinitis pigmentosa. RPB's continued support will help bring gene therapy to patients with other retinal diseases.

The Road Ahead, with an Eye on the Rearview Mirror

It is more than a happy coincidence that, in our 50th year committed to the restoration of sight and preservation of vision, RPB researchers report that 12 patients treated with gene therapy for an inherited retinal degeneration have regained significant sight, and that a gene therapy cure for color blindness has been proven possible.

When RPB embarked on our mission, we pledged resources to provide the time, tools and environment necessary for our awardees to work, and for their creativity to flourish. Today, our scientists are reporting discoveries and conducting clinical trials that promise to deliver betterthan-ever patient care.

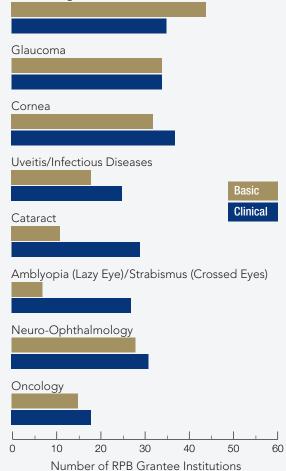
And yet, even as we reflect on our golden anniversary, we recognize the cresting wave of aging baby boomers, representing a surge in the number of people who will develop age-related diseases of the eye. The urgent need of anyone confronting vision loss remains our motivation.

Our renewed efforts will continue to arm practicing ophthalmologists with tools developed by our basic and clinical researchers. RPB extends a lifeline to those scientists and, by extension, to patients. We will continue to do this for as long as it takes to fulfill our mission.

Diane S. Swift, President

RPB-SUPPORTED RESEARCH REPORTED DURING 2009

Retinal Degeneration/ Vascular Disease



Hundreds of RPB-supported vision scientists throughout the U.S. are investigating the areas of basic and clinical research graphed above. 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.

The RPB Research Program

500 years ago, RPB's first survey of the nation's top eye research institutions disclosed three major impediments to the prevention of eye disease: lack of adequate lab facilities, lack of talented and trained manpower, and lack of unrestricted funds for promising projects. Since then, RPB has allocated hundreds of millions of dollars to address these needs.

"RPB has developed an army of promising researchers through our Research Program," says Dr. Harold Spalter, Chairman of RPB's Scientific Advisory Panel.

RPB's Program is constantly refined to address urgent and emerging needs within the vision community. "We have regularly taken the pulse of eye research across this country, and have created new grant categories or unique awards to maintain its vitality," says Spalter.

Examples abound. Since 1984, the Jules and Doris Stein RPB Professorship has been available to department chairs as a powerful tool to recruit accomplished basic scientists into ophthalmology. In 1993, RPB began awarding Medical Student Fellowships to attract potential researchers into ophthalmology. More recently, RPB was able to realize a benefactor's vision and stimulate disease-specific studies by creating the Walt and Lilly Disney Award for Amblyopia Research. Says Spalter, "I know of no other eye research organization as responsive."

Joseph M. Miller, M.D., M.P.H., University of Arizona College of Medicine, recipient of a Walt and Lilly Disney Award for Amblyopia Research, develops child-friendly vision testing tools. Here, he is measuring the astigmatism of an infant with a device that measures corneal curvature while allowing eye contact with the child.

E

2009 Advances in Eye Research

In 2009, the patient above, along with 11 vision-compromised patients with a rare form of *Leber's Congenital Amaurosis*, continued treatment with gene therapy in one eye. Each patient experienced dramatic restoration of sight with no significant adverse effects. And there was more encouraging news. While there had been some concern that previous exposure to the virus used to carry the gene therapy might set off a damaging immune system response, studies have demonstrated the therapy's safety.

In every Annual Report since 1960, we have presented advances in eye research. The earliest success stories included a development ranked by the American Medical Association as one of the top ten medical advances of 1962: a drug originally synthesized as a possible cancer treatment was found effective against herpes simplex keratitis. That same year, scientists achieved the first successful imaging of the bloodstreams in the retina (magnified 1,000 times), while others used a laser to repair torn retinas. A year later, the first reliable recordings of specific brain responses in visual field testing were reported.

Many of today's breakthroughs are built on earlier findings. Almost none would have been possible without the 50 years of support from RPB grants. The following briefs are culled from published studies as well as the year-end summaries of ongoing work that RPB requires of its grantees.

2009

Active individual grantees: 155 Active grantee institutions: 57 Published studies citing RPB: 950

Retinal diseases, including Age-Related Macular Degeneration (AMD)

RPB researchers have finalized the world's first complete volume of retinal neuronal connectivity, providing a thorough blueprint of how the retina is constructed and allowing science, for the first time in 150 years of study, to define what is normal for retinal circuitry.

Investigators confirmed that compounds called polyphenols (found in plants, including berries and tea) may assist in delaying, slowing or treating certain types of retinal degenerations, including *retinitis pigmentosa*.

Drugs used in psychiatry and neurology as mood stabilizers and anti-epileptics may provide a novel treatment for preserving vision in individuals with *ischemic injury* (shortage of the blood supply) to the retina, according to RPB scientists.

Damaging, excessive blood vessel growth (neovascularization), a defining feature of **wet AMD**, **retinopathy of prematurity**, and proliferative **diabetic retinopathy** may be inhibited by some non-steroidal anti-inflammatory drugs (NSAIDs), according to RPB-supported investigators.



RPB funds were applied to the development of a new device to image the distribution of the macular carotenoids, lutein and xeaxanthin, in the living human eye. This device is the only one approved for use in the NEI-sponsored AREDS-2 study, designed to assess the effects of these oral supplements as well as omega-3 fatty acids. RPB researchers have taken the first step in creating a technique to remove fatty by-products that accumulate over long periods in the retinal pigment epithelium and contribute to the development of *AMD*.

