Columbia University Medical Center

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The Edward S. Harkness Eye Institute and the
Department of Ophthalmology in the
College of Physicians and Surgeons

Viewpoint

Spring/Summer 2006

Saving the Sight of Diabetics

It was a "happy coincidence" that brought George Bresnick, M.D., M.P.A. and his wife, Geraldine "Geri" Hendriksen to Columbia to collaborate on a new community diabetic retinopathy telemedicine screening program.

Dr. Bresnick, former chairman of ophthalmology at the universities of Rochester and Wisconsin, and Ms. Hendriksen, a successful community health professional, are the founders of Vision for All, Inc., a not-for-profit established in 1996 with the goal of providing affordable eye care to high-risk, elderly and medically underserved individuals. The couple first piloted a free eye care program in inner-city Rochester, later expanding their efforts to

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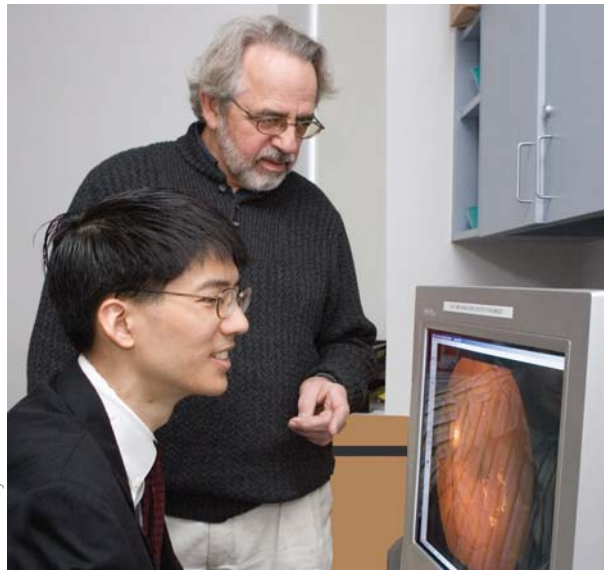

C. Manley

Michael Chiang, M.D., M.A. and George Bresnick, M.D., M.P.A.

Apprehending the Silent Thief

Glaucoma, a silent and insidious thief of vision, occurs when the retinal ganglion cell bodies of the optic nerve begin to die, leading to slow but progressive loss of vision. According to Research to Prevent Blindness, glaucoma is one of the leading causes of irreversible blindness

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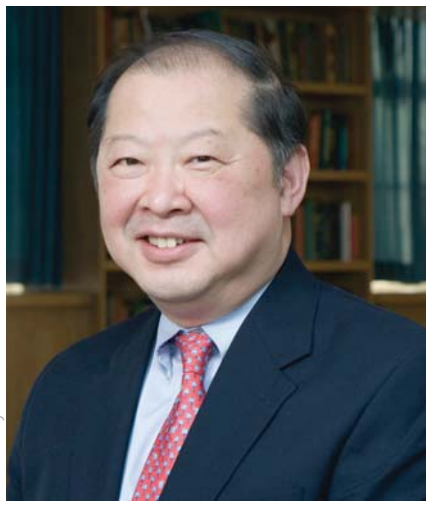
View from the Chair

Dear Friends,


C. Manley
Stanley Chang, M.D.

Vision is one of the most precious gifts of life. For many diseases of the eye, early diagnosis is the best defense against unnecessary vision loss.

With this issue of *Viewpoint*, we are excited to report on several research and screening initiatives designed to diagnose and safeguard vision in vulnerable populations. Dr. George Bresnick and his wife Geri Hendriksen, founders of Vision for All, are partnering with Dr. Michael Chiang to create a new diabetic retinopathy screening program using telemedicine for the Washington Heights community. Dr. James Tsai is pioneering a novel technological device for early detection of glaucoma that is ready to enter Phase 2 clinical trials. Dr. Rando Allikmets' team has discovered yet another gene related to age-related macular degeneration (AMD).

Our "Vision for the Future" — a $50 million capital campaign for the Department — is well underway, thanks to the leadership of our co-chairmen, Howard L. Clark, Jr., Shirlee Brown and Homer McK. Rees. We thrive on the generosity of dear friends and current and former patients. Your campaign gifts will support research programs, faculty development and state-of-the-art facilities. Additionally, we thank you for your considerable support of the Department of Ophthalmology's Annual Fund.

We are especially grateful for the opportunity to work toward preserving the gift of vision for so many, and extend sincere thanks for your dedication and commitment to our work in advancing ophthalmology and vision care.

With best wishes to you and yours,

Stanley Chang, M.D.
K.K. Tse and Ku Teh Ying Professor
Edward S. Harkness Professor
Chairman, Department of Ophthalmology

A Treasured Gift to Vision

"A sighted eye is a gift," says B. Dobli Srinivasan, M.D., Ph.D., Director of Ambulatory Eye Care at the Harkness Eye Institute. Dr. Srinivasan has dedicated his career to protecting sight, one of life's most precious gifts. After more than four decades at the Harkness Eye Institute in research, clinical practice and now directing residents in the ITT Eye Clinic, he plans to retire in June to southern California with his wife, Sheila, to enjoy warmer weather and family nearby.

Dr. Srinivasan's multi-faceted career as a scientist, physician and faculty member at Columbia began with pre-medicine studies at Bard College in the late 1950s, where he met Laszlo Bito, Ph.D. (the retired Columbia scientist perhaps best known for developing Xalatan for the treatment of glaucoma). As Dr. Bito tells the story, George Smelser, Ph.D., Professor of Anatomy at Columbia and Director of Ophthalmology Research, came to Bard to give a lecture on the eye. Both men were impressed and intrigued, and it was this initial exposure to ophthalmology that spurred the young Srinivasan to pursue a position as a research assistant in George Smelser's laboratory in the Ophthalmology Department. Laszlo Bito joined that laboratory shortly thereafter, and both enrolled in the graduate program in Cell Physiology and Biophysics.

