

VIEWPOINT



Winter
2002

THE DEPARTMENT OF OPHTHALMOLOGY Columbia University
The Edward S. Harkness Eye Institute

First Miranda Wong Tang Professor Appointed

Richard E. Braunstein, MD, a nationally recognized expert on corneal eye diseases and LASIK vision correction, has been named the first Miranda Wong Tang Assistant Professor of Clinical Ophthalmology. The academic position was established with funds from Mrs. Tang, a long-time supporter and founding member of the Department's Board of Advisors.

The new appointment was celebrated at a luncheon on October 3 at ASTRA. Mrs. Tang and her family were joined for the occasion by Dr. Braunstein and Dr. Stanley Chang, Edward S. Harkness
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(l-r) Amy Braunstein and Dr. Richard Braunstein, Hamburg Tang, Miranda Wong Tang, and Dr. Stanley Chang.

Partnerships for Vision

On November 17, the Department of Ophthalmology held a “Vision Research Summit” to explore ways of sharing knowledge, specialized talents and resources through increased interdepartmental collaborations. Coordinated by Abraham Spector, PhD, Malcolm P. Aldrich Research Professor, and John Flynn, MD, Anne S. Cohen Professor of Pediatric Ophthalmology, the symposium’s participants included leading scientists in a range of disciplines that concern vision research.

“There is an amazingly broad area of scientific investigation on both Columbia campuses that relates to some portion of the visual system—anywhere from the front of the eye to deep inside the brain,” says Dr. Flynn. “Our

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In This Issue

**CORRECTING
LASIK
CORRECTIONS**

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**TRAINING
EXCELLENCE**

Dear Friends:

During these difficult times, support from family, friends and colleagues takes on increased significance. As we adjust to a changed world, we seek guidance and strength from those closest to us. Enduring values and long-held commitments become ever more important in our daily lives.

While we've all been shaken by the horror of recent events, my colleagues and I are firm in our commitment to find improved ways of preventing and treating vision loss. Maintaining excellence in ophthalmology research, training and care continues to be our highest priority. A recent symposium sponsored by the Department of Ophthalmology underscores our efforts. Drawing senior ophthalmology faculty and scientists from other Columbia departments, the gathering provided a unique opportunity to promote new interdisciplinary partnerships in vision research.

In this issue of *Ophthalmology*, we describe just a few of the many collaborative projects already in progress between researchers in the Department of Ophthalmology and scientists working in related fields. We've also taken the opportunity to offer highlights of our outstanding resident training program and to share new insight into complications that sometimes occur with LASIK vision correction and how Columbia specialists provide expert care to treat these cases.

As we enter a new year, I thank all of you for your continuing friendship and support. I hope 2002 brings peace, happiness and well-being to you and your family.

Sincerely,

Stanley Chang, M.D.
Edward S. Harkness Professor
Department of Ophthalmology Chairman

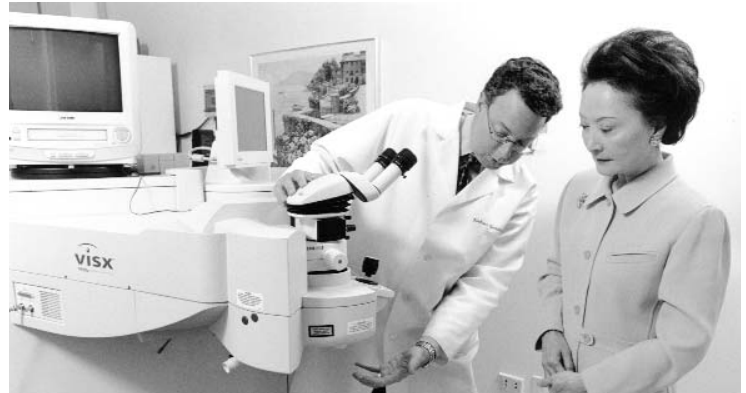
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Tang Professor Appointed, cont.