An RPB-supported investigation has produced data suggesting that the broad spectrum antibiotic, minocycline, may be useful in the treatment of photoreceptor degeneration associated with *retinal detachment*, up to 24 hours after the retina has become detached.

Eye Movement Disorders

Researchers studying the formation of extraocular muscles are seeking to identify the regulators of muscle regeneration in order to treat *strabismus* (crossed eyes) and *amblyopia* (lazy eye).

Cataract

Evidence indicates that patients over the age of 50 who have had vitrectomy surgery (removal of the vitreous gel which fills the eye) are prone to develop *nuclear cataracts*. Scientists now report that it should be feasible to delay or prevent these cataracts, possibly by supplementing a form of vitamin C—ascorbate—to the vitreous cavity in the middle of the eye.

Cornea

RPB-supported findings reveal for the first time that allergic asthma is a risk factor for corneal graft rejection. The findings also identify therapeutic targets for neutralizing immune factors that contribute to **corneal graft** rejection.

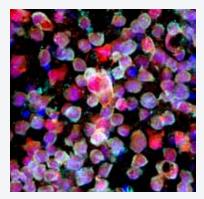
Advances in gene therapy

RPB researchers' use of gene therapy to cure color blindness in the lab was cited as the No.3 scientific discovery of 2009 by *Time Magazine*. Successful tests of gene therapy have opened the door to treating a range of eye diseases. Clinical trials are being formed to treat patients with *achromatopsia* (inability to distinguish colors). Other gene therapy trials are in the works to treat those with *retinoschisis* (splitting of the retina) and *diabetic retinopathy*.



For millions of people with color blindness (mostly afflicting men) gene therapy may allow them to see and use the full spectrum of crayons (*top*) as opposed to the drab colors they now see (*bottom*) and, more important, to enter careers requiring accurate color discrimination, which currently inhibits their employment.

Advances in stem cell therapy



iPS cells at four weeks into their development as photoreceptor cells. As science unravels the biological mechanisms of eye development and disease progression, the ability to regenerate damaged tissue through stem cell therapy becomes ever more possible.

At one RPB-sponsored lab, investigators have grown retinal cells from stem cells. At another, they have directed retinal pigment epithelium cells into becoming

photoreceptor-like cells. Still other scientists report success at integrating newly generated retinal ganglion cells into the circuitry of the retina and brain.

In a development that holds great promise for the entire field of regenerative medicine, RPB researchers are focusing on a new type of stem cells: induced pluripotent stem cells (iPS cells). These are made by inserting stem cell genes into skin fibroblasts (the most common type of cell found in connective tissue), resulting in cells that have all the qualities of embryonic stem cells. Mature, functioning photoreceptor cells have been grown using this method. More important, iPS cells can generate patient-specific stem cells, eliminating the risk of rejection by the body's immune system. Scientists have demonstrated that Rapamycin, a drug used to prevent rejection of transplanted organs, can be used to prevent *corneal scarring* following corneal transplantation.

Researchers found that topical trichostatin A, applied immediately after laser refractive therapy, may help prevent *corneal haze*, a common postsurgery complication.

Diabetic Eye Disease

Preliminary evidence indicates diabetic patients who smoke may be risking the acceleration of retinal disease due to the potential additive effects of chronic exposure to both high blood sugar and nicotine.

Data gathered over a 25-year period suggest that sustained blood sugar and blood pressure control may be beneficial in reducing the incidence of *macular edema*, a significant cause of visual impairment in persons with diabetes.

Dry Eye

For the first time, researchers identified a specific protein in the lacrimal gland that can cause *dry eye* in *Sjogren's syndrome*. The finding will allow them to identify therapeutic interventions.



Glaucoma

RPB researchers have established that communication between the optic nerve and brain is challenged very early in *glaucoma* and can be rescued by medication. Their central finding—that glaucoma likely originates in the brain—represents a paradigm shift in the current understanding of the disease and opens the door to neuroprotective therapies.

Ocular Cancer

Researchers suggest that patients undergoing certain radiation treatment for an eye cancer known as *choroidal melanoma* should be monitored for several years to allow early identification and management of *corneoscleral necrosis* (premature cell death—a significant complication recently described by an RPB research team).

RPB-supported findings indicate that an available drug used to inhibit the growth of leaky blood vessels may be useful as an adjunct therapy for *micrometastatic eye melanoma*.

Uveitis and Ocular Inflammation

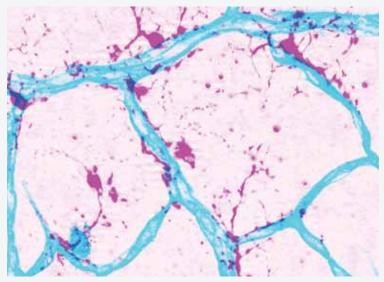
An RPB award was one of two key grants used to finance the Systemic Immunosuppressive Therapy for Eye Diseases (SITE) Cohort Study, the largest group of *ocular inflammation* patients ever assembled. The results support wider use of immunosuppressive drugs for treatment of difficult cases of ocular inflammation that need long-term treatment.

Drug Delivery Systems

While some scientists are developing new ophthalmic drugs, others are seeking ways to efficiently deliver these agents to the eye. One group has demonstrated that a single injection containing thermo-sensitive hydrogel may be useful in improving the delivery of multiple agents to intraocular tissues.