"Dobli pursued both the M.D. and Ph.D. degrees, while I stayed with the Ph.D. program. After our graduations, Dobli completed two years of military service in the Coast Guard, including a trip to the Antarctic, while I spent two years of post-doctoral training," Dr. Bito explains. "Then we each returned to Columbia, Dobli in clinical work and I in basic research. Those were heady years after Sputnik, when science was held in especially high regard."

C. Manley

B. Dobli Srinivasan, M.D., Ph.D.

Prasad Kulkarni, Ph.D., now a professor of ophthalmology at the University of Louisville, recalls, "I first met Dobli in 1976 when I joined Dr. Ken Eakins' lab as a post-doctoral fellow at the Harkness Eye Institute. Dobli and I each had NIH grants and worked together to investigate eicosanoids and prostaglandins and their involvement in ocular inflammation. Together we had a lot of fun and I learned from him the insight and importance of basic research and its implications for clinical research. We also consulted as a team and were instrumental in the development of anti-inflammatory drugs like diclofenac and flurbiprofen for use in the eye."

Dr. Srinivasan agrees. "I had a great time doing research for almost 25 years, from

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Basic Science Course Draws International Residents and Experts

Despite New York's short days and cold weather, Winter Intersession at the Harkness Eye Institute is anything but dull. During their break from clinical practice, 26 talented medical residents from the New York metropolitan region and as far away as Denmark, Jamaica, Kuwait, Portugal and Sweden filled the Flanzer Auditorium and surrounding classrooms and laboratories to participate in the annual Basic Science Course in Ophthalmology (BSCO).

Organized by Stephen Tsang, M.D., Ph.D. and coordinated by Levin Santos, the BSCO is an intense and fascinating four-week course designed to immerse participants in the fundamentals of ophthalmic science and their application to patient care.

"Since 1941, the Columbia University Department of Ophthalmology has offered the Basic Science Course in Ophthalmology. Originally intended primarily for residents, it has proven valuable to the broader visual sciences community," explains Dr. Tsang. "The Harkness Eye Institute's mission is a synergistic triangle that combines education of the world's future leaders in ophthalmology with unparalleled patient care and cutting-edge vision research. This course fulfills that mission perfectly."

Participants receive intensive instruction from a stellar international faculty of more than 80 clinicians and scientists. The rigorous course schedule runs Monday through Saturday during the four weeks of the course, and includes more than one hundred lecture hours, plus laboratory studies in ocular anatomy and histology, two days of training in orbital dissection and two days of instruction in retinoscopy and refraction. Participants also perform cataract surgery and lens implantation on

C. Manley

L to R: Stanley Chang, M.D.; Graham E. Holder, Ph.D.; Robert Braunstein, M.D.; Stephen Tsang, M.D., Ph.D.; Alan C. Bird, M.D.; Lucian Del Priore, M.D., Ph.D.; Gaetano Barile, M.D.

Basic Science Course *(con't.)*

pig eyes during a one-day session in the "Phaco wet lab" under faculty guidance.

The curriculum and faculty are selected by Columbia scientists and clinicians, including John T. Flynn, M.D., Jan P. Koniarek, Ph.D., James C. Tsai, M.D., Joseph Walrath, M.D., and the late Basil V. Worgul, Ph.D. [See *In Memoriam*, page 19.]

"This course was truly an exceptional experience that encompasses much more than the exposure to didactic teaching," remarks Suzanna Airiani, M.D., a Harkness Eye Institute resident who participated in this year's course. "The first few months of my training involved mastering basic ophthalmic skills and clinical examinations. This course augmented that training with intensive instruction in the basic sciences underlying ophthalmic practice and research." She adds, "The orbital dissection training was a marvelous hands-on opportunity to interact with and learn from top eye center experts."

In addition to the many Columbia faculty who offered their expertise, this year's invited faculty included **Professor Alan C. Bird** and **Sir Stewart Duke-Elder Professor Anthony T. Moore**, both from University College London; **Graham E. Holder, Ph.D.**, Director of Electrodiagnosic Department at Moorfields Eye Hospital in London; **Robert Nussenblatt, M.D.**, Director of Immunology at the National Eye Institute (NEI), National Institutes of Health (NIH); and **Joseph L. Demer, M.D., Ph.D.**, Chief, Comprehensive Ophthalmology Division at the Jules Stein Eye Institute, UCLA.

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L to R: BSCO Faculty member Irene Maumenee, M.D., Marcus Kivitalo, M.D. of Ornskoldsvik, Sweden, and Stephen Tsang, M.D., Ph.D. at the course graduation ceremony.

"The curriculum incorporates current understanding and knowledge within a clinically relevant framework," explains Dr. Airiani. "The curriculum provided a firm and experiential grounding in the fundamentals, plus additional emphasis on molecular and clinical genetics, cellular biology, epidemiology, pharmacology, refractive and cataract surgery and clinical testing modalities." She concludes, "This course was excellent preparation for the mandatory ophthalmic knowledge assessment program, and the opportunity to sharpen my knowledge of basic science with such esteemed faculty has been invaluable."

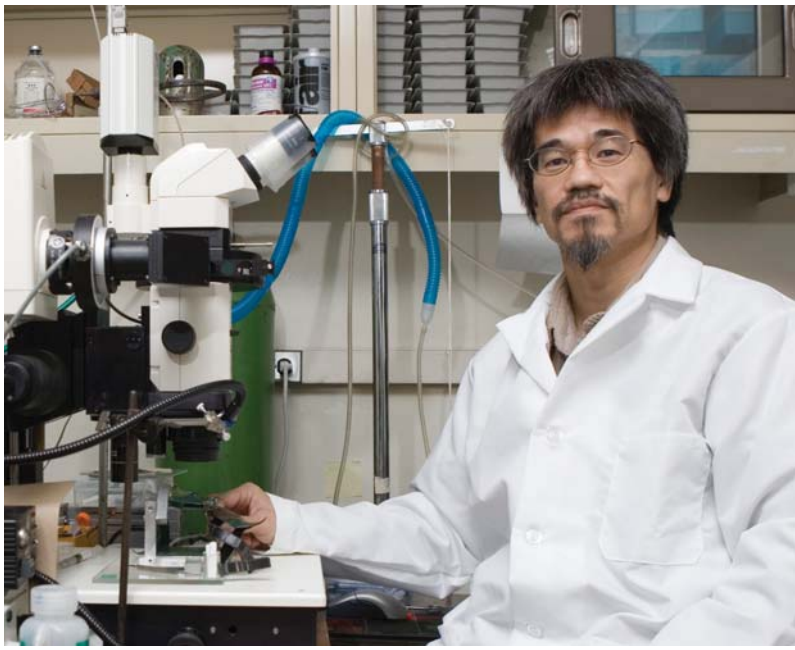
The website for the Basic Science Course in Ophthalmology can be found at: http://www.cumc.columbia.edu/dept/eye/education/edu_bsc.html.