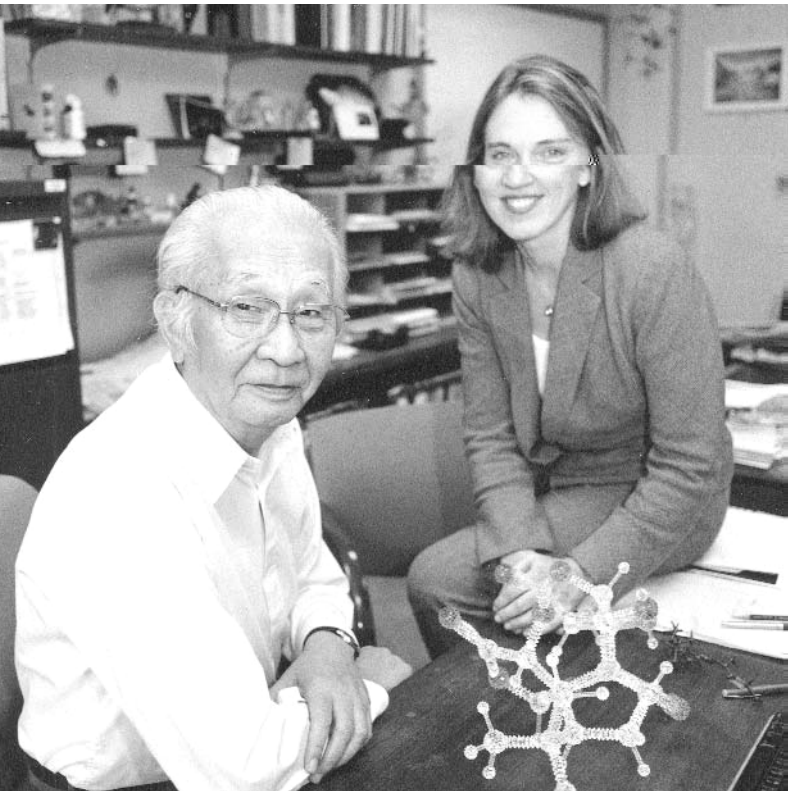


Mrs. Miranda Wong Tang gets a crash course in LASIK vision correction from Dr. Richard E. Braunstein.

Professor and Department of Ophthalmology Chairman, and many other Columbia faculty and friends. Dr. Chang expressed deep appreciation to Mrs. Tang for her untiring commitment to advancing knowledge about eye disease through scientific research. He emphasized that as an endowed position, the Tang Assistant Professorship will provide critical support for the incumbent, particularly at mid-career, the most productive years for a clinician scientist. "The Miranda Wong Tang Assistant Professorship will help to advance Dr. Braunstein's important work in developing new diagnostic and treatment strategies for corneal disease," said Dr. Chang.

Dr. Braunstein, a graduate of Columbia's College of Physicians & Surgeons, has served on the ophthalmology faculty since 1994. He is Director of the Department of Ophthalmology's Division of Refractive Surgery and of the Edward S. Harkness Eye Institute's Residency Training Program, and a member of the Department's Board of Advisors. He has published and lectured extensively on corneal disease and its treatment, and is principal investigator for three clinical trials in the LASIK vision correction procedure. ■

Partnerships for Vision, cont.



Dr. Koji Nakanishi and Dr. Janet Sparrow team up to investigate retinal disease.

goal is to build on common interests.”

Columbia’s Department of Ophthalmology has a rich tradition of fostering collaborative enterprise. Promising projects between vision experts and specialists in other fields are uncovering new information about the eye and improving prospects for sight preservation and treatment.

Two Perspectives on a Perilous Molecule

For the past five years, Columbia researchers Janet Sparrow, PhD, Associate Professor of Ophthalmology, and Koji Nakanishi, PhD, Cen-

tennial Professor of Chemistry, each have been bringing their individual points of view to the study of a vitamin A derivative, called A2E.

A substance that collects in the retinas of aging eyes, A2E occurs with particular abundance in patients with retinal disorders such as age-related macular degeneration, Stargardt’s disease and at least one form of retinitis pigmentosa. A2E builds up inside retinal pigment epithelial (RPE) cells, which maintain healthy vision by nourishing and otherwise “nursing” the retina’s light-sensing rods and cones. The accumulating substance was thought to be harmless, until a 1996 paper by Dr. Nakanishi, which confirmed A2E’s molecular structure, raised questions about its potentially damaging effects. Subsequent research by Dr. Sparrow showed that far from being a benign presence in aging retinal tissue, A2E acts as a corrosive detergent that damages the membranes of RPE cells.