Beyond the eye

An RPB researcher studying blood vessel development in the eye translated those findings into a breakthrough development in kidney regeneration. There are no effective treatments for acute kidney injury, a growing problem in hospitals and clinics. "This [...] pathway may be important to tissue regeneration and repair in other organs, including the heart, lung and intestine," said the researcher.



A type of macrophage called a microglial cell (shown here in purple) is closely associated with blood vessels in the retina (shown in blue). Cells of this type elicit repair responses after kidney injury and likely have the same kind of repair activity in many organs.

Lifestyle research: A guide to eye health

Based on the premise that education about the causes of eye disease can improve prevention, the timely dissemination of eye research developments has been one of RPB's goals since the beginning. In 2009, RPB distributed a "Guide to Eye Health," a fact sheet containing recent findings on "lifestyle" risk factors for eye disease. Since its publication, even more lifestyle news has come to light.

RPB researchers have suggested that drinking and smoking may accelerate the risk of **AMD** with increasing age, and that even smokers aged 80 and over should quit or face an ever-rising risk of macular degeneration.

A study indicated that nutrient-rich diets, rather than vitamins and minerals taken as supplements, are related to having less severe *cataracts*.

Scientists found that high caloric and sodium intakes appear to be associated with the progression of *retinal disease* among African American patients with type 1 diabetes.

Investigators reported that improving vitamin D levels in the blood (from moderate exposure to the sun, walking outdoors and consuming vitamin D-containing foods and supplements) was related to lower risk for early stages of *age-related macular degeneration*.

A study confirmed that omega-3 fatty acids (found in fish such as salmon, mackerel or tuna, and



The "Guide to Eye Health" can be ordered from RPB's Web site, www.rpbusa.org.

in walnuts, flax seed and other foods) can prevent and treat *retinopathy* and improve retinal function in type 2 diabetes.

Researchers reported that resveratrol, a plant compound found in red wine, peanuts, and many berries, may counteract age-related effects and reduce intraocular pressure, suggesting it may be useful as a treatment for *glaucoma*.

New Grants 2009

The Jules and Doris Stein RPB Professorship

is RPB's premier award, providing up to \$700,000 across seven years with a possible additional \$150,000 in matching funds to equip lab space. It is designed to foster translational research by recruiting outstanding basic scientists to conduct clinically relevant research in a department of ophthalmology. In 2009, there were four active RPB Stein Professors.

Paulo A. Ferreira, Ph.D.

Duke University School of Medicine

Dr. Ferreira (*above*) seeks to understand the genetic and molecular bases of diseases affecting neurons of the retina and causing visual impairment. Many of his findings have medical implications far beyond vision science. "Among other advances, we have identified molecular processes that contribute to the protection of light-sensing neurons from light-elicited damage and aging. These advancements will define novel therapeutic targets and approaches to delay the onset or cure a variety of visual disorders," says Ferreria.

James L. Funderburgh, Ph.D.

University of Pittsburgh School of Medicine Identified trabecular meshwork stem cells, opening the path for stem cell therapy reduction of intraocular pressure and prevention of *glaucoma*.

Irina A. Pikuleva, Ph.D.

Case Western Reserve University School of Medicine

Identified the most abundant enzyme involved in eliminating cholesterol from the retina; will start developing therapeutic

strategies to enhance its function in order to prevent or slow progression of *AMD*.

David S. Williams, Ph.D.

David Geffen School of Medicine at UCLA

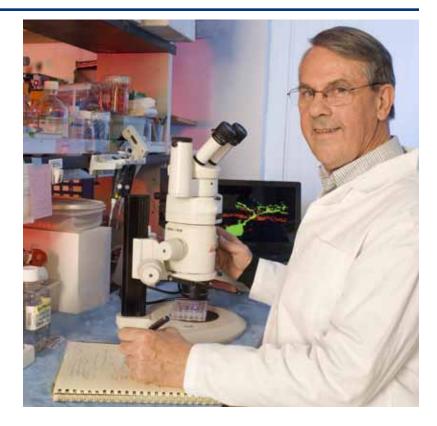
Investigated the effects of the metabolite oxaloacetate on lifespan, with the prospect of using it as a treatment to retard *retinal degenerations*.

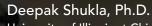
The RPB Walt and Lilly Disney Award for Amblyopia Research

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.

David R. Copenhagen, Ph.D.

University of California, San Francisco, School of Medicine Amblyopia develops in children, usually before they can speak, making it particularly difficult to detect. The condition can lead to a permanent loss of visual function and is thought to result from incomplete or malformed connections between neurons in the visual system. "Recently, we found that a specific hormone-like factor called a neurotrophin plays a key role in the normal maturation of neural connections in the retina during postnatal development," says Dr. Copenhagen, "and we are investigating pharmacological and genetic approaches to new therapies."





University of Illinois at Chicago

"We are investigating the molecular and cellular basis for the spread of ocular herpes within the human eye. We have been able to establish that cells respond to *ocular herpes* infection by enhancing the number of cellular projections (filopodia). The virus, in turn, uses this opportunity to travel along filopodia to reach the cell body."

RPB Lew R. Wasserman Merit Awards

provide \$60,000 to mid-career scientists, creating a continuum of financial resources for them to build on earlier work and maintain a research career.

Shiming Chen, Ph.D.

Washington University in Saint Louis School of Medicine Determining how mutations of CRX (the master regulator gene for photoreceptor function and survival) cause disease in order to test the effectiveness of gene therapy.

Reza Dana, M.D., M.P.H., M.Sc.

Harvard Medical School

Developing novel and effective treatments that control inflammation and immunity in *dry eye* disease.

David C. Musch, Ph.D., M.P.H.

The Regents of the University of Michigan School of Medicine Determining if the location of damage from *glaucoma* is important in predicting disease progression.

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 eye researchers.