Spotlight: Takayuki Nagasaki, Ph.D.

How does the cornea maintain its transparency and health? That is the question that Takayuki Nagasaki, Ph.D., is trying to answer. Dr. Nagasaki, Assistant Professor of Ophthalmic Science (in Ophthalmology) and Director of the Anterior Segment Biology Laboratory at Columbia, is investigating how the cornea and the conjunctiva maintain tissue and mass to achieve a state of healthy equilibrium known as "homeostasis."

"Our research is aimed toward understanding the physiology of the surface of the eye at a molecular and cellular level with the goal of providing better management of injuries and diseases of the cornea and the conjunctiva. The knowledge gained from this basic science research will also improve keratorefractive surgery such as PRK and LASIK," Dr. Nagasaki explains.

The cornea is the eye's window — the transparent dome-shaped refracting surface at the front of the eye that provides two-thirds of the eye's focusing power. The conjunctiva, also thin and transparent, is a mucous membrane that lubricates the eye, beginning at the outer edge of the cornea and extending to cover the sclera (the white of the eye) and the inside of the eyelids.



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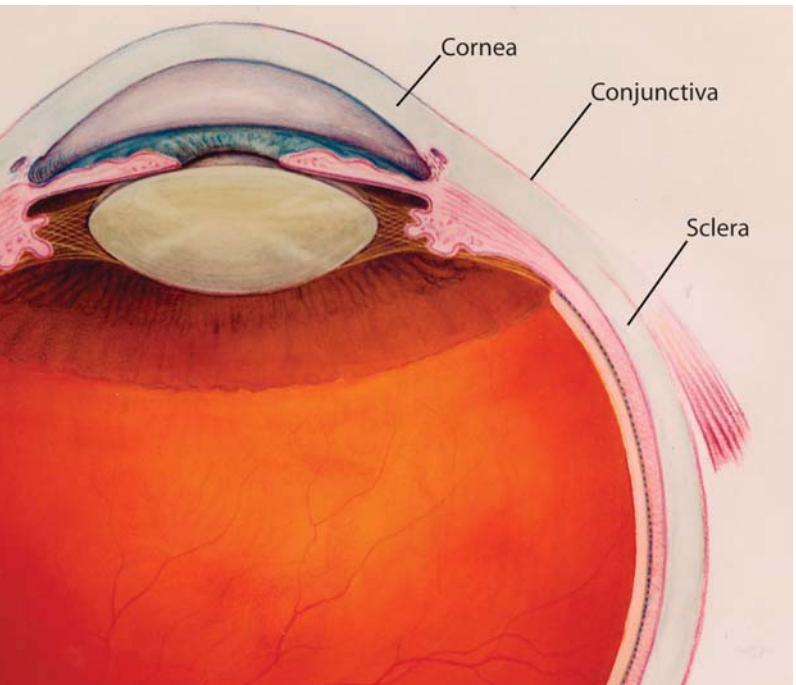
Takayuki Nagasaki, Ph.D.



National Eye Institute, NIH

Although the cornea and conjunctiva are adjacent tissues, their individual epithelial stem cells (the cells responsible for regeneration and wound healing) behave very differently. In the cornea, epithelial stem cells are concentrated in the limbus, the border between the cornea and the sclera. These cells divide and migrate toward the center of the cornea at a rate of 30 micrometers per day. In the conjunctiva, epithelial cells are distributed uniformly and divide, but do not move.

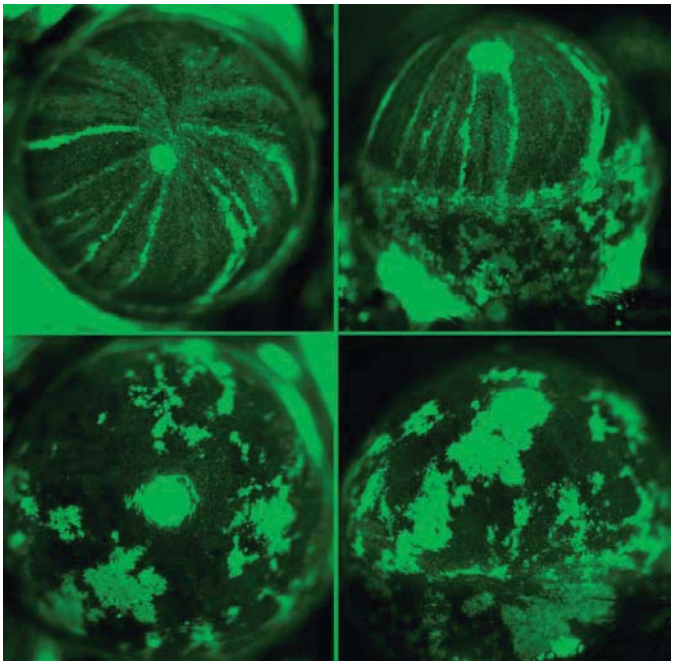
"Ocular surface homeostasis involves three parameters — cell movement, cell division and cell loss. We know that continuous movement of the epithelial stem cells is

Spotlight: Takayuki Nagasaki, Ph.D. *(con't.)*

essential to the cornea's ability to stay transparent," Dr. Nagasaki asserts. He uses a technique called *in vivo time lapse fluorescence microscopy* to track the progression of the stem cells in the eyes of mice. These "transgenic" mice are genetically engineered and bred so that the cells of interest will be fluorescent and readily traceable under the microscope. By creating a time lapse sequence, Dr. Nagasaki can observe individual epithelial stem cell movement in a living animal, tracking the rate and direction of movement over the course of several months. In mice, this movement from limbus to cornea center takes approximately eight weeks; in humans, more than six months.

