Joan Schneeweiss was first diagnosed with Stargardt disease, a form of juvenile macular degeneration, at the age of 18. Turning to the Edward S. Harkness Eye Institute, she underwent rigorous testing with John H. Dunnington, M.D. and later with Charles Campbell, M.D., Ph.D., both former chairmen of the Institute, but was told that there was little that could be done to preserve her vision.

A few years ago, Mrs. Schneeweiss came to Stanley Chang, M.D., knowing of his expertise in retinal disorders. A simple genetic screening confirmed the clinical diagnosis and introduced her to the exciting research into causes and treatments for Stargardt and other retinal diseases taking place in the Department of Ophthalmology.

“Our relationship with Columbia goes back some 40 years,” notes Mrs. Schneeweiss. In the 1970s, Mrs. Schneeweiss and her husband Michael, both native New Yorkers, became involved with Columbia philanthropically when they collaborated with several other couples to establish the Babies Heart Fund at the Babies and Children’s Hospital of New York (now the Morgan Stanley Children’s Hospital of New York-Presbyterian). Later, they established the Joan and Michael Schneeweiss Center for Adult Congenital Heart Disease to address the specialized needs of adult congenital heart disease patients.

On July 10, “Superman” and his team paid a visit to the Edward S. Harkness Eye Institute for the grand re-opening of the newly renovated Children’s Eye Clinic, which was closed after a devastating flood in 2004. David Wicklow, the New York Presbyterian architect who supervised the renovation, along with several members of the construction crew who worked tirelessly to complete the job on time, received “Superman” t-shirts at the ribbon-cutting ceremony in recognition of their efforts. The light-hearted celebration and fun didn’t stop with the Superman t-shirts. Millie Soto, R.N., the charge nurse who oversees the Clinic’s operations, arranged for refreshments, balloons, face painting and medals for the young patients in attendance.

“For three years, we have been struggling with the lack of available space to treat the 2,500 young people we see annually in the Children’s Eye Clinic,” said John T. Flynn, M.D., Chief of the Division of Pediatric Ophthalmology, who conducted the ribbon-cutting ceremony with assistance from Amilia Schrier, M.D., Hugh Moss, M.D. and Michael Chiang, M.D., M.A. During the time that the clinic was closed, doctors saw their young patients out of one examining room borrowed from the Institute’s JJT Eye Clinic, which already serves more than 26,000 patients each year. “Now, thanks to a very generous gift from an anonymous donor who matched the contributions of New York-Presbyterian Hospital and the Department of Ophthalmology, we have a beautifully renovated space, an additional exam room and the best state-of-the-art ophthalmologic equipment in any children’s eye clinic I’ve worked in during my 40-year career.”

The renovated Children’s Eye Clinic re-opened on July 10. L to R: John T. Flynn, M.D., Amilia Schrier, M.D., Hugh Moss, M.D., Millie Soto, R.N., David Wicklow
of adults who have been treated for congenital heart diseases since childhood. After meeting Dr. Chang and Rando Allikmets, Ph.D., Mr. and Mrs. Schneeweiss decided to turn their attention to ophthalmology.

"Joan and I have been married for over 50 years, and I’ve observed her struggle with this disease. She’s very gallant and courageous," adds Mr. Schneeweiss. "We both felt it was very important to support retinal research for the next generation and generations to come. We just want to help others avoid suffering with degenerative vision loss."

Mrs. Schneeweiss explains, "We decided to create the Schneeweiss Research Fund because there are so many people struggling with retinal disorders. I know a lot of older people who have age-related macular degeneration, and it is quite burdensome." Rando Allikmets, Ph.D. and Stephen H. Tsang, M.D., Ph.D., are the two scientists whose research is funded in part by the Schneeweiss Research Fund. "Their work sounds both promising and exciting." 

Stargardt Disease Gene Therapy Nearing Clinical Trials

In 1997, Rando Allikmets, Ph.D. broke the genetic “secret code” of Stargardt disease. His discovery of the ABCR (ABCA4) gene launched several new research efforts into the molecular genetic fundamentals of Stargardt disease, age-related macular degeneration (AMD), cone-rod dystrophy and retinitis pigmentosa.