In their continuing collaboration, Drs. Sparrow and Nakanishi are working together to study the role of light in the precarious biochemical mix of A2E and RPE cells. But each approaches the research from a different angle, which, says Dr. Sparrow, is what makes their work so much fun. Dr. Nakanishi, the chemist, is intrigued by the unique structural changes that occur when particular light rays combine with A2E. Dr. Sparrow, the biologist, is eager to understand how these light-gener-

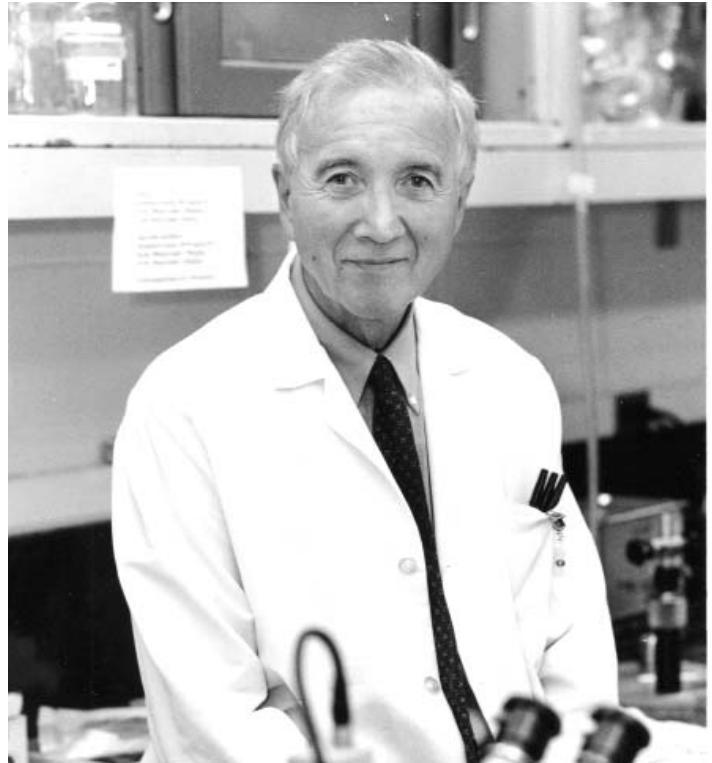
ated changes in A2E inflict their damage on RPE cells. What they each learn in the laboratory may one day be used to keep A2E from taking a toll on sight.

“As science becomes more specialized,” says Dr. Sparrow, “there is a need for multiple areas of expertise to answer questions that are asked. Collaboration is the only way science can flourish.”

Gene Therapy Express

When we think of a virus, we’re most likely to think of the minute, disease-causing organisms responsible for a range of illnesses—from ordinary colds and flu to HIV/AIDS and other life-threatening conditions. But, paradoxically, researchers are now turning to the common virus for its potential to deliver beneficial, sight-saving treatments.

In a cutting-edge gene therapy project, Department of Ophthalmology Professor Peter Gouras, MD; Louis V. Gerstner, Jr., Scholar Rando Allikmets, PhD; and Higgins Professor of Biochemistry and Molecular Biophysics, Stephen Goff, PhD, are engineering viruses to act as DNA-carrying transporters that substitute healthy genes for those that are defective. “Imagine curing Stargardt’s disease,” says an animated Dr. Gouras. “This is a hereditary condition that causes vision loss in kids. It’s thrilling to work on a strategy that may one day save their eyesight.”



Dr. Peter Gouras is developing a “magic bullet” for retinal disorders.

Researchers believe that genetic engineering offers promising treatment solutions for many diseases, including those affecting sight. “It may require thousands of experiments,” says Dr. Gouras, “but success will come.”

