



Viewpoint

SPRING/SUMMER 2008

Clinical Corner: It's All in the Eyes

"To an artist, the eye is the most important organ," notes John Richardson, the friend and eminent biographer of Pablo Picasso. Mr. Richardson recently authored *A Life of Picasso: The Triumphant Years, 1917-1932*, the third in an acclaimed biographical series that spans more than 50 years of the artist's life.

Mr. Richardson shared these and other recollections of the inimitable artist at a lecture and cocktail reception on January 22nd for the Department of Ophthalmology hosted by Advisory Board member William Acquavella at the Acquavella Galleries in New York City. The event, which also included time for book signing, was attended by more than 100 friends and donors to the Department.

"Picasso had these amazing eyes – in any photograph you can see this extraordinary hypnotic look he had. Picasso knew he had these hypnotic eyes and the intense gaze that is known in Spanish as *mirada fuerte*. He used his eyes to enormous effect to seduce, caress or



L to R: Françoise Gilot, Thomas Knapp, John Richardson

even frighten people," Mr. Richardson explains, noting that Picasso's eyes and their importance to his work is a principal theme of all three biographical volumes.

Mr. Richardson, who recently turned 84 and divides his time between New York City and Connecticut, trained as an artist at the Slade School of Fine Art in London, but later exchanged his paint brush for the pen and a career as a writer and art critic. In 1949, he moved to Provence in France, and collaborated with

cubist expert and art collector Douglas Cooper to create a private museum at the Château de Castille near Avignon. At that time he was developing friendships with prominent 20th-century artists including Picasso, Georges Braque, and Fernand Leger. In the 1960s, Mr. Richardson set up the U.S. operations of Christie's in New York City.

In addition to his Picasso biographies, Mr. Richardson is the author of a memoir, an essay collection

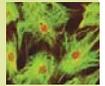
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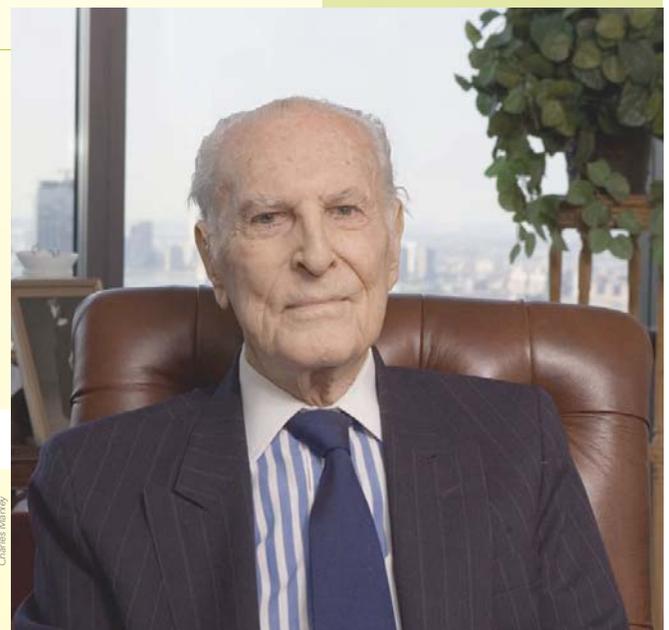
Richard Deems lost sight in his left eye 25 years ago due to a retinal detachment. When vision in his right eye began to fail a year ago, he turned to Columbia University's Department of Ophthalmology and Stanley Chang, M.D.