"Every single cell on the corneal surface is moving centripetally," Dr. Nagasaki continues. "It appears that many of them die off on their way to the center. We are trying to understand why the movement from limbus to cornea center happens. At the same time, we are looking at why the stem cells in the conjunctiva do not move." He points out that the cornea and conjunctiva are continuous structures without much of a defined boundary between the two. In addition to tracking the stem cell movement, Dr. Nagasaki is researching why and how the corneal stem cells move to the central cornea, rather than to the conjunctiva.

"By studying this process in the normal eye, we gain insight into the eye's natural regenerative and wound healing abilities," notes Dr. Nagasaki. "This will help us to better understand what is going wrong in the diseased eye."



T. Nagasaki

Top left: A live image of a normal mouse eye viewed from the apex, genetically modified to show fluorescent cells. Radial stripes become visible because some epithelial cells are bright while others are dim, showing the texture of the iris. Corneal epithelial cells move from the limbus to the central cornea. The central bright spot is due to the fluorescence of lens cells, which is mostly blocked by the pigmented iris, but not at the pupil.

Top right: A normal eye viewed from the side shows both cornea (top half) and conjunctiva (bottom half), separated by the limbus (where corneal epithelial stem cells are located, but not conjunctival epithelial stem cells). Radial stripes in the cornea originate at the limbus. The conjunctiva has arbitrary patterns without any stripes.

Bottom: An abnormal eye from the apex (*left*) and from the side (*right*). In this experimentally generated disease condition there are no stripes in the cornea. A cornea like this will usually become vascularized and lose transparency.

New Fellows Join Department

Howard Fine, M.D., from Parsippany, NJ, is a Vitreoretinal Clinical Fellow. He holds undergraduate degrees in chemical engineering and biology from the Massachusetts Institute of Technology, a graduate degree in health sciences in clinical trials from Duke University and earned his medical degree from Harvard Medical School. He completed his residency at Wilmer Eye Institute at Johns Hopkins University and participated in Phase 1 and 2 clinical trials related to uveitis in the Clinical Research Training Program of the National Eye Institute.

C. Manley

Howard Fine, M.D.

"I am excited to have joined the team at Columbia as a retina fellow under the leadership of Dr. Stanley Chang, Dr. Lawrence Yannuzzi and the outstanding retina faculty," Dr. Fine states. "I find this to be an exhilarating time to be entering the field as we are learning to treat previously blinding diseases and will increasingly be able to preserve and restore sight for our patients."

Dublin native **David Keegan, M.D., Ph.D.** is a Vitreoretinal Clinical Fellow. He received his M.D. from the Royal College of Surgeons in Ireland, and holds a master's degree in medical science from University College Dublin. As part of his Ph.D. in ophthalmology from University College London, Dr. Keegan researched methods of retinal cell transplantation. Dr. Keegan has also held vitreoretinal surgery and medical retina fellowships at Moorfields Eye Hospital in London under Professor Alan C. Bird and other top experts.

C. Manley

David Keegan, M.D., Ph.D.

"I came to Columbia to work with Dr. Chang and his team — it truly is a privilege and that is not an overstatement," says Dr. Keegan. "I feel very fortunate to have the opportunity to see different approaches to the spectrum of vitreoretinal diseases."

Natalia Elkin, M.D., a native New Yorker, is a Clinical Fellow in Glaucoma. She earned a B.A. from New York University *summa cum laude* and her M.D. from SUNY Downstate Medical Center in Brooklyn. First a resident in internal medicine at Long Island Jewish

New Fellows Join Department *(con't.)*

C. Manley

Natalia Elkin, M.D.

Medical Center, she completed another residency in ophthalmology at Montefiore Medical Center and served as Chief Resident during her final year.

Dr. Elkin works closely in clinical and surgical practice with Drs. James Tsai, Max Forbes, Lama Al-Aswad and Rajendra K. Bansal. She is also actively involved in the Department's free glaucoma screenings in the community.

Kira Manusis, M.D., another New York native, is a Clinical Fellow in Anterior Segment. Dr. Manusis earned a B.S. degree from Brooklyn College *summa cum laude* and her M.D. from New York University School of Medicine. Following an internship in medicine at Cabrini Medical Center, she completed her ophthalmology residency at the New York Eye & Ear Infirmary.

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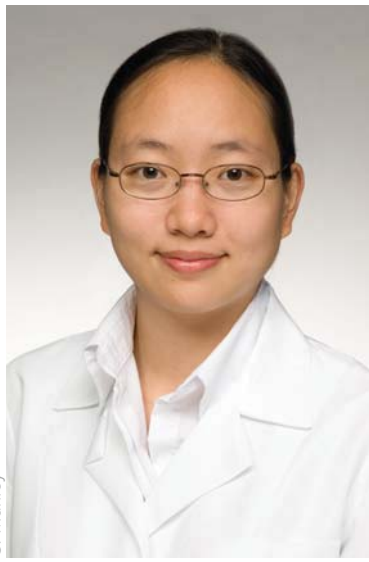
Kira Manusis, M.D.

Dr. Manusis works with Dr. Richard Braunstein and his colleagues, performing refractive and anterior segment surgery and serving as a supervising and attending physician for residents.



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Lookjan Riansuwan, M.D.

Born in Thailand, **Lookjan Riansuwan, M.D.** is a Research Fellow in Glaucoma. She earned her medical degree and completed her residency in ophthalmology at the Faculty of Medicine Siriraj Hospital of Mahidol University in Bangkok. Certified by the Board of Ophthalmology in Thailand, Dr. Riansuwan has practiced at the Somdej Prapinkloa Naval Hospital in Bangkok and lectured on basic ophthalmology for nurses.

Dr. Riansuwan's personal interest in glaucoma stems from the fact that East Asians suffer the world's highest rate of blindness from primary angle closure glaucoma. She works with Columbia glaucoma physicians and scientists with the goal of returning to Thailand to better serve her patients there.