Finding a way to introduce submicroscopically small genes into the tiny nuclei of retinal cells poses significant challenges. Drs. Gouras, Allikmets and Goff are investigating the potential of a “magic bullet” vector, called lentivirus, to safely and effectively deliver genes to targeted retinal tissue. According to



the researchers, lentivirus is well-suited to the transport of larger genes, such as ABCR. In 1997, Dr. Allikmets's investigations revealed a link between ABCR and Stargardt's disease. "As a growing number of retinal disorders are tied to ABCR mutations," Dr. Allikmets says, "there is increasing interest in the gene's therapeutic potential."

Measures for Sight

"I've seen patients who, for years, thought they had a neurological disease when, in fact, their problems were caused by retinal dysfunction," says

Jeffrey Odel, MD, Associate Clinical Professor of Ophthalmology. Collaborating with Donald C. Hood, PhD, James F. Bender Professor

of Psychology, and Vivienne C. Greenstein, PhD, Assistant Professor of Clinical Ophthalmology, Dr. Odel is evaluating the use of innovative, noninvasive approaches to diagnose and monitor patients whose baffling symptoms need a closer look.

Based on existing electroretinographic technology, the new techniques, multifocal electroretinography (mERG) and multifocal visual evoked potential (mVEP), can be used to pinpoint exact geographic locations in the retina, optic nerve or brain that may be

responding to light stimulation. Drs. Odel, Hood and Greenstein are evaluating mERG and mVEP to determine their effectiveness in diagnosing and monitoring vision disorders, including retinal vascular disease, retinitis pigmentosa and glaucoma. They are also using the technology to diagnose and evaluate experimental treatments for multiple sclerosis, a neurological disease that is often first manifested by impaired or double vision. Identifying disorders at their earliest stages is increasingly important, explains Dr. Odel, because of new treatments that may prevent disease progression.

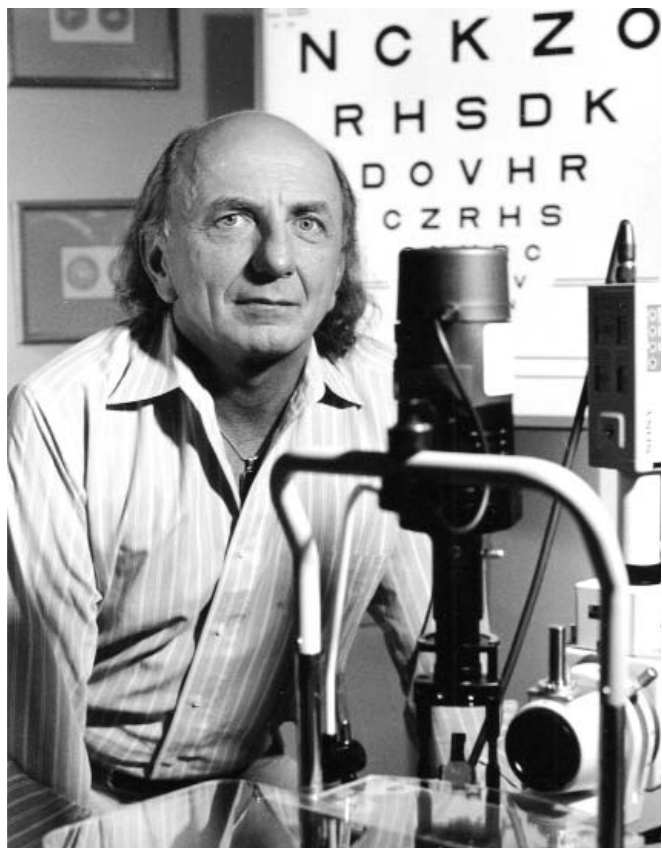
"I've seen patients who thought they had a neurological disease when, in fact, their problems were caused by retinal dysfunction."

An Inside Look at Outside Hazards

Professor of Radiation Biology Basil V. Worgul, PhD, has devoted his career to studying the effects

of various chemical and physical agents on the eye. Interested in cell growth and differentiation, Dr. Worgul hypothesizes that a lifetime of exposure to radiation and other gene-damaging agents could collectively contribute to the development of many age-related cataracts.