"Last year, my right eye, my good eye, was giving me trouble because it started to bleed. For two weeks, I had no eyesight at all, no vision. It

was devastating," explains Mr. Deems. "When my doctor in New York threw up his hands, I said to him, 'Well, do you think I should consult Dr. Stanley Chang?' And he said, 'By all means, he is the number one man when it comes to retinal surgery.' So I went to Dr. Chang in November of 2006, and I've been his patient ever since. I've got pretty good vision now – not as

Richard Deems

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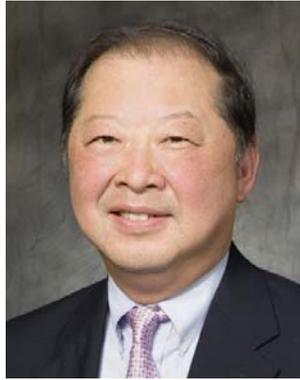


Charles Marbury

Dear Friends,

Diabetes, the chronic and systemic disease characterized by elevated high blood sugar due to defective insulin production, affects 20.8 million children and adults in the United States, according to the American Diabetes Association. Of that total, some 6.2 million remain undiagnosed. Another 54 million have pre-diabetes. Diabetes is devastating to the body; left untreated, it can set off a destructive chain of events leading to heart disease, stroke, kidney disease, nervous system damage and blindness.

The delicate tissues of the retina are especially sensitive to damage from diabetes. The Center for Disease Control and Prevention estimates that diabetic retinopathy is the cause of 12,000 to 24,000 new cases of blindness each year – half of which could have been prevented with early intervention. The physicians and scientists of the Department of Ophthalmology are deeply committed to Columbia University Medical Center's larger goal of finding a cure for diabetes, and to early intervention and new treatments.



Charles Manley

In this issue of *Viewpoint*, we profile Gaetano Barile, M.D., a retinal specialist and vitreoretinal surgeon whose groundbreaking research has yielded important new knowledge about the mechanisms of diabetes, particularly as it relates to the eye. His work has been funded by the Eye Surgery Fund, the Glaubinger and Irving Scholar Funds and the Juvenile Diabetes Research Foundation. A new gift from The Hearst Foundation, Inc. will hasten his efforts to find new treatments for diabetic retinopathy. We also feature first-time donor Richard Deems and art historian John Richardson, author of *A Life of Picasso: The Triumphant Years, 1917-1932*. Mr. Richardson spoke about his research for the book at a special book-signing event for the Department hosted by our Advisory Board member, William Acquavella.

As we celebrate the 75th anniversary of the founding of the Edward S. Harkness Eye Institute, I extend renewed gratitude to each of you – patients, friends and donors – for your continued generosity and support, on behalf of the faculty and staff of the Department of Ophthalmology. We recognize and appreciate the trust and faith you place in our hands, and we are grateful for the honor of working with you. Thank you again for all that you do.

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

It's All in the Eyes continued from page 1

and books on Manet and Braque. He is one of *Vanity Fair's* contributing editors and has written for *The New York Review of Books* and *The New Yorker*.

Mr. Richardson acknowledges how important his own vision has been to his work and career. He recalls, "About five years ago, my sight was getting worse and I was getting quite concerned about it. I was having a drink with my old friend Bill Acquavella and told him that I was having trouble with my eyes. He pulled out a grid and asked me what I saw. I said, 'The whole thing is twirling and whirling and not making any sense at all.' He told me that I must see Dr. Chang right away."

Mr. Richardson followed up on that suggestion and, after a visit to Stanley Chang, M.D., was diagnosed with neovascular or "wet" age-related macular degeneration (AMD). Wet

AMD is characterized by an overgrowth of blood vessels that form under the macula on the retina and leak blood and fluid, leading to scar tissue and visual distortions. Mr. Richardson chose to become a patient in what was then one of the Lucentis clinical trials, and he received monthly injections in his left eye by Gaetano



Maie-Lee Chen and John Richardson

Barile, M.D. with "remarkable results." He emphasizes that other patients should not be afraid of the injection – the benefits far out-



Charles Manley

L to R: William Acquavella; Amelia Schrier, M.D.; David Pearce, M.D.; Jane Heffner; Stanley Chang, M.D.

weigh the initial fear, and the injection is really quite tolerable.