Allikmets' Team Discovers Second AMD Gene

Rando Allikmets, Ph.D., Director of the Molecular Genetics Laboratory, has reported the results of a new study that is being published in *Nature Genetics* that shows that two genes — Factor H and Factor B — play a role in nearly three-quarters of all AMD cases.

The study, which included a genetic analysis of 1,300 people, showed decisively that while Factor H [see *Viewpoint* Fall 2005] inhibits immune response to infection, Factor B, a complementary gene, acts as an activator. Both genes have protective and risk-increasing variants, meaning that a protective Factor B variation can protect against AMD, even if one carries a risk-increasing variant of Factor H, and vice versa. Still, 74% of the study's subjects with AMD had either the Factor H or the Factor B risk variant (or both), but no protective variants of either gene.

"These findings are significant because they absolutely confirm the roles of these two genes and, consequently, the central role of a specific immune response pathway, in the development of AMD. We confirmed this association not just statistically and genetically but, most importantly, pinpointed the biological origin of the disease," added Dr. Allikmets. "In just a few short years, we've gone from knowing very little about what causes AMD to knowing quite a lot. We now have clear targets for early therapeutic intervention."

Special thanks to Elizabeth Streich of CUMC's Office of External Affairs.

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Faculty News

Jorge Fischbarg, M.D., Ph.D., the Laszlo Z. Bito Professor of Physiology and Cellular Biophysics (in Ophthalmology) and Director of Membrane Biology Laboratory, is the editor of a book titled, **"The Biology of the Eye,"** published by Elsevier.

C. Manley

John T. Flynn, M.D.

John T. Flynn, M.D., Vice Chairman of the Department of Ophthalmology and Chief of Pediatric Ophthalmology, received the Marshall M. Parks Medal from **The Foundation of the American Association for Pediatric Ophthalmology and Strabismus**. This medal is conferred on those who have made extraordinary contributions to the field and to the care of children and adults with strabismus.

Max Forbes, M.D., Professor Emeritus and the former head of the Glaucoma Division, was awarded the **American**

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C. Manley

Max Forbes, M.D.

Glaucoma Society's President's Award for his scientific achievement and continued service to the Glaucoma Society and the field of ophthalmology. The fourth recipient of the award, Dr. Forbes is a founding member of the Society.

James C. Tsai, M.D., Director of the Glaucoma Division, was recently named to the Board of Directors of **The Glaucoma Foundation**, the premiere not-for-profit organization dedicated to fighting glaucoma through its research support and patient outreach. "It is an absolute gift to have Jim on our board," says Scott Christensen, the Foundation's President and CEO. The Glaucoma Foundation, which recently celebrated its 20th anniversary, is based in lower Manhattan, with chapters in Chicago, Dallas/Fort Worth and Long Island.

Stephen L. Trokel, M.D., Vice Chairman of the Department of Ophthalmology and

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Promotions

Rando Allikmets, Ph.D., received tenure as Associate Professor of Ophthalmic Science (in Ophthalmology and Pathology & Cell Biology).

Rajendra Bansal, M.D., promoted to Associate Clinical Professor of Ophthalmology.

Lucian Del Priore, M.D., Ph.D., received tenure as Professor of Clinical Ophthalmology.

George Florakis, M.D., promoted to Clinical Professor of Ophthalmology.

Song Eun Lee, Ph.D., promoted to Associate Research Scientist.

Eli Marcovici, M.D., promoted to Assistant Clinical Professor of Ophthalmology.

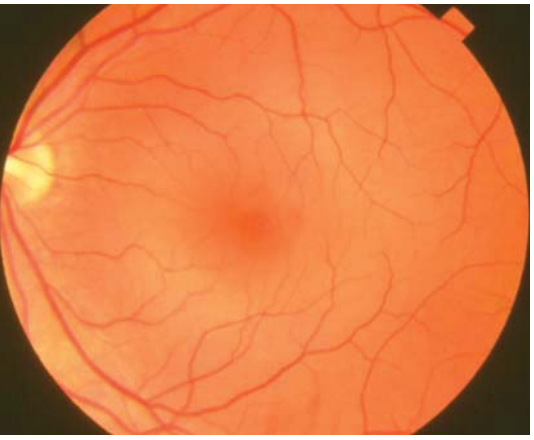
Takayuki Nagasaki, Ph.D., promoted to Assistant Professor of Ophthalmic Science (in Ophthalmology).

Richard Silverstein, M.D., Ph.D., promoted to Assistant Clinical Professor of Ophthalmology.

R. Theodore Smith, M.D., Ph.D., promoted to Associate Clinical Professor of Ophthalmology (in Biomedical Engineering).

Li Wu, M.D., M.Sc., promoted to Senior Staff Associate.

Saving the Sight of Diabetics *(con't. from page 1)*



National Eye Institute, NIH

Fundus photograph of a normal retina.

Boston, the West Indies and Mexico.

"Last fall I contacted Dr. James Tsai for advice on establishing a glaucoma program on the island of Nevis in the West Indies," notes Dr. Bresnick. "As we talked further, the discussion turned to our program to screen for diabetic retinopathy in Mexico. Dr. Tsai immediately saw the potential for Columbia and set the wheels in motion by bringing Dr. Stanley Chang into the conversation."

Diabetic retinopathy is the leading cause of blindness in working-age Americans, even though it is highly treatable by laser when caught in time. Retinal blood vessels are particularly sensitive to cellular damage from high blood sugar; in fact, nearly all Type 1 diabetic patients and over 60% of Type 2 diabetic patients will develop retinopathy within the first 20 years of onset. The American Academy of Ophthalmology and the American Diabetes Association strongly recommend that diabetic patients obtain annual ophthalmology examinations for early detection and treatment of retinopathy, yet numerous studies have shown that fewer than half of diabetic patients actually do so.