Working with Eric J. Hall, PhD, Higgins Professor of Radiation Biophysics in the Department of Radiation Oncology, Dr. Worgul is looking at genetic factors that affect variability in individual sensitivity to radiation. Their studies have broad implications—from



Dr. Basil Worgul is studying the gene-damaging impact of environmental agents on the eye.

helping to determine optimal radiation dosages for patients undergoing cancer treatment to preventing those with lower-than-normal radiation tolerance from taking needless occupational risks. Dr. Worgul is also collaborating with Charles S. Hesdorffer, MD, Associate Professor of Clinical Medicine, to evaluate the ocular effects of agents used in bone marrow transplantation procedures for certain types of cancer, including radiation, chemotherapeutic drugs and steroids. “Now that an increasing number of patients are surviving cancer,” he says, “we’re becoming more

attuned to ensuring good quality-of-life following cancer and its treatment. It’s important to know the impact of specific therapies on vision before choosing the best overall course of treatment.”

Fashioning a Model

One of the early steps in studying new treatments is to assess their safety and effectiveness in laboratory animals. For the past few years, researchers have been using sophisticated genetic engineering techniques to create “knockout” mice and other animal models that mimic many hereditary diseases. Gaetano Barile, MD, Assistant Professor of Clinical Ophthalmology, and Ann Marie Schmidt, MD, Associate Professor of Surgery, have been collaborating to develop just such a model for the study of diabetic retinopathy.

“The biggest risk factor for vision loss from diabetes is the duration of the disease,” says Dr. Barile. His laboratory partnership with Dr. Schmidt, a pioneer in the scientific investigation of diabetes and its complications, has helped to generate colonies of laboratory mice to study the complex biochemical changes that gradually lead to vision loss from diabetes. But more than sharing lab space, Drs. Barile and Schmidt discuss techniques, overcome hurdles and generate new ideas. “Dr. Schmidt’s interest in ophthalmology,” says Dr. Barile, “and my interest in basic research move the process forward. Everyone benefits.” ■



When LASIK Corrections Need Correcting

The introduction of LASIK surgery and its development as a relatively routine ophthalmological procedure over the past decade is a milestone in vision correction. It has made it possible for many people who were previously dependent on vision aids to take off their glasses and throw away their contact lenses.

An acronym for laser-assisted in situ keratomileusis, LASIK is refractive surgery that reshapes the cornea to rectify vision problems including both near and farsightedness and astigmatism. The procedure begins by cutting an ultra-thin circular flap on the corneal surface with a tiny motorized blade called a microkeratome. A hinge is left at one end of this flap so that it can be folded back to expose the middle section of the cornea, the stroma. When the flap is lifted, the surgeon applies an excimer laser to the stroma, producing computer-controlled pulses that vaporize tissue from the area. This ablation of the stroma continues until its contours match measurements determined prior to the operation that will restore the patient's visual acuity. Once the operation is completed, the corneal flap is returned to its original position to accelerate the healing process.

LASIK has been effective in a majority of cases and patients are enthusiastic about

the results. Occasionally, however, the outcome may not be completely satisfactory and, in such cases, some further surgical adjustment is called for. Richard E. Braunstein, MD, Miranda Wong Tang Assistant Professor of Clinical Ophthalmology, is a nationally recognized expert in performing LASIK surgery and in managing its complications. Under his supervision, surgeons in Columbia's Department of Ophthalmology have developed a special knowledge and skill in working with patients who come to Columbia for help when they have suffered poor results from refractive surgery. Dr. Braunstein emphasizes that fewer than one percent of patients who have undergone the LASIK procedure at Columbia have experienced any difficulty following its completion.

