



Giving Back for the Gift of Sight: Barbara and Donald Jonas Support New Stem Cell Research

Philanthropy is one of the most powerful ways for patients to thank physicians for their care. But the major gift that Donald and Barbara Jonas have dedicated to support the research of Stephen H. Tsang, M.D., Ph. D. is more than an expression of gratitude. It is an investment in the likelihood that within a few years, Dr. Tsang's groundbreaking stem cell research will lead to a cure for degenerative retinal diseases, especially the one affecting Mr. Jonas.



Barbara and Donald Jonas

For the past decade, Donald Jonas has been living with Late Onset Retinal Dystrophy (LORD), a rare hereditary condition that destroys the cells responsible for peripheral vision and depth perception. "I can see looking ahead, but if I'm on the golf course and there's a ball six inches to the

side of my shoe, I can't see it," said Mr. Jonas, a retired retail executive who, together with his wife Barbara, has a long history of philanthropic involvement with the arts, education, nursing and medical causes.

When he learned of Dr. Tsang's research for a therapy to treat the disease that has been destroying his sight, he knew he had to help. He was determined to do everything he could to spare others from the progressive vision loss that has marked the past decade of his life.

"This is something that I feel strongly about, especially when I think of younger people who could possibly have a cure in their lifetime," Mr. Jonas said. "It is gratifying to

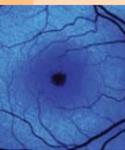
▶ *continued on page 3*

INSIDE

View from the Chair **2**

Science Insight **3**

Using the Retina's Natural Fluorescent Light to Measure and Treat Disease



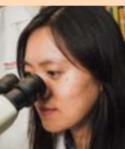
Visionaries & Luminaries **4**

Stephen Tsang, M.D., Ph.D. Manipulates Genes to Treat Eye Disease



Faculty Spotlight **6**

Ophthalmological Research in the Era of Sequestration



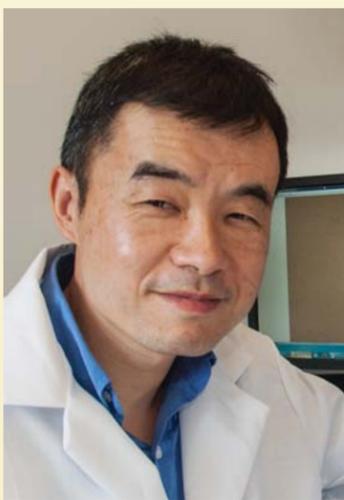
In Memoriam **8**

Louis Flanzer



Xin Zhang, Ph.D., Genetics Expert, Joins Department's Research Staff

One thing that the distinguished research scientist Xin Zhang, Ph.D. will not be doing in his new post as Associate Professor of Ophthalmic Sciences in Ophthalmology, Pathology & Cell Biology, is tether himself to the laboratory. Indeed, Dr. Zhang plans to conduct his award-winning research on the genetics of eye disease within the Department's clinical program, with the hope of bridging the gap between laboratory science and clinical care.



Xin Zhang, Ph.D.

In this era of translational medicine, Dr. Zhang, like a growing number of scientists, is working to give his

research more immediate clinical applicability: to pave a path from the bench to the bedside. "I hope to use the clinical experience of my new

colleagues to stimulate research, so it will have greater impact and elevate the level of our work," he said.

Jack Cioffi, M.D., Chairman of the Department, views recruitment of scientists such as Dr. Zhang as imperative to the success of the department.

"The close collaboration between clinicians and scientists provides our best chance to prevent, treat and cure complex diseases of the eye," said Dr. Cioffi.

"The Harkness Eye Institute has a long history of innovative clinical research, and scientists like Dr. Zhang will build upon this tradition."

Dr. Zhang earned his undergraduate degree in physics from Beijing University in 1991. After beginning his graduate studies in physics at The Johns Hopkins University, he switched to biology, in which he eventually received his doctorate in 1998. He found the manipulation of genes, which he had begun exploring during his early days as a graduate student, more satisfying than studying E. coli on an agar plate. In the early 2000s, during his post doctoral fellowship in the department of medicine's division of genetics at Harvard Medical School, he became particularly interested in the manipulation of genes from the eye—

mouse eyes, to be exact—and, subsequently, in the genetic underpinnings of eye disease.

The work was especially exciting, because the changes that resulted from gene manipulation were easily visible. "Looking at the eye, you can really tell something is happening," Dr. Zhang said. "When you manipulate genes within the eye's lens, what frequently happens is the development of a cataract. Clearly, you can see white stuff in the lens. So, you can have a visual appreciation of what you're doing." In humans, the same is true. Small genetic changes can lead to big changes within the structures of the eye. "You have a single nucleotide change in the human genome that consists of three billion DNA base pairs and, as a consequence, patients may not have an iris."