"I am hugely grateful to Dr. Chang and Dr. Barile," says Mr. Richardson with emotion, as he is now also being treated for AMD in his right eye. "I wouldn't have been able to finish this third volume of biography if it hadn't been for their care. They are so compassionate and attentive, yet sensible and down-to-earth. One never has a minute's worry around them. I always know everything is going to be alright." And well it should be, as Mr. Richardson is already at work on the fourth volume of the Picasso biography. ■

Hearst Foundation Funds Diabetes Vision Research

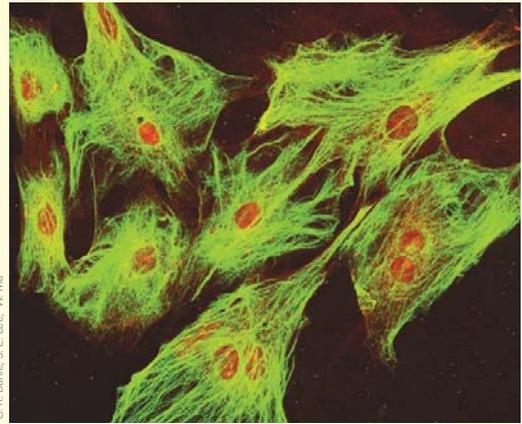
Diabetic retinopathy, a common complication of diabetes mellitus, is the leading cause of vision loss in working-age Americans. It is estimated that one in 29 Americans over the age of 40 has some degree of diabetic retinopathy, fueled in part by our nation's diabetes epidemic. Visual loss from diabetic retinopathy is typically painless, and it can occur slowly and insidiously or attack suddenly. Regular ophthalmic exams are crucial to early diagnosis, as interventions such as laser therapy can be used to slow or stabilize diabetic retinopathy. Despite the importance of vision to patients with diabetes, there is not yet a FDA-approved pharmacologic agent to treat diabetic complications in the retina.

In December, The Hearst Foundation, Inc. awarded the Department of Ophthalmology a grant to further support Gaetano Barile, M.D.'s research to uncover the disease processes behind the retinal complications of diabetes.

Dr. Barile is studying the role of advanced glycation end products (AGEs) and their receptor (RAGE) in the progression of diabetic complications in the

retina. "The duration and severity of hyperglycemia [high glucose or "sugar"] is the major factor in the development of retinopathy in patients with diabetes," explains Dr. Barile. One metabolic consequence of hyperglycemia is the accelerated formation of AGEs, proteins in the body which are abnormally altered by high blood glucose levels. In patients with diabetes, AGEs may accumulate and ultimately bind to RAGE, a receptor on the surface of certain cells. This process can trigger cellular dysfunction and often destructive inflammation in body tissues.

Dr. Barile and his team have made seminal contributions to the field with studies that first identified RAGE expression in the native Müller cells of the retina and then showed increased RAGE expression in diabetic retinas. The Müller cell is a critical support cell that aids the function of adjacent retinal cells, including light signal-transmitting neurons and blood vessels that supply nutrients to the metabolically active retina. Dr. Barile states, "Increasingly, diabetic retinopathy is recognized as a neuro-vascular disorder, a disease that encompasses interrelated vascular and neural dysfunction prior to the clinical development of retinopathy. Our identification of RAGE in the Müller cell supports this hypothesis and suggests that its perturbation in the retina can upset a delicate neuro-vascular balance. We replicated neuronal and vascular dysfunction in our models and observed that reduction of RAGE activation is beneficial. We believe that stabilizing the Müller cell in the human retina via RAGE antagonism



G. R. Barile, S. E. Lee, W. Ma

Retinal Müller cells in culture in vitro, exhibiting their fine cytoskeletal processes with an immunolabel for the protein vimentin. Müller cells are glial cells that provide critical structural and physiologic support to the neural retina.