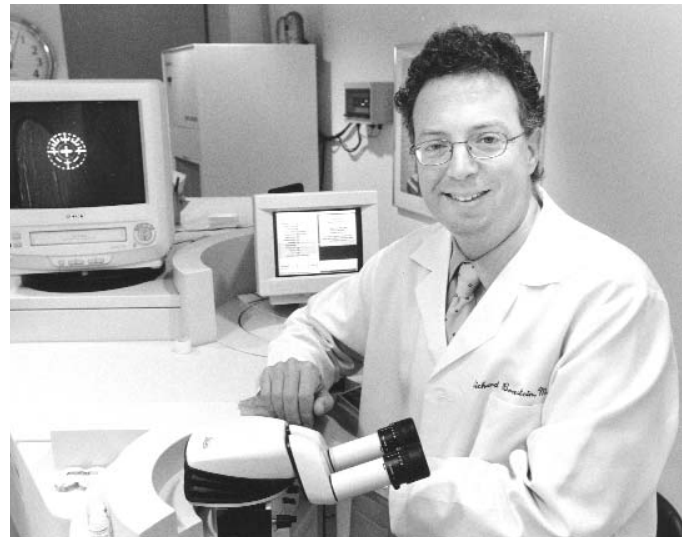
Dr. Braunstein says that an unexpected response to the surgery is usually the culprit when vision is not improved after LASIK. "There is not just one, but rather an array of less than acceptable consequences that are possible in the aftermath of such surgery," he says. "We see a wide variety of such problems, in addition to patients who have had straightforward overcorrections or undercorrections." Saying "most problems are minor and easily corrected," Dr. Braunstein adds that



"there are also some for which new treatments must be developed."

Dr. Braunstein described a recent case, in which the vision of a 43-year-old patient who was nearsighted in both eyes failed to improve following his LASIK surgery. When the patient came to Columbia for a consultation, Dr. Braunstein discovered that a cataract had developed in one eye as a result of the procedure, and that the corneal flap created for surgery in the other eye was wrinkled. The problems were causing blurred vision and allowing a severe glare of light to interfere with the patient's sight. "We did cataract surgery in the eye with worse vision and obtained an excellent result," reports Dr. Braunstein, adding that "we are now planning a procedure to correct the wrinkling by stretching and resuturing the flap."

According to Dr. Amilia Schrier, Assistant Professor of Clinical Ophthalmology, who is also involved in treating LASIK-connected problems, one of the worst possible complications of LASIK surgery is a corneal infection. "Certain infectious diseases" she explains, "can affect the cornea, infiltrating and breaking down corneal tissue." But Dr. Schrier also points out that such infections are highly unusual. When they do occur, how-

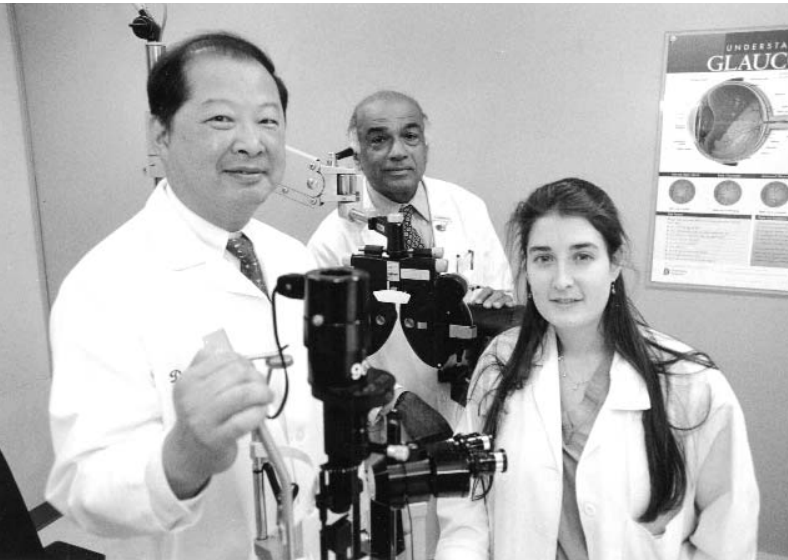


Dr. Richard E. Braunstein

ever, diagnosis and treatment can be difficult because of the infection's location beneath the corneal flap. Consequently, she says that "There are a number of management decisions involved, such as whether or not to remove the flap," and that "treatment options include topical steroids, antiviral drops or oral medications."

Meanwhile Columbia's ophthalmologic surgeons are in the vanguard refining LASIK surgery to insure that any problems caused by the procedure are minimal and easily overcome. ■

Training Excellence



Chief Resident Donna Siracuse with Drs. Stanley Chang (left) and B. Dobl Srinivasan in the Eye Clinic.

Fostering relationships between attending physicians and the residents they mentor plays an integral role in the Department of Ophthalmology's training program. When residents are given steady access to the expertise and informed judgement of more experienced colleagues, it is patients who ultimately benefit, as they are ensured of receiving the highest quality care.