"George and Geri brought their proposal to our doorstep at exactly the right time. We had been considering how to implement a diabetic retinopathy screening program after seeing so many cases of advanced retinopathy in the clinic," confirms Dr. Chang. "Simultaneously, Dr. Michael Chiang's success with the Retinopathy of Prematurity telemedicine study has proven the viability and effectiveness of telemedicine as a screening tool [see 2005 Fall/Winter *Viewpoint*]. We are excited by the potential of combining the power of telemedicine with the effectiveness of Vision for All's community outreach in Washington Heights."

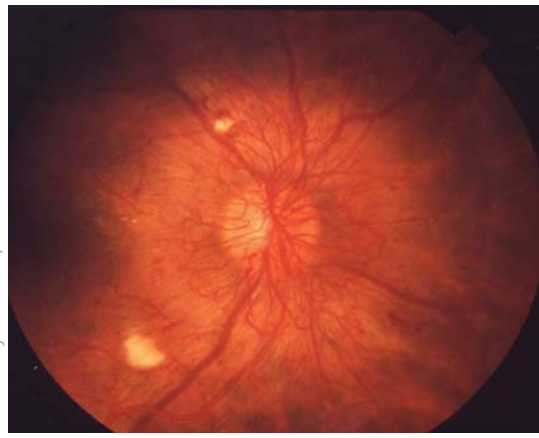
The Harkness Eye Institute already provides low-cost and free vision care to the largely Hispanic Washington Heights population through the ITT Eye Clinic. Yet the challenge lies in reaching diabetic patients who may not be aware of the Eye Clinic's services, or even that their vision is at risk.

"Although many of the community's diabetes patients are having their diabetes monitored at New York-Presbyterian Hospital medical clinics several times per year, roughly 60% of the patients are not obtaining the necessary retina exams at the Eye Clinic. Sadly, many do not come to us until the situation is dire, when the retinopathy is advanced and the

Saving the Sight of Diabetics *(con't.)*

vision is already severely compromised," states Dr. Bresnick. "In order to treat diabetic patients with laser most effectively, the patients must be seen before the retinopathy has progressed to an advanced stage. This requires regular retinal examinations, as severe retinopathy can develop without any visual symptoms until serious bleeding occurs in the eye. Since so many patients fail to come to the Eye Clinic for preventive care, the most effective way to preserve their vision is to bring the eye screening to them."

Michael Chiang, M.D., M.A., Assistant Professor of Ophthalmology and Biomedical Informatics, is leading the operational aspects of the two-year project for Columbia's ophthalmology and biomedical informatics departments, with the goal of proving the efficacy of telemedicine diagnosis for diabetic retinopathy screening. Telemedicine diagnosis of diabetic retinopathy involves obtaining digital photographs of patients' retinas during a standard visit with their primary care physician, and then transmitting those images via the Internet to a remote screening center for reading and grading by trained experts. All that is necessary is a willing patient, a standard ophthalmic fundus camera operated by a qualified technician, a computer and an Internet connection. Experts anywhere in the world can make an accurate assessment based solely on the retinal photographs, thanks to the universally accepted standards for reading and grading retina photographs developed at the University of Wisconsin in the early 1970s where Dr. Bresnick was a member of the research team.



National Eye Institute, NIH

Proliferative retinopathy, an advanced form of diabetic retinopathy, occurs when abnormal new blood vessels and scar tissue form on the surface of the retina.

Dr. Bresnick feels fortunate to have participated in that early research. "We conducted a series of collaborative clinical trials supported by the National Eye Institute that decisively showed the effectiveness of laser treatment in preserving vision for diabetic patients with proliferative diabetic retinopathy or macular edema," he explains.

Dr. Bresnick continues, "A crucial part of these studies involved developing standardized and reproducible methods to record and grade the severity of the retinopathy in each patient. The stereo-retinal photographic technique and grading system developed at the University of Wisconsin has become recognized as the 'gold standard' for diabetic retinopathy evaluation." Dr. Chiang agrees, emphasizing that this grading protocol is at the very core of the telemedicine diabetic

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Saving the Sight of Diabetics *(con't. from page 13)*

retinopathy screening study at Columbia. Without universally accepted grading standards, reliable remote diagnosis simply would not be possible.

Thanks to generous funding from the Russell Berrie Foundation, approximately 3,000 diabetic patients will be screened annually for diabetic retinopathy at community medical clinics operated by the Ambulatory Care Networks Corporation (ACNC) at Columbia University Medical Center. The resulting retina photographs will be uploaded via the Internet to Inoveon, a telemedicine company based in Oklahoma City with a reading center in Nashville, where trained experts will read, grade and provide the results to patients' primary care physicians. In turn, the physicians will refer their patients to the Eye Clinic to ensure that they receive appropriate ophthalmic treatment.

"We have two main goals for the project. The first is to detect potentially blinding disorders in the high-risk diabetic population and steer those patients toward treatment in time to save their vision," states Dr. Chiang. "The second is to look at several research questions related to the main outcomes of the study, such as, will the availability of a telemedicine screening system within a primary care setting increase the likelihood that diabetics will have their eyes examined? Can telemedicine provided in this setting improve our ability to diagnose this treatable disease? How well can we implement this system within existing medical workflows? Will it be economically self-sustaining? Access to a high-volume patient population and a strong research infrastructure makes Columbia the perfect real world environment in which to conduct this study and address these questions."

Simultaneously, through Vision for All, Dr. Bresnick and Ms. Hendriksen are building the community networks necessary to reach diabetic individuals in Washington Heights who are not receiving regular medical care or whose eyes are not yet being monitored. "Geri and I are working with various organizations to offer initial screenings and retina exams in conjunction with diabetes education at various community sites. We then facilitate appointments and visits to an ophthalmologist for appropriate eye care. But making sure the patient actually makes the trip to the Eye Clinic for follow-up care is one of the hardest things to do. There are a number of educational and socioeconomic barriers," observes Dr. Bresnick, noting that fear and financial worries top the list.

Dr. Chiang is optimistic. "The Columbia ophthalmology clinic has a longstanding commitment to working with the public, and never turns away someone in need of treatment due to lack of ability to pay. This is the driving force behind the telemedicine diabetic retinopathy screening program that we are all working to implement."