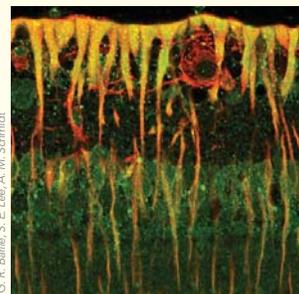
may help to diminish the complications that occur in diabetic retinopathy."

With the support of The Hearst Foundation, Dr. Barile will continue to focus on defining the precise pathophysiologic role of RAGE in retinal diseases, particularly diabetic retinopathy. The

goal is to better ascertain this pathway as a target for new drug therapies.

Mason Granger, program director of grants for The Hearst Foundation, says, "Over the years, The Hearst Foundation has been extremely committed to investments and grants in the area of health care, particularly the application of research to patient care. We are proud to support the excellent work of Columbia's Department of Ophthalmology, and indeed, all of Columbia's important endeavors and

schools. The Foundation's highest priorities include support for education and research efforts that improve patient care. This grant ties these interests together in a way that we believe has a great deal of power to affect people's lives in a very positive way." ■



G. R. Barile, S. E. Lee, A. M. Schmidt

Co-localization of immunohistochemical antibodies to RAGE (green) and vimentin (red) appears most prominently as yellow fluorescence in the Müller cells spanning the neural retina of the pig (inner retina superiorly and outer retina inferiorly in this retinal section).

Visionary Giving continued from page 1

good as I'd like, but for an older person, I can read the *New York Times* and do what business I do, so it is quite satisfactory."

At 95, Mr. Deems remains active as a trustee of The Hearst Foundation, Inc. and a director of the Hearst Corporation, where he has worked for the last 69 years, most recently as head of Hearst Magazines. "I came as a temp and decided to stay," he quips.

Mr. Deems is so grateful for his vision that he and his wife Jean made a generous gift to the

Department of Ophthalmology last spring. Additionally, as a trustee of The Hearst Foundation, Mr. Deems recommended the Foundation's support of Gaetano Barile, M.D.'s research in diabetic retinopathy and Columbia University Medical Center's larger institutional goal of finding a cure for diabetes. "Over the last 25 years, I've become very interested in ophthalmology, understandably," notes Mr. Deems. He developed close friendships with the prominent ophthalmologists who treated him during this period,

including Weill Cornell ophthalmology chairman D. Jackson Coleman, M.D., one of Dr. Chang's teachers and mentors.

In speaking about his motivation in supporting vision research at Columbia, Mr. Deems remarks, "In my opinion, there is no one more knowledgeable than Dr. Chang. I like the way he's bringing along other young doctors, and the leadership that he provides to them is so important. I think some of his genius rubs off on them." ■

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Chang Receives Castle Connolly "Physician of the Year" Award

Stanley Chang, M.D. was one of three physicians honored with the prestigious Castle Connolly "National Physician of the Year Award for Clinical Excellence" at a dinner in New York City on March 18. Two other physicians were recognized for lifetime achievement.

The award acknowledged Dr. Chang's many contributions to medicine and ophthalmology in particular, reflecting both his outstanding professional achievements and those of the Department of Ophthalmology. Honorees were selected from among the more than 600,000 physicians currently practicing in the United States. Nominations were solicited from the executive and medical leadership of the nation's premier medical

centers and specialty hospitals and from all physicians profiled in the Castle Connolly publications *America's Top Doctors* and

America's Top Doctors for Cancer, with final selections made by the Castle Connolly Medical Advisory Board. ■



Arthur Hull Hayes Jr., M.D., former Commissioner of the U.S. Food and Drug Administration and former Provost and Dean of New York Medical College, presents Stanley Chang, M.D. with the "Physician of the Year" award.