"Over 500 mutations in ABCR underlie a continuum of retinal diagnoses, ranging from Stargardt disease and AMD, to retinitis pigmentosa," Dr. Allikmets explains. Working with a multicenter study team, he discovered two additional genes that are responsible for nearly three-quarters of all AMD cases, and Dr. Allikmets has created microchip-based sequencing and genotyping for fast and effective screening for multiple retinal diseases.

With support from the Foundation Fighting Blindness and the Schneeweiss Research Fund, Dr. Allikmets and his team (including Janet Sparrow, Ph.D. and Peter Gouras, M.D.) have now developed a potential new gene therapy for Stargardt disease that delivers a normal gene to the eye via lentiviral vectors. A lentivirus is one type of virus useful for gene therapy because the undesirable contents can be removed and the remaining virus shell is used as a transporter vehicle for the replacement gene.

In preclinical research, Dr. Allikmets and his team showed that delivery of a normal ABCA4 gene to the retinas of mice bred with the genetic modification of Stargardt disease successfully integrated within 20-30% of all photoreceptors, with a drastic reduction in A2E accumulation. A2E is a component of lipofuscin, and has been implicated in photoreceptor degeneration and resulting vision loss. Additional research in larger animal models has demonstrated the effectiveness of the lentiviral delivery method. Dr. Allikmets and his team are now collaborating with Oxford BioMedica, a biopharmaceutical company, to launch a Phase I human study of the StarGen® gene therapy for Stargardt disease, which may occur as early as 2008.

"We began the StarGen project five or six years ago with a grant from the Foundation Fighting Blindness. Mr. and Mrs. Schneeweiss added their support three years ago, which more than doubled the resources available for the project and helped us to expand at a crucial time," said Dr. Allikmets.

In this issue of Viewpoint, we are delighted to feature Joan and Michael Schneeweiss, steadfast Columbia donors whose support has co-funded the development of a new gene therapy for Stargardt disease with Rando Allikmets, Ph.D., and stem cell research for retinitis pigmentosa with Stephen H. Tsang, M.D., M.D. We also highlight the research endeavors supported by the Eye Surgery Fund, established by Daniel B. Kirby, M.D., a world-renowned cataract surgeon in his day and the deceased father-in-law of Dukes Wooters, a cherished member of our Advisory Board. Gifted vitreoretinal surgeon and physician William M. Schiff, M.D. is profiled in the Faculty Spotlight.

Finally, we celebrate the re-opening of our Children’s Clinic and fondly remember Arthur Gerard DeVoe, M.D., department chairman from 1959-1974, who passed away in September at the age of 98.

With renewed thanks and appreciation for your generosity to the Department this year, I extend my deepest thanks on behalf of the physicians, scientists, nurses, staff and patients of the Edward S. Harkness Eye Institute. Your gifts provide the foundation for the extraordinary research and clinical achievements of our faculty and the exceptional outcomes our patients enjoy. I am honored to have your trust and partnership as we work together toward preserving vision. Again, thank you most sincerely for all that you do.

With best wishes to you and yours for a joyous holiday season and happy and healthy New Year.

Stanley Chang, M.D.
K.K. Tse and Ku Teh Ying Professor
Edward S. Harkness Professor
Chairman, Department of Ophthalmology
Philanthropic Focus:
Kirby Legacy Thrives at Columbia

"From 1928 to his death in 1953, Daniel B. Kirby, M.D. was recognized as the foremost cataract surgeon in the world," states Dukes Wooters, speaking of his late father-in-law, the renowned New York ophthalmologist for whom New York University’s Eye Institute is named.

Mr. Wooters is a longtime member of the Department of Ophthalmology’s Advisory Board at Columbia. The retired founder and CEO of Cotton Incorporated and recently retired executive at Galen Associates, a private equity firm, continues, "He had great skill in his hands, and traveled the world teaching his techniques to his colleagues." Modern cataract surgery techniques involve removing the diseased lens via a slit in the cornea and replacing it with a new intraocular lens. However, during Dr. Kirby’s era, surgeons with steady hands had to precisely excise the film of the cataract from the eye with a scalpel.