Edward Chaum, M.D., Ph.D.

University of Tennessee Health Science Center

Developing Internet-based, automated methods for diagnosing blinding eye diseases.

P. Michael Iuvone, Ph.D.

Emory University School of Medicine

Utilizing circadian rhythms and neuromodulators in the retina to develop novel treatment strategies for blinding diseases such as *AMD*.



Robert W. Massof, Ph.D.

The Johns Hopkins University School of Medicine Measuring quality of life for a large, multi-center clinical trial on *low vision* rehabilitation.

Julia E. Richards, Ph.D.

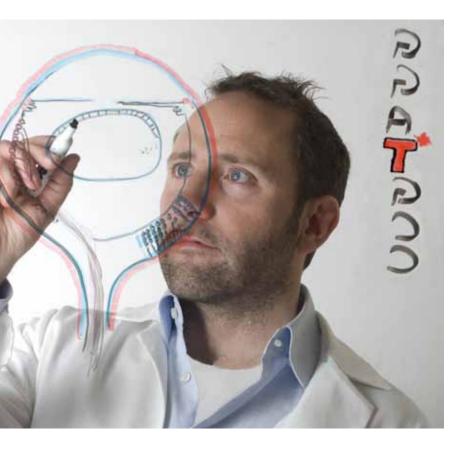
The Regents of the University of Michigan School of Medicine Determining if non-ocular conditions are genetically associated with early middle age onset of *open angle-glaucoma*.

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 *agerelated macular degeneration*. This year's recipient is Jayakrishna Ambati, M.D. (pictured at left), University of Kentucky College of Medicine. "My lab will be pursuing information about the precise mechanism of action of small interfering RNAs that may lead to new treatments for ocular *angiogenesis* [excessive blood vessel growth]. We will also continue our pursuit of biomarkers for the progression of AMD and examine various compounds for their ability to suppress *angiogenesis* in diseases of the cornea. All of these studies will enhance our understanding of fundamental vascular biology."

RPB Career Development Awards

provide \$200,000 across four years to outstanding young clinical and basic scientists conducting research in departments of ophthalmology. They are valuable recruiting tools for chairs of departments of ophthalmology.



Alon Kahana, M.D., Ph.D.

The Regents of the University of Michigan School of Medicine Developing new tools for diagnosis and treatment of extraocular muscle and orbital disorders in *amblyopia* and eye movement disorders, using regenerative medicine technologies.

Aparna Lakkaraju, Ph.D.

University of Wisconsin-Madison School of Medicine Understanding cholesterol homeostasis in the retinal pigment endothelium and assessing whether cholesterolmodifying drugs like statins will be beneficial to the treatment of AMD.

Holly L. Rosenzweig, Ph.D.

Oregon Health & Science University School of Medicine Investigating the role of the NOD2 gene in *auto-inflammatory eye disease* and its connection to skin and joint diseases.

Douglas Gould, Ph.D. (pictured at left)

University of California, San Francisco, School of Medicine Dr. Gould's lab is testing a novel theory that misfolded mutant proteins lead to oxidative stress in tissues key to AMD. "We are developing and using unique and valuable tools to understand the basic disruption of normal bodily functions in retinal diseases. Our goal is to discover new cellular mechanisms that can be exploited to delay or prevent vision loss in patients."

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.

Audrey Bernstein, Ph.D.

William & Mary Greve Scholar Award Mount Sinai School of Medicine Addressing ways to promote wound healing of the cornea after LASIK-induced *corneal edema*.

Meredith Gregory-Ksander, Ph.D.

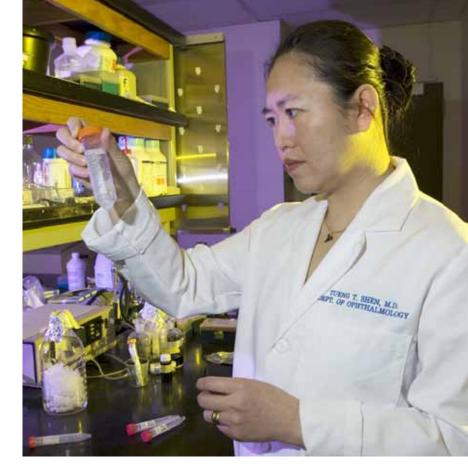
Sybil B. Harrington Scholar Award Harvard Medical School Determining how the corneal epithelial barrier to infection is maintained and how bacteria penetrate this barrier.

Albert S. Jun, M.D., Ph.D.

Dolly Green Scholar Award The Johns Hopkins University School of Medicine Studying basic cellular defects in *Fuchs' dystrophy* to develop non-surgical treatments for the disease.

David N. Zacks, M.D., Ph.D.

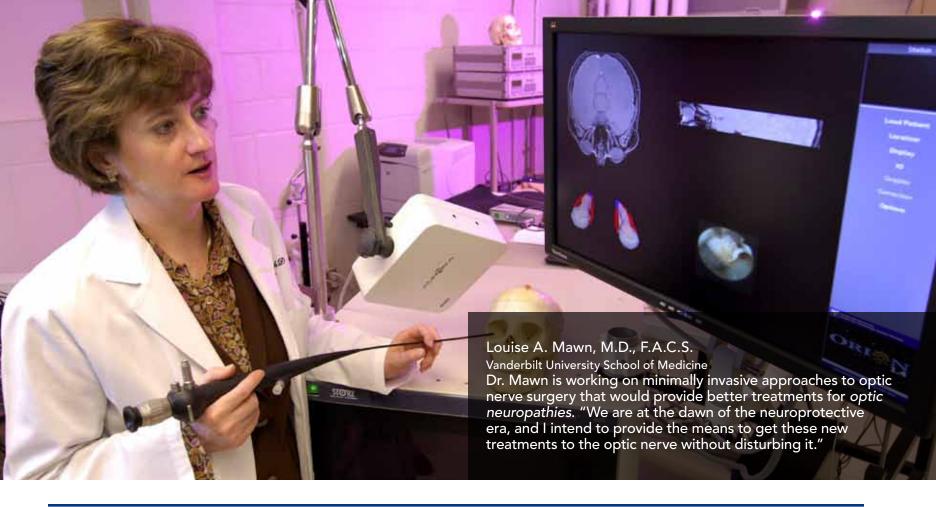
Sybil B. Harrington Scholar Award The Regents of the University of Michigan School of Medicine Laying the foundation for the development of human clinical trials for photoreceptor neuroprotective therapy.