L to R:

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Lars Leksell Professor and Distinguished Professor, University of Pittsburgh; Director, Center for Image-Guided Neurosurgery, University of Pittsburgh Medical Center;

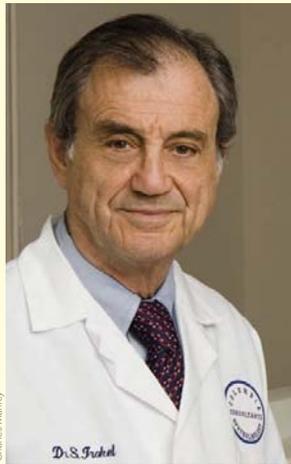
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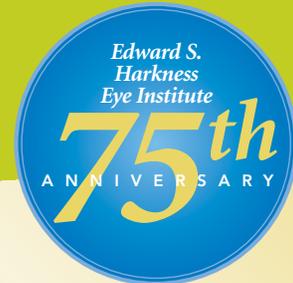
Trokel Inducted Into ASCRS Hall of Fame

On April 5, Stephen Trokel, M.D. was inducted into the American Society of Cataracts and Refractive Surgery's "Hall of Fame" at an award ceremony in Chicago. Established in 1999, the ASCRS has recognized more than 30 scientists and physicians who have made seminal contributions to the field of cataract and refractive surgery. Hall of Fame inductees are chosen by their peers from more than 30,000 ophthalmologists worldwide.

Dr. Stephen Trokel is widely regarded for his pioneering work in the development and application of excimer lasers in corneal refractive surgery and as the first ophthalmologist to recognize the significance of such an application. Dr. Trokel's vision and exhaustive research have made laser vision correction a realistic alternative to glasses and contact lenses for millions worldwide. He remains an innovator working to further develop and implement new technology. In 1999, he was named one of the 20th century's most influential ophthalmologists. ■



Stephen Trokel, M.D.



Save the Date!

Join us as we celebrate the Edward S. Harkness Eye Institute's 75th Anniversary at a Gala Benefit

Thursday, September 18, 2008 at the Metropolitan Club

For more information, please call (212) 305-7827

Telemedicine Screening System Detects Eye Disease at the Primary Care Level

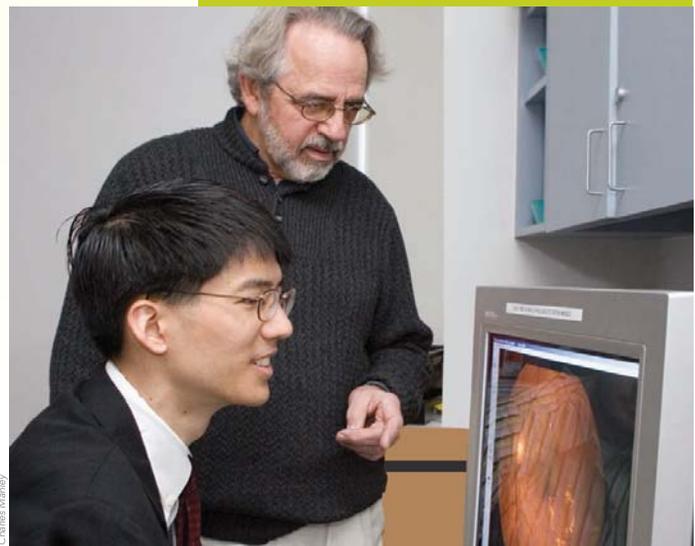
An innovative telemedicine screening system designed to diagnose diabetic retinopathy in the convenience of the primary care setting has proven to be highly successful in detecting this and other eye diseases. Michael Chiang, M.D., M.A. and George Bresnick, M.D., M.P.A., in collaboration with the Department of Medicine and Inoveon Corporation, developed this telemedicine system to reach the estimated 39% of diabetic patients in a primary care clinic at Columbia who were not receiving the recommended annual dilated eye examinations.

Telemedicine is a means to deliver rapid and cost-effective ophthalmic screenings to those most at risk. Digital retinal photographs are taken during standard primary care visits and then uploaded to the Internet to a telemedicine reading center, where trained experts read, grade and return the results to the physician.