According to Mr. Wooters, the widower of Dr. Kirby’s daughter Betty, his father-in-law was a great man who was devoted to both his family and his patients. In fact, many of Dr. Kirby’s patients were so grateful for his compassion and skill in restoring clear vision that they wanted to return the gift, hence the birth of the Eye Surgery Fund. As the Fund’s President, Mr. Wooters is joined on the board by many family members, including Billie and Peter Mullen, Sister Joan Kirby and four of Dr. Kirby’s grandchildren.

For the last nine years, the Eye Surgery Fund has been supporting the work of three Eye Institute faculty members and a Kirby Fellow. This year, the Fund is sponsoring the research of Gaetano Barile, M.D., Konstantin Petrukhin, Ph.D. and Stephen H. Tsang, M.D., Ph.D. [see Stargardt Sters, cover], as well as Kirby Fellow, Nuno Gomes, M.D.

Dr. Barile’s research focuses on the role that hyperglycemia, the state of elevated blood sugar that occurs in patients with diabetes mellitus, plays in the development of diabetic retinopathy and other related complications. Hyperglycemia accelerates the formation of advanced glycation end products (AGEs), a byproduct of metabolic processes. RAGE, a cell-surface receptor, binds with AGEs and a class of pro-inflammatory mediators. In patients with diabetes, AGEs accumulate and ultimately bind to their receptors, triggering cellular dysfunction and amplifying these detrimental effects by also increasing cellular receptor expression in a vicious cycle.

Dr. Barile and his research team have created a genetic mouse model that mimics the neural and vascular changes of diabetic retinopathy in humans. Even in mice with early nonproliferative diabetic retinopathy (NPDR), they have observed increased RAGE axis activity in the retina, particularly along the vitreoretinal interface.

Importantly, they identified the Müller cell, a structural cell that contributes to critical physiologic functions in the retina, as the native cell expressing RAGE. Their experiments suggest that RAGE damage in the retina impairs retinal neuronal function, perhaps even before lesions in the retinal vessels (a clinical indicator of diabetic retinopathy) can be detected. This new understanding of the havoc that hyperglycemia can wreak on the retina has important implications for persons with diabetes struggling to control their blood sugar levels.

Dr. Barile’s study also links hyperlipidemia (elevated levels of cholesterol and other lipid fats in the bloodstream) to increased severity of diabetic retinopathy. “We observed that the classic anatomic retinal lesions of nonproliferative diabetic retinopathy developed at the highest rate in mice with elevated blood sugar and cholesterol. These findings strongly suggest that high cholesterol can accelerate the progression and severity of diabetic retinopathy in humans,” he cautions. He hypothesizes that disrupting the RAGE axis may reduce neurovascular damage, offering an important therapeutic target for intervention.

Since joining the Department last year, Dr. Petrukhin, the former head of ophthalmic research at Merck Research Laboratories, is developing small molecule treatments for age-related macular degeneration (AMD).

“RNR is the drug target for the treatment of AMD and other diseases that involve the degeneration of photoreceptor cells,” says Dr. Petrukhin. His line of research is focused on screening thousands of small molecule compounds (“agonists”) for their ability to bind to retina-specific nuclear receptor (RNR) in much the same way as a key fits into a lock. Once identified, a successful agonist would be further refined into a medication that will interact with RNR to halt photoreceptor degeneration. [See Viewpoint Fall 2006/Winter 2007.]

Dr. Gomes, a Portuguese native, received his medical degree from Instituto de Ciências Biomédicas Abel Salazar in Porto, Portugal. Following two years as a general medical resident at Porto’s Hospital de Santo António, he began a four-year residency in ophthalmology at Hospital de São João, also in Porto, specializing in vitreoretinal surgery and medical retina, as well as in cataract surgery.
Loiacono Named Administrative Director

The Department of Ophthalmology is pleased to welcome Salvatore Loiacono, Jr. as its new Administrative Director. Originally from Brooklyn, NY, and now residing in New Jersey, Mr. Loiacono holds an undergraduate degree in health care administration from St. John’s University and is pursuing a graduate degree in public administration at Baruch College with a focus on health care policy. His impressive career as a health care administrator began at Mount Sinai Medical Center in New York City and progressed to Jersey Shore University Medical Center in Neptune, NJ, where he served as Department Administrator for Obstetrics/Gynecology & Surgery.