After completing his fellowship at Harvard, Dr. Zhang's career took an opportune turn: In 2003, Kenneth Cornetta, M.D., the new chairman in

▶ *continued on page 2*

Dear Friends,

As I write this, government agencies across the country are cutting a total of \$85 billion from their budgets, in compliance with the mandatory, across-the-board spending cuts known as sequestration. Among these agencies is the National Institutes of Health (NIH), the lifeblood of academic research.

Research is at the core of every great ophthalmology department, and ours is no exception. The research coming out of Columbia Ophthalmology is breaking important ground in the understanding and treatment of eye disease. During the past few years, our faculty has been using mouse models to explore the etiology of conditions such as retinitis pigmentosa, age-related macular degeneration, and Stargardt disease. By manipulating genes in these mice, which are genetically similar to humans, our scientists are working to understand why some people acquire eye disease, and find new ways to treat it.



This translational approach to research—blending scientific inquiry with clinical evidence—drives our Department. World-renowned geneticist Xin Zhang, Ph.D. joined us specifically because he wanted to work with our clinical faculty, while continuing his award-winning research on the genetics of eye disease. Stephen Tsang, M.D., Ph.D., another distinguished scientist who is “bringing the bench to the bedside,” is working to prevent blindness by using gene therapy and stem cell transplantation to treat a variety of inherited degenerative retinal diseases in mice, including retinitis pigmentosa and late onset retinal dystrophy.

Dr. Tsang is the embodiment of the clinician-scientist, but this model doesn't always occur in one person. The Department is full of partnerships among clinicians and scientists, who exchange ideas and collaborate on research. There is perhaps no better example of this type of collaboration in the country than the retinal genetics group developed under the guidance of Stanley Chang, M.D. Dr. Chang, an accomplished clinician-scientist in his own right, saw the need for innovative genetic research aimed at retinal degenerations. Through collabora-

tions with investigators, such as Rando Allikmets, Ph.D. and Janet Sparrow, Ph.D., clinician-scientist teams were created where vexing clinical questions were addressed both in the clinic and in the laboratory. This collaborative model will remain the focus as we expand our research capabilities in the future.

Such collaboration makes the Department exciting not only for senior faculty, but for the students and postdocs they mentor. The recent loss of \$1.7 billion from the NIH budget threatens the livelihood of our faculty, their innovations, and their ability to train young scientists. Just 15 years ago, 40% of NIH grants were funded; today, it's one in ten. Now, philanthropic dollars matter more than ever.

Indeed, we owe our deep appreciation to supporters like Donald and Barbara Jonas, whose generosity has led to state-of-the-art facilities and programs throughout Columbia's medical center. Thanks to the Jonases' most recent gift, Dr. Tsang has the support he needs to move his stem cell research to clinical trials in a few years.

We are also profoundly grateful to Colbey Plutzer, a courageous and caring high school senior from Syosset, Long Island, who received a diagnosis of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) when she was just 11 years old. In gratitude to Dr. Chang, who successfully halted the disease, Colbey has launched a bold fundraising campaign for research into a cure for the disease that nearly destroyed her sight.

The tremendous generosity of our donors, including the late Louis Flanzer, who with his wife Gloria funded the Flanzer Eye Center and the Flanzer Vision Care Center, makes our work possible. As the NIH tightens its belt, our reliance on such generosity will grow, so we can continue to translate cutting-edge research into pioneering patient care.

Sincerely,

A handwritten signature in blue ink that reads "Jack Cioffi".

G.A. (Jack) Cioffi, M.D.
Jean and Richard Deems Professor
Edward S. Harkness Professor
Chairman, Department of Ophthalmology

Genetics Expert Joins Department's Research Staff *continued from page 1*

the department of medical and molecular genetics at the Indiana University School of Medicine, appointed Dr. Zhang as his first recruit. Two years later, Dr. Zhang became a primary investigator at the School's Stark Neuroscience Institute. By 2011, he was the David D. Weaver Investigator in genetics. And, by the next year, he was an associate professor in the department of biochemistry and molecular biology.