The program was launched in March 2007. Now, a year later, Drs. Chiang and Bresnick have performed 230 telemedicine examinations on diabetic patients and detected 29 patients with severe diabetic retinopathy. Those patients were immediately referred to retina specialist Reza Iranmanesh, M.D. for

further care. While reviewing these retinal images, Drs. Chiang and Bresnick also referred many other patients for follow-up due to suspicion for glaucoma or other ocular disease that may have gone otherwise undetected.

Based on the initial success of this endeavor, Drs. Chiang, Bresnick and Iranmanesh intend to expand this telemedicine program to other Columbia University primary care medical clinics. Their overall goals are to improve early detection of diabetic retinopathy while it is still easily treatable, and to understand how these advanced technologies can best be applied to make ophthalmic care more accessible to patients. ■



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



Gaetano R. Barile, M.D.

Faculty Spotlight: Gaetano R. Barile, M.D.

It was a serendipitous research opportunity with Stanley Chang, M.D. at Cornell University Medical College in the late 1980s that inspired New York area native Gaetano “Guy” Barile, M.D. to choose ophthalmology as his specialty. “As a medical student, I was exposed to the spectrum of fields of medicine, but the elegant surgery and commitment to restoring vision that Dr. Chang demonstrated captured my interest. The importance of vision to patients and the precision of microsurgical interventions further stimulated me to pursue ophthalmology,” says Dr. Barile.

Following an internship at what is now Columbia University Medical Center, Dr. Barile completed the residency program at Manhattan Eye, Ear and Throat Hospital, where he experienced strong clinical training under many excellent attending physicians. In fact, he recalls performing his first cataract surgery with Amilia Schrier, M.D., now the Director of Ambulatory Eye Care at the ITT Eye Clinic at the Harkness Eye Institute. “Amilia was a fantastic teacher and role model for me during my residency, and it’s really an honor to have her as a colleague here at Columbia,” says Dr. Barile.

While completing a subsequent retina fellowship under Dr. Chang, Dr. Barile was awarded the prestigious Heed Foundation Ophthalmic Fellowship, and he made the transition with Dr. Chang from St. Luke’s-Roosevelt Hospital to Columbia, later joining the faculty of the Department of Ophthalmology. With Dr. Chang’s encouragement, Dr. Barile pursued

additional retinal training at Moorfields Eye Hospital in London. There, he had the opportunity to work with Professor Alan Bird, an internationally recognized expert in the field of medical retinal diseases. “It was really a wonderful experience for me,” he says. “In the clinics at Moorfields, we were seeing patients from all over the United Kingdom with a whole host of retinal disorders. I was able to really hone diagnostic skills and learn about unusual diseases.”

Dr. Barile is now an Associate Professor of Clinical Ophthalmology and the Glaubinger Scholar in Retinal Research at Columbia. From 2002-2005 he was the Herbert Irving Assistant Professor. He is recognized by Castle Connolly as one of New York’s “Top Doctors” for his expertise as a retinal specialist and vitreoretinal surgeon. He comments, “What is most exciting for me is when we’re able to meaningfully improve vision in people who have lost sight due to complications of visually threatening disease, such as diabetic retinopathy, retinal detachment or macular degeneration.”

In addition to his surgical and office practice, Dr. Barile collaborates with colleague William M. Schiff, M.D. [see Fall/Winter 2007 *Viewpoint*] on clinical research to improve anatomic and physiologic outcomes in vitrectomy and retinal detachment surgery. He also has a longstanding interest in macular degeneration, collaborating with Rando Allikmets, Ph.D. and R. Theodore Smith, M.D., Ph.D. in the Columbia Macular Genetics Study, and serving as a principal investigator of several clinical research trials at the Eye Institute, including Genentech’s pivotal Lucentis studies. “We expect that the treatments we pursue will have a real clinical impact on manifestations of these blinding disorders,” he says.