“One of the most significant challenges in health care administration is balancing multiple missions while maintaining a break-even operating margin,” explains Mr. Loiacono, whose business aptitude and passion for health care management surfaced during his undergraduate years and early in his career under mentorship from a professor and colleagues. “Even as federal funding and reimbursement from managed care insurers continue to decline, the Department of Ophthalmology remains committed to our three-pronged mission: cutting-edge vision research, stellar medical education and superb patient care. I believe it is important to provide high quality health care for everyone. The challenge of fulfilling these objectives with limited resources means we must look for efficiencies where we can; we also rely more on the tremendous generosity of our donors.”

“Sal brings a sophisticated combination of experience and business acumen to this position,” notes Stanley Chang, M.D. “He is sensitive to cultural, political and professional diversity and recognizes that a unified team can accomplish more than a group of individuals.”

“I believe it is important to provide high quality health care for everyone. The challenge of fulfilling these objectives with limited resources means we must look for efficiencies where we can; we also rely more on the tremendous generosity of our donors.”

Salvatore Loiacono, Jr.

Faculty News

Ophthalmology residents honored Frantz Lerebours, M.D., Instructor in Clinical Ophthalmology and Associate Attending Physician at Harlem Hospital, at a luncheon in June for his dedicated service in teaching ophthalmic surgery to residents of the Edward S. Harkness Eye Institute. Dr. Lerebours, a board certified ophthalmologist, holds a medical degree from the Université d’Etat d’Haiti and completed his residency at Harlem Hospital. He joined the Columbia faculty and Harlem Hospital’s attending staff in 1986, following fellowships in retina and vitreous at Beth Israel Hospital and Mount Sinai School of Medicine.

Stephen H. Tsang, M.D., Ph.D., Assistant Professor of Clinical Ophthalmology and the Joel Hoffman Scholar, is the recipient of the 2007 Foundation Fighting Blindness Career Development Award for a project titled, “Stem Cell Therapy for Early Onset Retinal Dystrophy in an Animal Model.” Dr. Tsang is investigating how stem cell-based therapy can potentially restore vision in retinitis pigmentosa by replacing diseased retinal cells with stem cells that will integrate with remaining host cells.

Ilyas Washington, Ph.D., Assistant Professor of Ophthalmic Science and the Michael Jaharis Scholar, received a prestigious Young Investigator Award from the Office of Naval Research to evaluate the effectiveness of his laboratory-developed chlorophyll analogs in enhancing near-infrared vision in animal models. He also received a grant from the International Retinal Research Foundation to study the ability of special vitamin A analogs in slowing the formation of lipofuscin in animal models as a strategy to retard the progression of AMD.

It is an honor and a privilege to work with the physicians and team members here at the Edward S. Harkness Eye Institute – the faculty, staff and leadership team are just a phenomenal group of people,” Mr. Loiacono says. “I really enjoy coming to work and am excited about my future here at Columbia University Medical Center.”

Salvatore Loiacono, Jr.
2007 Employee of the Year

Patients at the Flanzer Eye Center might recognize Megan Ann Smyser as one of the kind, smiling ophthalmic technicians who screens and conducts vision tests for patients before they are seen by their ophthalmologist. Ms. Smyser, a transplanted New Yorker who grew up in a military family, initially intended to pursue optometry, but fell in love with ophthalmology at Columbia six years ago. A self-described “people-person,” Ms. Smyser was recently named “Employee of the Year” for her hard work, expertise and consistent efforts to create a patient-friendly environment.

“This new employee award program is designed to recognize team members who exceed expectations,” says Salvatore Loiacono, Administrative Director. “Megan works hard to provide patients with the best experience possible. Physicians, patients and team members always speak highly of her work ethic and technical clinical judgment. We are proud to have her as a valued member of our team.”

Congratulations to Megan Smyser on a job well done!