Tueng T. Shen, M.D., Ph.D. (pictured above)

Ernest & Elizabeth Althouse Scholar Award University of Washington School of Medicine

Dr. Shen combines ophthalmology, bioengineering and electrical engineering to develop new treatment options for people with eye disorders. "We now have a contact lens wireless monitoring device that can transmit continuous information about intraocular pressure and glucose levels to expand our understanding of diseases like *glaucoma*. We are also creating intraocular replacement lenses that continually release post-operative medications. And we are refining the next generation of artificial corneas to help millions who suffer from corneal blindness regain sight."



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.

Louis Robert Pasquale, M.D.

Harvard Medical School

Defining gene-environment interactions and delineating the genetic architecture of *primary open angle-glaucoma*.

Terry Smith, M.D.

The Regents of the University of Michigan School of Medicine Developing therapies for patients with sight threatening *Graves disease*.

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.

Kathleen Berg

University of Minnesota, Academic Health Center, Medical School Investigating the cause of infantile *nystagmus*, characterized by involuntary eye movements, which can reduce vision.

Lloyd Cuzzo

Keck School of Medicine of the University of Southern California Identifying the role of certain proteins in the development of *optic neuropathy* in Alzheimer's disease.

Asim Visal Farooq

University of Illinois at Chicago Investigating entry receptors used by the *herpes simplex* virus (HSV-1) to enter the corneal epithelium.

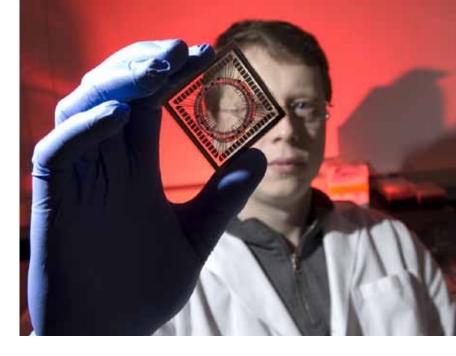
Varsha Manjunath

Tufts University School of Medicine

Investigating the outer retina/retinal pigment epithelium complex in *dry AMD* employing a new one-micron, ultra-high resolution (OCT) prototype.

RPB Research Sabbatical Grants provide

\$50,000 each to mid-career researchers involved in educational and scientific programs that either enhance their scientific expertise or allow them to pursue a new ophthalmic research career path.



Jack Sychev (pictured above)

University of Washington School of Medicine

Using light-absorbing compounds as nano-switches, coupled with pharmacological agents, to restore light sensation to cells.

Peter Hao Tang

Medical University of South Carolina

Developing a technique to improve the delivery of multiple therapeutic agents to intraocular tissues in the treatment of *retinal disease*.

Eric A. Pierce, M.D., Ph.D.

University of Pennsylvania School of Medicine

Dr. Pierce will travel to the Vision Institute, Inserm-Pierre and Marie Curie University and to the Nijmegen Center for Molecular Life Sciences, Radboud University, Netherlands, where he will be identifying the genetic causes of inherited retinal degenerations to determine how mutations cause death of photoreceptor cells.

The Grants Review Process

RPB relies on a diverse group of experts to review applications, a practice begun by Dr. Stein. To maintain objectivity, ad hoc committees (rotating panels composed of chairs of departments of ophthalmology) review applications and offer recommendations to the Scientific Advisory Panel. That panel—made up of eminent scientists from wide-ranging fields—passes recommendations to the RPB Board of Trustees for final approval.

IN MEMORIAM: STEVEN M. PODOS, M.D.

The Research to Prevent Blindness Board of Trustees and staff are saddened at the passing of Dr. Steven M. Podos. Dr. Podos held many significant positions in the field of glaucoma research, and served on RPB's Scientific Advisory Panel.

2009 RPB Ad Hoc Committee Members

Dimitri T. Azar, M.D., University of Illinois at Chicago
William T. Driebe, M.D., University of Florida College of Medicine
David L. Epstein, M.D., Duke University School of Medicine
Barrett G. Haik, M.D., University of Tennessee Health Science Center
Shalesh Kaushal, M.D., Ph.D., University of Massachusetts Memorial Medical Center
Lanning B. Kline, M.D., University of California, Davis, School of Medicine
Mark J. Mannis, M.D., University of California, Davis, School of Medicine
Stephen D. McLeod, M.D., University of North Carolina at Chapel Hill School of Medicine
Timothy W. Olsen, M.D., Emory University of Pittsburgh School of Medicine
Joel S. Schuman, M.D., Vanderbilt University School of Medicine
James C. Tsai, M.D., Yale University School of Medicine
Russell N. Van Gelder, M.D., Ph.D., University of Washington School of Medicine

2009 RPB Scientific Advisory Panel

HAROLD F. SPALTER, M.D., Chair

Emeritus Professor of Clinical Ophthalmology Columbia University College of Physicians & Surgeons

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

JOHN E. DOWLING, Ph.D.