In terms of basic science or “bench” research, Dr. Barile and his team are investigating the role of the RAGE receptor in retinal disease such as diabetic retinopathy. [See “Hearst

Foundation Funds Diabetes Vision Research,” page 3.] “We started out looking at the RAGE receptor as primarily an issue of diabetic complications, but it turns out that it also may be relevant in macular degeneration,” Dr. Barile explains. Recent studies demonstrated that RAGE activation can increase retinal pigment epithelial cell secretion of VEGF, a protein that induces leaky blood vessels and new blood vessel growth seen in neovascular or “wet” macular degeneration and that has been successfully targeted with “anti-VEGF” therapy such as Lucentis. “In research, you have to stay flexible in your thoughts – sometimes preconceived notions can be challenged,” Dr. Barile notes. “In the case of RAGE, there are retinal cell-specific effects that may require disease-specific approaches to future treatments.”

Dr. Barile finds the collegial relationships among attending physicians, fellows, residents and staff at the Eye Institute particularly satisfying. “I am privileged to work with some of the most talented people in the field on a daily basis. Their commitment to patient care, teaching and research is amazing. It’s hard to imagine a more stimulating setting for me as a physician.”

However, the most gratifying and important interactions for Dr. Barile are his daily encounters with patients who are living with eye disease. “I have been fortunate to meet really interesting and inspiring patients in my practice. As doctors, if we sit down and listen to our patients, we can learn a lot about biology, medicine and even life,” he observes. “Our patients offer insights that inspire and challenge us as physicians and scientists to do as much as we can, as quickly as possible, to find solutions for their sight-threatening conditions.” ■

Doris Duke Clinical Research Fellows

Louis K. Chang, M.D., Ph.D. is a Vitreoretinal Clinical Fellow who is originally from Newton, MA. He earned his undergraduate degree in biological sciences from Stanford University, where his research was funded by the Howard Hughes Medical Institute. He went on to earn his M.D. and Ph.D. in neuroscience as part of the medical scientist training program at Washington University School of Medicine.



Louis K. Chang, M.D., Ph.D.

Following an internship at Harbor-UCLA Medical Center, Dr. Chang completed his residency in ophthalmology at the Jules Stein Eye Institute of the University of California at Los Angeles (UCLA), where he was recognized for his excellence in ophthalmic surgery. At Columbia, he is a Heed Fellow with sponsorship from the Heed Ophthalmic Foundation.

Dr. Louis Chang works closely with Stanley Chang, M.D., William Schiff, M.D. and Gaetano Barile, M.D., seeing retinal patients and performing vitreoretinal surgery. He specializes in medical and surgical treatment of diseases of the retina and vitreous. "I am extremely fortunate to have the opportunity to learn from some of the best and brightest minds in the field and to work with the outstanding residents and staff at Columbia," says Dr. Chang.



Ankoor Shah

Three talented medical students from Columbia's College of Physicians and Surgeons are taking a year from their medical studies to conduct vision research under department faculty with support from the Doris Duke Clinical Research Fellowship Program.

Joann Kang, from Denver, CO, earned her undergraduate degree in biology with honors in research at Cornell University. Ms. Kang's previous research experiences have included the study of cysteine regulation at Cornell University; novel cancer therapies at the National Cancer Institute; and glioma potentiation at Columbia through a National Institutes of Health (NIH) Fellowship Training Grant. The American Medical Student Association recently honored her with the best clinical research award for the research she conducted in the Department of Ophthalmology.

Ms. Kang works closely with Richard Braunstein, M.D. and Rando Allikmets, Ph.D. on the development of a screening tool for corneal dystrophies and keratoconus using genotyping microarray technology. This genetic disease "chip" will allow simultaneous screening of all currently known disease-associated genetic variants in patients and in the general population, facilitating prospective diagnosis and future treatment options.