Appointments

Michael Chiang, M.D., M.A.
named the Herbert Irving Assistant Professor of Ophthalmology and Biomedical Informatics

Howard Fine, M.D.
named the Helen and Martin Kimmel Assistant Professor of Clinical Ophthalmology

Pamela Gallin, M.D.
promoted to Clinical Professor of Ophthalmology and Pediatrics

Kirby Legacy Thrives at Columbia continued from page 3

Now the Kirby Fellow at Columbia, he is collaborating with several faculty members on a number of research efforts, including animal models of retinal degeneration, retinal function in patients with Stargardt disease and environmental factors associated with the formation of a macular pucker.

“The Kirby Fellowship is providing me with unparalleled opportunities to participate in both clinical and basic science research,” notes Dr. Gomes. “I feel very lucky and honored to work closely with Dr. Chang and the other faculty members. These are some of the world’s finest surgeons and physician-scientists. I am thrilled to have this opportunity and grateful to Mr. Wooters and Dr. Kirby for their generosity.”

Mr. Wooters is a staunch supporter of Dr. Chang’s leadership of the Edward S. Harkness Eye Institute, as well as a grateful patient himself. “Dr. Chang restored my eyesight,” says Mr. Wooters, who retired just a year ago at age 89 and stays abreast of current business trends. “There is not a better way to continue Dr. Kirby’s legacy than to support Dr. Chang’s fine faculty in these important research endeavors.”

Kirby Legacy Thrives at Columbia
complex retinal detachments caused by diabetes, trauma, proliferative vitreoretinopathy (PVR), and other medical conditions. Retinal tears and detachments are painless, yet serious and sight-threatening conditions that require precise, timely and skilled surgical intervention to preserve vision. Many of Dr. Schiff’s patients have been referred to him by other retina specialists who know of Columbia’s and his reputation for success in treating difficult cases. “In many of these patients, it is not realistic to expect that we will be able to restore 20/20 vision,” notes Dr. Schiff soberly. “Rather, we hope the patients can recover ambulatory vision, which is enough vision to help them get around independently. Even with this limited achievement, patients are very grateful. This is especially true when patients have turned to me at a point where they understand that there is a risk of blindness. In those circumstances, the ability to recover some vision is indeed very meaningful.”

Dr. Schiff also sees younger patients who have experienced severe trauma to the eye. “With these patients in particular, we have had some incredible successes in restoring vision when others have said that such an outcome was not possible. Often these are our most grateful patients—they are young and desperate to get their vision back,” he says. “Every situation is different and every eye is unique. We frequently modify conventional techniques to confront the immediate challenge to restore the patient’s vision.” He notes that Columbia has some of the best surgical outcomes in the country with complex retinal detachments. While studying history as an undergraduate at Cornell University, Dr. Schiff discovered his passion for medicine through a part-time campus job with an orthopedic surgeon who treated athletes. “I really enjoyed shadowing the doctor, and I became totally captivated by the possibilities of medicine. I saw athletes with injuries turn the corner towards health and return to the field,” he says.

Dr. Schiff went on to earn his medical degree from New York University School of Medicine and complete a medical internship at St. Luke’s Hospital in New York City. “For a brief time, I thought I would go into orthopedics,” he explains. “But I was fascinated by the human eye and preferred the fine motor skills and movements necessary in eye surgery.” Dr. Schiff completed his residency in ophthalmology at The New York Eye and Ear Infirmary under Joseph Walsh, M.D., whom he credits as an important mentor. In 1994, he began a fellowship in vitreoretinal surgery and diseases under Dr. Chang at New York Hospital/Cornell Medical Center, later moving to Columbia with him. “Stan Chang is an outstanding mentor,” says Dr. Schiff with genuine admiration and appreciation.