A Treasured Gift to Vision *(con't. from page 3)*

graduate school onward. Those were the halcyon days of research." After pursuing research for many years, he started in clinical practice under the mentorship of A. Gerard DeVoe, M.D., the ophthalmology department chair during the 1960s.

Dr. DeVoe reminisces, "I enjoyed working with Dr. Srinivasan during his clinical days. He is a wonderful person, straightforward and honest, extremely conscientious. He is a fine surgeon and has a gentle manner with patients. I could always count on him to do whatever needed to be done. I don't think you'll find anyone more loyal to the Eye Institute."

K. H. Boyd

Dr. Srinivasan examines a patient in the ITT Eye Clinic

Dr. DeVoe introduced Dr. Srinivasan to Rand Araskog, the now-retired chairman and chief executive officer of ITT Corporation and a founding member of the Department's Board of Advisors. Over the years, they have developed a special bond, and Mr. Araskog credits Dr. Srinivasan with preserving his vision. In fact, Mr. Araskog and his wife established the A. Gerard DeVoe-B. Dobli Srinivasan Directorship of Ambulatory Eye Care in 2004 to honor both doctors. "Dr. Srinivasan's kindness and humility constantly show through in his work. He really deserves the adjective 'selfless,'" reflects Mr. Araskog. "He always talks with fervor about the fact that a sighted eye is a gift to be treated with the greatest of care. This belief expands beyond his professionalism and toward his genuine concern for the individual and what being able to see means to a lifetime. He has had a major impact on my life."

Dr. Srinivasan became involved on a volunteer basis with the Eye Clinic that serves the Washington Heights community during Dr. DeVoe's tenure. In 1990, under the chairmanship of Anthony Donn, M.D., Dr. Srinivasan accepted the Eye Clinic directorship, and with it, the responsibility for treating 21,000 patients annually, as well as teaching and supervising nine to ten residents each year.

"One of the best decisions I ever made was to ask Dr. Srinivasan to become the director of the Eye Clinic," states Dr. Donn. "Prior to that, the clinic had been run on a volunteer basis by the attending physicians. Putting Dobli in charge of supervising residents brought the quality of the residency program to a new level."

Dr. Srinivasan clearly enjoys mentoring his residents. "I get a big kick out of learning

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Faculty News *(con't. from page 11)*

Director of Columbia Vision Correction, delivered the keynote lecture at the **American Society for Laser Medicine and Surgery's** (ASLMS) 26th Annual Meeting in Boston in April. Dr. Trokel is the first ophthalmologist to recognize the significance of the excimer laser in corneal refractive surgery. In 1999, he was nominated by over 30,000 of his peers as one of the twentieth century's most influential ophthalmologists.

Stephen Tsang, M.D., Ph.D., Assistant Professor of Ophthalmology, has been selected by the **Association for Research in Vision and Ophthalmology** (ARVO) to receive its inaugural ARVO/Alcon Early Clinician Scientist Research Award. He will present his winning paper at the ARVO Annual Meeting in late April.

A Treasured Gift to Vision *(con't. from page 15)*

from them. They keep me going! It is gratifying to see them blossom; by their third year, they are superb ophthalmologists."

Amilia Schrier, M.D., who has taught residents in the clinic with Dr. Srinivasan since 1998, will become the new DeVoe-Srinivasan Director of Ambulatory Care and assume responsibility for the ITT Eye Clinic when Dr. Srinivasan retires at the end of June. She says, "Dr. Srinivasan is a physician's physician; his knowledge, judgment and contributions are second to none. There is not a day that goes by that he is not called upon to offer his opinion and recommendations on challenging cases. His self-assurance gives all of us — colleagues, attending physicians and residents — the confidence to perform and be the best that we can be."

Eric Wolf, M.D., Chief Resident in the ITT Eye Clinic, concurs. "Dr. Srini, as he is affectionately known, is respected and loved by all of his students and patients and has achieved a fatherly status in the eyes of his residents and colleagues. He is a veritable institution within this medical center and will not be forgotten."

Reflecting on his career, Dr. Srinivasan says, "I have thoroughly enjoyed my career at Columbia — the research, the clinical work, the residents, my colleagues. I feel very lucky to have had so many wonderful opportunities." He plans to continue his involvement in ophthalmology and public health, albeit on a more relaxed level.

"Dr. Srinivasan has been a pillar of this department," states Dr. Stanley Chang. "His steadfast dedication to teaching residents and medical students, and strong commitment to serving the community has set a high standard for scholarly activity over for four decades. We wish him a happy and healthy retirement!"

Apprehending the Silent Thief *(con't. from page 1)*

in the United States, affecting some 2.2 million Americans, with as many as 2 million more not yet diagnosed.

Although elevated pressure within the eye has long been considered a tell-tale symptom of glaucoma, recent research has shown that one in three glaucoma cases occur in persons with normal intraocular pressure. This alarming statistic has led James C. Tsai, M.D., Director of the Glaucoma Division at Columbia, and his mentor, Max Forbes, M.D., former glaucoma division director, to redouble their efforts in pursuit of a multi-dimensional approach to apprehending the "silent thief."

"There are three facets to our clinical and research efforts in the Glaucoma Division. The first involves implementing aggressive glaucoma screening outreach with funding from the Friends of the Congressional Glaucoma Caucus Foundation and other organizations to detect and begin treating the disease earlier, before significant vision loss occurs [see *Viewpoint* Spring 2005]. The second is basic science research, both to understand retinal ganglion cell loss and to discover new compounds or drugs with potential neuroprotective and neuroregenerative effects," explains Dr. Tsai [see *Viewpoint* Fall 2005]. "The third is translational research and goes hand in hand with the basic science neuroprotection research. How do you demonstrate that a person's glaucoma is

V. Zemon

Vance Zemon, Ph.D. demonstrates the icVEP

stable or getting worse? What we're trying to do is develop new treatments and technologies that are more sensitive and specific to the early detection and worsening of glaucoma, and the Harkness Eye Institute has developed a highly accurate and sensitive prototype device to do just that."