Professor of Neurosciences, Department of Molecular and Cellular Biology, Harvard University

ROBERT FOLBERG, M.D.

Founding Dean, Oakland University William Beaumont School of Medicine Professor, Departments of Biomedical Sciences, Pathology & Ophthalmology

EVE J. HIGGINBOTHAM, S.M., M.D.

Senior Vice President & Executive Dean for Health Sciences Howard University

HAIG H. KAZAZIAN, Jr., M.D.

Professor, Department of Genetics University of Pennsylvania School of Medicine

GORDON K. KLINTWORTH, M.D., Ph.D.

Professor, Departments of Pathology & Ophthalmology Duke University School of Medicine

ANTHONY MOORE, MA, FRCS, FRCOphth, FMedSci

Division of Inherited Eye Disease Institute of Ophthalmology, University College of London

KRZYSZTOF PALCZEWSKI, Ph.D.

Professor & Chair, Department of Pharmacology Case Western Reserve University

STEPHEN J. RYAN, M.D.

President, Doheny Eye Institute Professor, Department of Ophthalmology Keck School of Medicine of the University of Southern California

SHEILA K. WEST, Ph.D.

Professor, Departments of Ophthalmology & Epidemiology Wilmer Eye Institute, The Johns Hopkins School of Medicine

Left to right: Palczewski, Anderson, Michael Gorin (M.D., Ph.D., Departments of Human Genetics & Ophthalmology, University of California, Los Angeles), Higginbotham, Spalter (seated), West, Folberg, Moore.



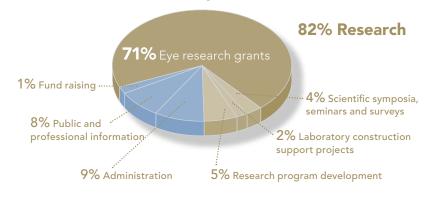
Network in Action

Retinopathy of prematurity (ROP), a leading cause of childhood blindness throughout the world, may develop in prematurely born infants. There are indications that the ROP rate may be increasing as a result of an increasing neonatal population, while the number of ophthalmologists performing examinations on these infants is diminishing. A team of RPB researchers is collaborating to counter both trends by developing reliable, quick, telemedical diagnostic approaches for ROP: Robison V. Paul Chan, M.D., F.A.C.S., of Weill-Cornell Medical College; Michael F. Chiang, M.D., of Columbia University; and Thomas C. Lee, M.D., of the University of Southern California. "We're looking at how to identify the disease better and learning more about how it develops," says Chan. "Treating these children can be stressful. You're not only trying to help these very young, very sick patients, but also their parents and families who are obviously extremely worried."



National Network of Eye Research

The flexibility of RPB support helps create a true national network of eye research. Grants from RPB enable departments of ophthalmology to enhance projectspecific grant work from other sources, magnifying the value of those grants. RPB support can also be used to promote collaborations with other research departments or even other schools. The adjacent list includes U.S. medical institutions that received new departmental grants, or new awards for individual investigators.



How RPB Funds Were Expended 1960-2009

State	RPB Grantee Institutions	Total Grants 2009	Total Support Including 2009		
ALABAMA	University of Alabama at Birmingham School of Medicine	\$ 100.000	\$3,435,000		
ARIZONA	University of Arizona College of Medicine	100,000	1,745,000		
CALIFORNIA	University of California, Davis, School of Medicine	100,000	3,073,900		
CALL ON NA	David Geffen School of Medicine at UCLA	100,000	7,890,750		
	University of California, Irvine, College of Medicine	200,000	535,000		
	University of California, San Diego, School of Medicine	100,000	2,760,000		
	University of California, San Diego, School of Medicine				
	University of California, San Francisco, School of Medicine	400,000*	5,789,256		
	Keck School of Medicine of the University of Southern California	130,000	4,233,500		
FLORIDA	University of Florida College of Medicine	100,000	3,225,600		
	University of Miami Miller School of Medicine	100,000	3,670,200		
GEORGIA	Emory University School of Medicine	175,000	3,287,100		
ILLINOIS	Northwestern University Feinberg School of Medicine	100,000	2,195,000		
	University of Illinois at Chicago	190,000	3,606,712		
INDIANA	Indiana University School of Medicine	100,000	2,539,000		
IOWA	The University of Iowa Carver College of Medicine	100,000	3,527,425		
KENTUCKY	University of Kentucky College of Medicine	175,000	1,070,000		
	University of Louisville School of Medicine	100,000	3,169,800		
LOUISIANA	Louisiana State University Health Sciences Center in New Orleans	100,000	2,182,100		
MARYLAND	The Johns Hopkins University School of Medicine	200,000	6,680,140		
MASSACHUSETTS	Harvard Medical School	275,000	6,745,215		
MASSACHUSEHIS					
	Tufts University School of Medicine	30,000	2,993,697		
MICHIGAN	The Regents of the University of Michigan School of Medicine	550,000*	4,823,050		
	Wayne State University School of Medicine	100,000	3,433,000		
MINNESOTA	Mayo Medical School	100,000	2,574,600		
	University of Minnesota, Academic Health Center, Medical School	130,000	2,728,701		
MISSOURI	University of Missouri-Columbia School of Medicine	100,000	1,812,300		
	Washington University in Saint Louis School of Medicine	160,000	5,997,900		
NEBRASKA	University of Nebraska Medical Center	100,000	1,440,000		
NEW JERSEY	University of Medicine & Dentistry of New Jersey Medical School	100,000	1,967,000		
NEW YORK	Columbia University College of Physicians & Surgeons	100,000	4,293,167		
-	Mount Sinai School of Medicine	160,000	3,645,700		
	University of Rochester School of Medicine & Dentistry	100,000	2,200,250		
	SUNY at Buffalo School of Medicine & Biomedical Sciences	100,000	480,000		
	SUNY Upstate Medical University	100,000	2,210,000		
NORTH CAROLINA	Duke University School of Medicine	100,000	5,713,350		
NORTH CAROLINA	Luciversity of Nerth Caroline at Change Hill School of Madicine	100,000	1 070 500		
	University of North Carolina at Chapel Hill School of Medicine	100,000	1,070,500		
OHIO	Case Western Reserve University School of Medicine	100,000	2,812,500		
	Cleveland Clinic Lerner College of Medicine	100,000	1,420,000		
	University of Cincinnati College of Medicine	100,000	1,086,750		
OKLAHOMA	University of Oklahoma Health Sciences Center	100,000	4,251,600		
OREGON	Oregon Health & Science University School of Medicine	300,000*	3,862,150		
PENNSYLVANIA	University of Pennsylvania School of Medicine	130,000	5,093,500		
	University of Pittsburgh School of Medicine	100,000	3,468,372		
SOUTH CAROLINA	Medical University of South Carolina	130,000	1,977,500		
TENNESSEE	University of Tennessee Health Science Center	175,000	1,935,000		
	Vanderbilt University School of Medicine	160,000	1,950,500		
TEXAS	Baylor College of Medicine	100,000	3,704,060		
	The University of Texas Southwestern Medical Center at Dallas	100,000	3,446,000		
UTAH	University of Utah Health Sciences Center	100,000	4,565,300		
WASHINGTON	University of Washington School of Medicine	200,000	2,962,638		
		200,000			
	West Virginia University School of Medicine		273,100		
WISCONSIN	Medical College of Wisconsin	100,000	3,664,215		
	University of Wisconsin-Madison School of Medicine	300,000*	4,158,750		
	*Includes a four-year \$200,000 Research to Prevent Blindness Career Developm	ent Award, payable at the rate of	\$50,000 per year.		