“Allikmets. “In our mouse models of Stargardt disease, the accumulation of lipofuscin (A2E) is very high. After the gene is delivered to the correct cells by injection, A2E levels decrease to very high. After the gene is delivered to the cor-”

Stem Cell Research

Retinitis pigmentosa (RP) is the most common cause of inherited blindness, named for the increased pigmentation that appears in the areas where retinal cell death occurs during late manifestation of the disease. Initial symptoms of RP include night blindness, due to the death of rod photoreceptor cells, resulting in “tunnel vision.” In later stages, RP destroys cone photoreceptor cells in the macula, responsible for fine central vision. “We believe that cell transplantation in the human retina has the potential to restore lost vision and provide treatment for advanced stages of retinal degeneration featuring signifi-
“cant photoreceptor neuronal loss,” says Dr. Tsang, noting that a major obstacle for this approach is the ability to produce sufficient patient specific photoreceptor cells for transplantation. Adult retinal stem cells reside in the ciliary body (the part of the human eye that changes the lens shape to focus light) and are one potential source of photoreceptors. However, significant progress remains to be made in coaxing adult stem cells to differentiate into photoreceptors. Columbia colleague Peter Gouras, M.D. successfully employed cell transplantation and gene therapy in the 1990s to stop the progression of RP in rat and mouse models. However, gene replacement therapy, such as the StarGen approach, can only be applied before the target cell degenerates, limiting the effectiveness of this approach for those with severe retinal degeneration. In contrast, stem cell transplantation has the potential to restore lost vision and provide treatment for advanced stages of retinal degeneration even in cases of significant photoreceptor and retinal pigment epithelium (RPE) loss. “We fully support stem cell research,” remarks Mrs. Schneeweiss, whose advanced Stargardt disease might improve if Dr. Tsang’s stem cell approach proves successful. The Schneeweiss Research Fund is especially important to Dr. Tsang at a time when federal grant funds for stem cells research is lacking. Dr. Tsang notes that future applications may include patient-specific stem cells obtained from fine-needle aspiration of their ciliary bodies in the operating room. He continues, “Based on our findings, we foresee the ability to manipulate patients’ own stem cells to cure their specific disease, without risk of rejection.”
The Department of Ophthalmology at Columbia mourns the loss of Arthur Gerard DeVoe, M.D., who passed away on September 19 in Gladwyne, PA, at the age of 98. Dr. DeVoe, a distinguished academic ophthalmologist, led the Department of Ophthalmology and the Edward S. Harkness Eye Institute as Chairman from 1959-1974, and was the first to hold the title of Edward S. Harkness Professor of Ophthalmology. Prior to his tenure at Columbia, Dr. DeVoe, a graduate of Phillips Exeter Academy, Yale University and Cornell University Medical College, served as Chairman and Professor of Ophthalmology at what was then known as New York University Post-Graduate Medical School.

Dr. DeVoe was widely regarded by the ophthalmic community as a gifted and compassionate physician and surgeon, world-renowned for his expertise in corneal and anterior segment diseases. In 1964, Dr. DeVoe established the Institute’s Corneal Clinic to better meld the expertise of basic scientists and clinicians into practical application. Such devices as the keratoprosthesis lens and wide field specular microscopy were examples of these collaborations. He also expanded resident training opportunities by effecting a merger with the Bronx VA Hospital’s eye service. As the driving force behind the construction of the Institute’s research wing for basic and clinical research, completed in 1968, he cemented the Institute’s commitment to vision research and continued to recruit world-class scientists with the intent of deepening the understanding of eye disorders and developing new vision-saving treatments.

Dr. DeVoe was chairman of the American Board of Ophthalmology from 1964-1966 and a member of the Board of Governors of the American College of Surgeons and the Pan-American Association of Ophthalmology. An international lecturer, he also served as associate editor of the Archives of Ophthalmology.

Joan Gilson, who established the Arthur Gerard DeVoe Lectureship at Columbia in 1999, remembers Dr. DeVoe fondly. “As a patient, I just liked him so much. He never rushed and always showed genuine concern for his patients. When he operated on my eyes, I had all the confidence in the world,” she says with warmth and admiration. “To me, his care represents the epitome of how a doctor would treat his patients. Even though he had many important professional obligations, I always knew I could call him at any time with a question or concern.”

“Gerry DeVoe leaves a great legacy of professionalism, integrity and clinical and scholarly excellence that has and will continue to set high standards for the Eye Institute,” states Stanley Chang, M.D. “He made extraordinary contributions to ophthalmology and vision science. We will dearly miss our beloved and respected colleague.”