The research that Dr. Zhang pioneered at Indiana University—and plans to continue at Columbia—has earned him wide recognition, as well as numerous awards from prestigious funders, such as the Ralph W. & Grace M. Showalter Research Trust Fund, the March of Dimes, and the American Diabetes Association. It focuses on the developmental aspects of eye disease, disorders of the lens, and congenital eye conditions. Dr. Zhang uses the eyes of genetically engineered mice for his studies, since there is a powerful genetic similarity

between mice and humans. His work involves manipulating and, in some cases, disabling genes to create disorders such as microphthalmia, also known as small eye; coloboma, a condition that causes a hole in the eye; or, aniridia, in which the eye has no iris. One of Dr. Zhang's primary goals is to understand the genetic mechanisms behind these conditions. By manipulating mouse eye genes, he hopes to determine how these eye diseases develop in mice and whether similar genetic disruptions in humans would lead to the same diseases. “So far, we're just extrapolating,” he said. “Given the clinical opportunities at Columbia and the immense needs of patients with eye disease, these are possibilities we can explore.”

In addition to his ongoing research, Dr. Zhang has brought to Columbia his research team, which includes three doctoral students and two postdoctoral fellows from Indiana University, as well as two R01 research grants from the National Eye

Institute. Now, at this stage in his academic career, he is interested in forming closer ties with other vision researchers at Columbia Ophthalmology. He especially looks forward to working closely with its clinicians, to better integrate his research into understanding how certain genetic mechanisms contribute to certain eye diseases. For example, he plans to compare certain congenital symptoms in patients with those from his mouse model to predict the development of human eye disease. He also plans to sequence patients' genes to see if they reveal the characteristic changes that point to the cause of disease.

Dr. Zhang's goal is to connect genetic insight with therapeutic response: to translate science into treatment. “In a clinical setting, I am looking for inspiration,” he said. “By interacting with clinicians, I hope to see problems as they exist. The most important information will come from the patients.” ■

Science Insight:

Using the Retina's Natural Fluorescent Light to Measure and Treat Disease

Researchers at Columbia Ophthalmology are breaking new diagnostic ground by using the natural fluorescence of the retina to identify a variety of eye diseases. Although the technology that detects the retina's ability to generate its own light—its autofluorescence—is not new, quantifying this light and using the resulting measurements to track and characterize the progression of eye diseases is an innovation that Janet Sparrow, Ph.D. and colleagues are pioneering.

“We can use autofluorescence emission to image the retina and see certain features of it,” said Dr. Sparrow, the Anthony Donn Professor of

Ophthalmic Science in the departments of Ophthalmology, and Pathology & Cell Biology. “As we're looking at an image, we can get an idea if there is ongoing disease. We can also monitor changes over time.”

Most objects in the environment are visible because they reflect, as opposed to emit, light. However, the retina—which exists within the eye's back wall, known as the fundus—can generate its own fluorescence.

The retina is composed of layers of cells. The deepest layer is called the retinal pigment epithelium (RPE), and the cells in this layer contain fluorescent compounds. When a blue light from a confocal scanning laser ophthalmoscope excites the fundus, and in doing so, the retina, it triggers the compounds embedded in the RPE, resulting in the emission of a golden fluorescence.

The retina's fluorescence increases with age. It also increases with some retinal diseases. As diseases progress, patterns of fluorescence

may change. However, the presence of fluorescent compounds in the RPE does not necessarily indicate disease. In fact, a certain amount of light-producing compounds in the eye indicates normal visual activity.

Changes in fundus autofluorescence can be used to diagnose disease. For example, in age-related macular degeneration (AMD), one of the most prevalent eye diseases among the elderly, cells in the RPE are among the first to die. Thus, an examination of the RPE in a patient with AMD will reveal areas of

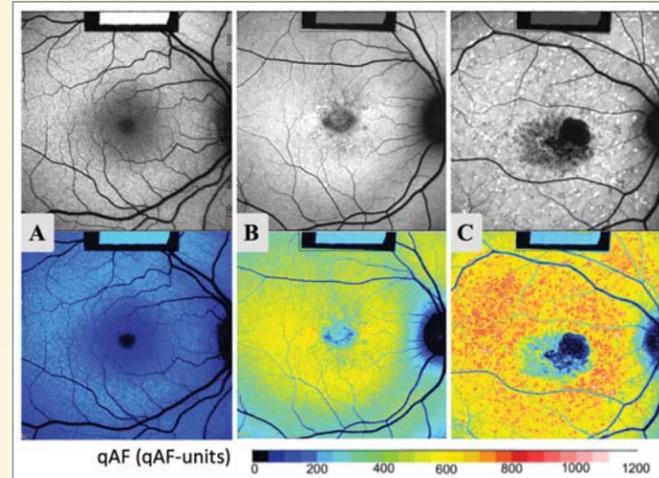
darkness instead of fluorescence. “My lab is looking at why these compounds form, why they exist in greater amounts in some individuals, why they are present with some diseases, and how they may be damaging to the RPE,” Dr. Sparrow noted.