RPB—RPBEF COMBINED BUDGET—2010

Research Grants and Other Program Allocations:

Unrestricted, Development and Challenge Grants to Medical Schools and Other Institutions\$	6,400,000
Research Professorships, Senior Scientific Investigators, Research Manpower and Visiting Professors Awards	5,115,000
Special Scientific Scholars and International Research Scholars Grants	500,000
Special, Emergency and LRW Grants	1,145,000
Direct Research Support	445,000
Research Program Development and Researc Facility Construction Grants	ch 360,000
Scientific Seminars, Surveys and Symposia	285,000
Public and Professional Information	675,000
Total Program Services	14,925,000

Management and General Allocations:

Salaries, Employee Benefits and Payroll Tax	201,325
Professional/Consultant Fees	1,162,500
Office Equipment/Supplies	8,825
Rent and Occupancy	45,000
Depreciation, Amortization and Insurance	23,000
Travel and Meetings	2,350
Telephone	2,000
Printing, Stationery, Postage and Shipping	3,000
Miscellaneous (Dues, Subscriptions, Other, etc.)	 20,000
Total Management and General	1,468,000
Fund Raising Allocations:	100,000
Total	 1,568,000
Grand Total	\$ 16,493,000

RESEARCH TO PREVENT BLINDNESS, INC. (RPB) RESEARCH TO PREVENT BLINDNESS ENDOWMENT FUND (RPBEF) COMBINED STATEMENT OF FINANCIAL POSITION DECEMBER 31, 2009

RPBEF RPB ASSETS Cash and cash equivalents 2,663,466 \$ 4,844,732 \$ Investments, at market value..... 16,416,149 221,309,693 *Amounts due from RPB..... 0 803.805 Interest receivable..... 68,256 1,018,075 Contributions receivable 194,824 0 Due from investment managers—net 0 0 Prepaid expenses and refundable deposits 0 0 Net fixed assets 46,241 0 Other assets..... 0 6,000 Total assets 19.394.936 227.976.305 LIABILITIES Accounts payable and accrued expenses..... 48.005 62.222 Due to investment managers—net..... 199.590 0 Grants payable 0 3,693,436 *Amounts due to RPBEF..... 803,805 0 Total current liabilities 851.810 3.955.248

NET ASSETS

Unrestricted net assets		
Unrestricted—general operating	8,350,240	121,080,108
Unrestricted—designated	0	48,386,712
Total unrestricted net assets	8,350,240	169,466,820
Temporarily restricted net assets	2,846,214	8,572,426
Permanently restricted net assets	7,346,672	45,981,811
Total net assets	18,543,126	224,021,057
Total liabilities and net assets	\$ 19,394,936	\$ 227,976,305

* Amounts due to RPBEF and from RPB are eliminated upon combination.