Ankoor Shah, from Niskayuna, NY, completed his undergraduate work at the University of Pennsylvania with a dual major in healthcare management and biology. At Columbia, he worked with Richard Braunstein,

M.D. on an NIH Training Fellowship and later with Lucian Del Priore, M.D., Ph.D., and received a Dean's Day Research Award. Under the mentorship of Dr. Del Priore, Mr. Shah is now

developing a mathematical model that applies Lineweaver-Burke plots from the field of biochemistry to disease processes in age-related macular degeneration (AMD). These models have been effective in predicting the rate of visual decline/gain with various treatments and comparing the success rates of these treatments in the

absence of clinical trial data. Concurrently, he is also designing new mathematical models to compare duration of action for Avastin and Lucentis, two leading anti-VEGF monoclonal antibody therapies available for the treatment of exudative "wet" AMD.

Steven Williams, a native of Miami, FL, completed his undergraduate degree at Harvard University in biochemical sciences before starting medical school at Columbia. With support from both the Doris Duke

Charitable Foundation and the Starr Foundation, Mr. Williams participates in clinical research on applications of telemedicine and retinal imaging for diagnosis of retinopathy of prematurity (ROP). His research focuses on the feasibility and accuracy of ROP diagnosis and computer-assisted analysis using retinal photography. Under the mentorship of Michael Chiang, M.D., M.A. and John T. Flynn, M.D., Mr. Williams is also involved in basic science research on ROP and is engaged in patient care experiences in the pediatric ophthalmology clinic. Following his final year of medical school, he plans to pursue residency training in ophthalmology. ■



Joann Kang



Steven Williams



A Legacy in Bloom

Mrs. Madelyn Medeot loved flower arranging, reading and dancing and had a soft spot for animals.

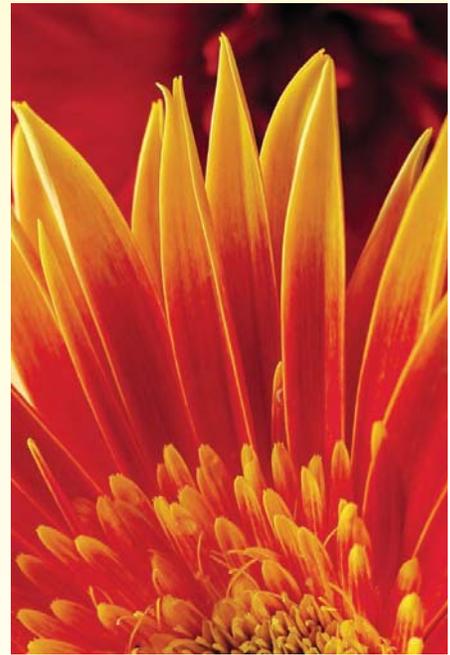
A longtime Westchester resident who worked as a legal secretary for the county's Department of Probation, Mrs. Medeot was also a devoted wife and mother, and enjoyed traveling in the United States with her husband Louis and son Mark.

Mrs. Medeot struggled for years with diabetes and related eye problems that dampened her enjoyment of these activities. After losing sight in one eye, she sought out Dr.

Chang, who worked to save vision in her second eye. Predeceased by both her husband and her son, Mrs. Medeot was so grateful for the care she received at the Edward S. Harkness Eye Institute, that she generously chose to name the Department of Ophthalmology in her will to create a bequest "for the study of diabetic blindness."

Sadly, Mrs. Medeot passed away in November 2007 at the age of 84. Yet her generosity and kindhearted compassion for those facing vision-robbing complications of diabetes live on through the important vision research her legacy is now

funding. While she may have lost most of her eyesight, her insight into how her good fortune and thoughtful estate planning could make a difference for others is truly extraordinary. ■



For more information about how a planned gift or bequest to the Department of Ophthalmology may benefit your estate plan, please contact Jane Heffner, Director of Development, at (212) 305-7827.

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Refractive Surgery/LASIK: 212.326.3320

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Viewpoint



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