"Residents work side by side with attending physicians, both in the general clinic and in the various subspecialty clinics," says Richard E. Braunstein, MD, Miranda Wong Tang Assistant Professor of Clinical Ophthalmology and Director of the Resident Training

Program. "This model provides an optimal teaching experience to attending physicians and helps residents improve their diagnostic and therapeutic skills." Residents serve as primary surgeons on major procedures under the guidance of practicing faculty members. They also rotate through the on-campus offices of specialists in each area of vision disorders, Dr. Braunstein notes.

Mastering a wide range of sophisticated instruments and technology used in departmental subspecialties is critical to becoming a full-fledged ophthalmologist, says Dr. B. Dobl Srinivasan, Professor of Clinical Ophthalmology and Director of Eye Clinics at Columbia. "There is no end to changes in ophthalmology," he explains. "Our field is very technique and instrument-oriented, so it is not just the biology but the tools that are taking a quantum-leap forward. But there is far more supervision by attending physicians than when I was a resident. That is one of the changes we've instituted in the clinic," he adds.

"There are always several attending physicians in the clinic and the operating room covering different specialties, and doctors in all the subspecialties are always available," says Chief Ophthalmology Resident Donna E. Siracuse, MD. She notes that simply observing and assisting attending physicians provides an



Remembering Seymour Milstein

Seymour Milstein, a loyal friend and generous benefactor of Columbia's Department of Ophthalmology, died on October 2, 2001, at the age of 81.

Chairman of The Milstein Group, a real estate and banking company, Mr. Milstein served as co-chairman of the Board of Trustees and chairman of the Executive Committee of the Emigrant Savings Bank. He was also a trustee and chairman emeritus of NewYork-Presbyterian Hospital and, from 1989 to 1996, chairman of The Presbyterian Hospital. A founding member of the Department of Ophthalmology's Board of Advisors, Mr. Milstein was also a member of the Columbia-Presbyterian Health Sciences Advisory Council.



Seymour Milstein

Mr. Milstein's visionary philanthropy provided extraordinary support for many Columbia-Presbyterian programs. He and his family gave Columbia-Presbyterian Medical Center its largest gift in history, a \$25 million contribution that funded construction of the Milstein Hospital Building. The family's exceptional generosity also helped to establish the Harkness Eye Institute's Flanzer Eye Center and renovate its operating rooms.

"Seymour Milstein was a leading supporter of our efforts to promote excellence in vision research, training and care," noted Stanley Chang, MD, Edward S. Harkness Professor and Chairman of Ophthalmology. "We will remember him for his many acts of kindness, outstanding dedication and enduring friendship." ■

Training Excellence, cont.

invaluable educational experience. "You don't always appreciate everything during your first year, but by your third year, once you are actually doing surgery yourself, you realize how many clinical and surgical pearls you glean from assisting the attending physicians," she says.

In addition to picking up tips from their veteran colleagues, residents participate in a rigorous course of instruction in the basic sciences, with opportunity for clinical research during their three-year tenure at Columbia. Learning in the classroom is complemented by an education in the clinic.

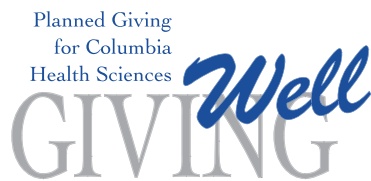
"There's no substitute for hands-on experience here," says Dr. Braunstein. ■

Columbia University in the City of New York

Edward S. Harkness Eye Institute

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Creating a Bequest for Ophthalmology at Columbia

- * Support important research
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Bequests to benefit ophthalmology at Columbia should specifically name “Columbia University in the City of New York,” and be directed to the Department of Ophthalmology. For example:

I give and bequeath to the Trustees of Columbia University in the City of New York, for its Department of Ophthalmology, the (amount of \$ _____) (% of my estate or trust), to support (research) or (education) or (fellowships, etc.) in honor of _____.

Contact **Susan Taylor** or **Elia Desruisseaux**, to work with you and your advisors to help plan your gift, at **(212) 304-7200** or **givingwell@columbia.edu**.