RPB—RPBEF	2009					
COMBINED STATEMENT OF ACTIVITIES		Unrestricted				
YEAR ENDED DECEMBER 31, 2009	General Operating	Designated	Total	Temporarily Restricted	Permanently Restricted	Total
Public support and revenue						
Public support						
Contributions		\$ —	\$ 1,140,964	\$ 1,368,382	\$ 1,607	\$ 2,510,953
Combined Federal Campaign	54,500	_	54,500	_		54,500
Ophthalmological associate memberships	130,200	_	130,200	_		130,200
Donated investments	59,745	_	59,745	_		59,745
Total public support	1,385,409		1,385,409	1,368,382	1,607	2,755,398
Revenue						
Interest and dividends	8,862,083	_	8,862,083	764,914	8,117	9,635,114
Other revenue	465,935		465,935	·	·	465,935
Total revenue	9,328,018		9,328,018	764,914	8,117	10,101,049
Net assets released from restrictions or designation						
Satisfaction of program restrictions or designations	1,292,892	(756,892)	536,000	(536,000)	_	_
Satisfaction of Matching Fund restrictions	1,000,000	(, 00,0,2)	1,000,000	(1,000,000)	_	_
Total net assets released from restrictions	.,		.,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	(1/000/000/		
or designation	2,292,892	(756,892)	1,536,000	(1,536,000)	_	_
Total public support and revenue	13,006,319	(756,892)	12,249,427	597,296	9,724	12,856,447
Expenses						
Program services						
Research grants, net of canceled grants						
of \$758,805 in 2009 and \$1,433,738 in 2008	7,621,214		7,621,214			7,621,214
Direct research support	409,829	_	409,829			409,829
Program development to stimulate laboratory	407,027		407,027			407,027
expansion and eye research activities	321,920	_	321,920	_		321,920
Scientific symposia, seminars and surveys	267,232		267,232			267,232
Laboratory construction support projects	13,457		13,457			13,457
Public and professional information	671,185		671,185			671,185
Total program services	9,304,837		9,304,837			9,304,837
Supporting services						
Management and general	1,215,732		1,215,732			1,215,732
Fund raising	88,193		88,193			88,193
Total supporting services	1,303,925		1,303,925			1,303,925
Total expenses	10,608,762		10,608,762			10,608,762
Excess (deficiency) of revenue over expenses	10,000,702		10,000,702			10,000,702
before realized gain (loss) and change in unrealized						
appreciation (depreciation) of investments	2,397,557	(756,892)	1,640,665	597,296	9,724	2,247,685
Realized gain (loss) and change in unrealized appreciation	_,,,	(,.,.)	.,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	,=/0	. ,. = .	_, ,500
(depreciation) of investments	28,692,176		28,692,176	(251,323)		28,440,853
Increase (decrease) in net assets	31,089,733	(756,892)	30,332,841	345,973	9,724	30,688,538
Net assets, beginning of year	98,340,615	49,143,604	147,484,219	11,072,667	53,318,759	211,875,645
Net assets, end of year	\$ 129,430,348	\$ 48,386,712	\$ 177,817,060	\$ 11,418,640	\$ 53,328,483	\$ 242,564,183
i vet assets, ena or year	Ψ IZ7,400,040	ψ 40,000,/12	φ 177,017,000	φ 11,410,040	ψ υυ,υΖυ,400	Ψ ZHZ,JUH,103

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 with RPB to Save Sight

For 50 years as the leading public foundation driving vision science, RPB has played a pivotal role in transforming and nourishing research efforts in this country. RPB's founder, Jules Stein, M.D., and the founding Board of Trustees, created an organization that could adapt to the needs of medical institutions, scientists, and patients.

Historically, RPB's programs have focused on five areas: providing unrestricted support to researchers; assisting in the financing and construction of new lab space; spurring the purchase and design of scientific equipment; creating a talented research corps; and raising awareness of eye research in the public and professional spheres through communications.

Since day one, RPB's core has been its Research Program, which has awarded thousands of grants to date.



RPB receives Allergan Foundation grant

Mr. Gavin Herbert, right, a former longtime Trustee of Research to Prevent Blindness, accepts a grant check from David Pyott, Chairman of Allergan Inc., of which Mr. Herbert is the founder. Contributors to our cause understand that our resources are strategically applied to scientists of maximum potential to pursue investigations with maximum effect. They also understand that giving to a research-focused organization is different from giving to a service-focused entity. Investing with RPB increases the possibility of someday eliminating our reason for being.

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.

"...only research can solve the stubborn mysteries of blindness."

—from RPB's first annual report, 1960

Endowment Funds

Generous contributors assure stability and continuity in the development of RPB's far-reaching programs. Existing funds include the following:

Jules and Doris Stein Endowment Fund\$ 45,087,782
Jules and Doris Stein Matching Fund7,774,030
Lew R. and Edie Wasserman Endowment Fund1,407,412
William and Mary Greve Memorial Fund519,943
Dolly Green Endowment Fund500,000
Sybil B. Harrington Endowment Funds
Desiree L. Franklin Endowment Fund138,700
Eugene G. Blackford Memorial Fund28,000
John D. and Patricia Sakona Endowment Fund75,453
David B. Sykes Family Endowment Fund205,454
Ernest E. and Elizabeth P. Althouse Memorial Fund2,193,667
William Mallory, Jr. Endowment Fund172,072



The Value of an Investment

"An RPB grant can be used in ways that other grants cannot. Other funding sources can be reticent to provide money to buy equipment, even essential equipment in many cases, so we may not have adequate tools to perform experiments that are really groundbreaking. Having the flexibility of RPB funds allows investigators, either singly or jointly, to buy equipment that substantially moves their research forward.

"With support from RPB, my lab is investigating corneal nerve repair. Corneal nerves can be damaged in a number of clinical situations, including eye surgery (LASIK vision correction, keratoplasty and cataract surgery), infections (herpes simplex and zoster), trauma, and dry eye syndrome. If there is loss of sensation related to this nerve damage it can lead to severe abnormalities of the ocular surface. So we're trying to figure out how we can regulate healing to improve outcomes with all types of corneal surgery."

Mark I. Rosenblatt, M.D., Ph.D., Weill-Cornell Medical College RPB Career Development Award 2008

A RECORD OF ECONOMY AND EFFICIENCY



RPB's fund raising cost ratio has been less than 2% for more than half a century of service. Its staff of nine is among the smallest of all major organizations in the voluntary health field.

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.