Drs. Tsai and Forbes have partnered with Vance Zemon, Ph.D. of Yeshiva University and George Hu, Ph.D. of Synabridge Corporation to develop the "isolated check visual evoked potential" instrument (icVEP), a fast and highly accurate glaucoma screening tool that measures electrical activity in the brain in response to visual stimuli. Columbia was the only center for the initial clinical trials funded by the National Institutes of Health (NIH), and achieved a 94% accuracy rate in separating glaucoma patients from the control group in Phase 1. Columbia is one of

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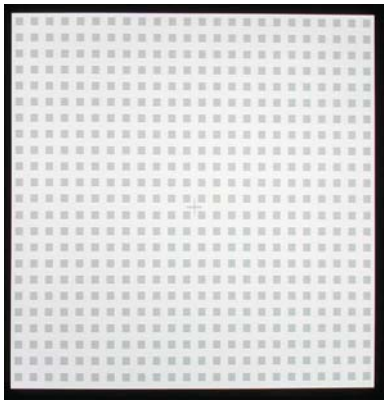
Apprehending the Silent Thief *(con't. from page 17)*

three collaborating institutions in Phase 2, which will test the efficacy and safety of the technology in a broader context.

The hypothesis behind the icVEP is that glaucoma patients with 20/20 visual acuity do not have the same visual function as those without glaucoma and 20/20 visual acuity. By measuring the responses in select visual pathways and applying complex statistical algorithms, Drs. Tsai and Zemon can quickly screen for glaucoma and also detect further visual decline — something that current screening methods cannot do. The icVEP concept builds on the success of Columbia's expertise in multifocal VEP pioneered by Columbia's Vivienne Greenstein, Ph.D. and Don Hood, Ph.D.



V. Zemon

The "check" pattern used with the icVEP

"A number of ganglion cell subpopulations exist in the retina, and we believe that these subpopulations represent parallel pathways for the transmission of visual information to the brain. One of these pathways — the magnocellular pathway — is known to be sensitive to low contrast and high frequency of stimulation and it is thought to be affected early in glaucoma," explains Dr. Zemon. "The magnocellular pathway has an ON-cell division for brightness perception, such as white on a black background, and an OFF-cell division for perception of dark objects on a lighter background. The icVEP measures the strength of electrical currents generated by the magnocellular pathway and then a signal-to-noise ratio is computed. If the result is greater than 1, then there is a true response in the brain. However, if a response is not found, the pathway is disrupted, indicating possible glaucomatous damage."

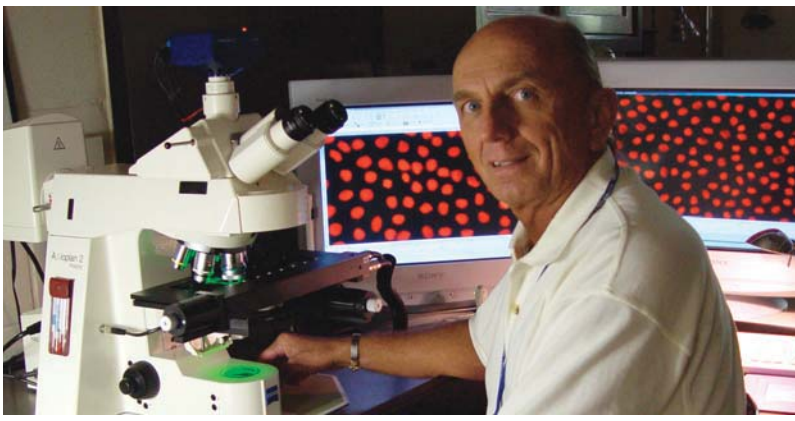
The icVEP device is a specialized computer combined with a carefully calibrated monitor. Input is received from two electrodes placed on the scalp of the subject — one over the visual cortex of the brain and the other over a neutral reference point on the top of the head. Once connected, the electrodes measure EEG brainwaves while the subject looks at an array of bright or dark isolated squares on the monitor. The "check" patterns appear and disappear during the testing, which involves the modulation of peak contrast over the course of eight two-second stimulus presentations per eye.

Dr. George Hu, a former student of Dr. Zemon, is the principal investigator on the NIH study and the engineer who designed the icVEP instrument. "George is the genius behind the icVEP. He has invented an efficient machine that collects data rapidly,

In Memoriam: Basil V. Worgul, Ph.D.

The Department of Ophthalmology mourns the loss of Basil Vladimir Worgul, Ph.D., who died of a heart attack at his home in Edgewater, NJ, on January 19, 2006 at the age of 58. He joined Columbia in 1974 and became a full professor in the departments of ophthalmology and radiology in 1990. He was also a director of the Ukrainian/American Chernobyl Ocular Study. He studied the effects of radiation on the eyes of some 12,000 clean-up workers exposed to radiation following the disaster.

"Dr. Worgul's most important contributions came early in his career through his research collaborations with the esteemed ophthalmologist, George Merriam, M.D.," observes Eric J. Hall, Ph.D., Director for the Center of Radiological Research at Columbia. "They made recommendations to NASA before the lunar missions about radiation protection, and were the first to show how very effective



Basil V. Worgul, Ph.D.

neutrons and HZE particles were in producing cataracts, even at low doses. After Dr. Merriam retired, Basil became the number one expert on radiation-induced cataracts in the United States."

"Basil Worgul made significant contributions to our understanding of cataract formation after radiation exposure," states Dr. Stanley Chang. "We will miss his brilliance and constant quest for new information."

Apprehending the Silent Thief *(con't.)*

rejects false information and automatically computes the signal-to-noise ratio to generate objective results," says Dr. Zemon with pride. "Unlike others studying VEP, we have synchronized data collection with the stimulus, meaning that we can obtain much cleaner signals from the brain and therefore achieve more reliable results. Yet the simplicity of the instrument ensures that any physicians' assistant can be trained to use it as a routine screening device within a primary care setting."

Dr. Tsai agrees. "If our clinical trials continue to be as successful as they already have been, the icVEP has the potential to revolutionize glaucoma detection for millions of people, as well as provide a reliable way to test new drug treatments. This is very exciting technology. We are really accomplishing our translational research goals."

Viewpoint

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