In addition to understanding the formation and alterations of retinal autofluorescence, Dr. Sparrow is researching its quantification. She is using these measurements to compare autofluorescence among patients with and without eye disease.

Co-investigator Rando Allikmets, Ph.D., Research Director of the Harkness Eye Institute, and William and Donna Acquavella Professor in the departments of Ophthalmology, and Pathology & Cell Biology, said, “In order to find a cure for disease, you need a qualitative picture and a quantitative picture—a clear understanding of what the disease looks like at its earliest stages and an estimate of its progression.”

Working with Dr. Francois Delori at Harvard, Columbia investigators began research in this area five years ago, with a study of 277 healthy males and females of various ethnic backgrounds and ages, up to 60 years. They measured levels of autofluorescence in patients' retinas to create a normative data base. Now, they are studying an additional 500 patients with retinal disorders, such as age-related macular degeneration, Best disease and Stargardt disease, and comparing levels of autofluorescence in their retinas with those of the healthy patients. “So far,” Dr. Sparrow commented, “we have examined this second group of patients only once. We are planning to bring them back to do a longitudinal study, to see how autofluorescence intensity might change over time and with age.”

Dr. Sparrow hopes that study results will inform the development of drugs to limit the formation of fluorescence-producing compounds, or at least neutralize their adverse effects. As Dr. Allikmets noted, “In the human eye and the animal model eye, measuring the amount of autofluorescence detects the progression of disease over time, as well as drug efficacy down the road.” ■



Quantified fundus autofluorescence images.

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Giving Back for the Gift of Sight *continued from page 1*

think our contribution may in some way help others from suffering the loss of vision.”

Dr. Tsang, the László Bitó Associate Professor of Ophthalmology, and Pathology & Cell Biology at Columbia University Medical Center, has been testing two promising treatments for degenerative retinal diseases. The treatment that he hopes will ultimately cure LORD involves injecting induced pluripotent stem (iPS) cells, which are generated from human skin biopsies, directly underneath the retinas of five-day-old, genetically engineered mice. Cells that are pluripotent can develop into any type of cell to help rebuild or otherwise aid organs and tissues throughout the body, such as the brain, heart, and even the retina. Dr. Tsang's goal is to use skin cells from LORD patients to cultivate iPS cells, and then to transplant these cells back into the patients. “Because the cells come from the same patient, the hope is that you won't have to worry about rejection,” Dr. Tsang said.

Mr. Jonas proved a willing donor. While undergoing surgery for basal cell carcinoma, he provided a sample of normal adjacent skin tissue for the cultivation of stem cells. The Food and Drug Administration does not yet allow iPS cell transplantation in humans; however, the couple's gift will allow Dr. Tsang to prepare data for human trials. “With the Jonas gift, we are trying to bring the future of medicine closer.”

The Jonases know that a cure for LORD may not arrive in their lifetime. But as Mrs. Jonas said, “We have total confidence in Dr. Tsang. We know he will do excellent work that will benefit untold numbers of patients in the future.”

Nationwide Impact, Columbia Roots

Dr. Tsang's research is one of many projects at Columbia that owe their support to the Jonases' commitment to research, training, and practice needs in today's health

▶ *continued on page 6*

Stephen Tsang, M.D., Ph.D. Manipulates Genes to Treat Eye Disease

Stephen Tsang, M.D., Ph.D., the László Bitó Associate Professor of Ophthalmology, and Pathology & Cell Biology, uses genetically engineered mice to model a variety of inherited degenerative retinal diseases, including retinitis pigmentosa and late onset retinal dystrophy, which lead to blindness.

Retinitis pigmentosa destroys the light-sensing photoreceptor cells that exist in the retina, and leads to vision loss. Mutations in some 56 genes—including *PDE6*—have been associated with retinitis pigmentosa, which affects about 1.5 million people worldwide. A defect in the *PDE6* enzyme complex is the third most common cause of this condition in humans. In mice, this same inherited disease occurs when there is a defect in one of the genes encoding for *Pde6*.

Dr. Tsang is working to find new treatments for photoreceptor degeneration in retinitis pigmentosa, as well as age-related macular degeneration and related retinal diseases. Because these diseases in humans and mice are similar, Dr. Tsang is researching human treatments by using mouse models to conduct experiments in gene therapy and stem cell transplantation.

His gene therapy work involves delivering a correct copy of the *Pde6* gene to the photoreceptor cells in the mouse retina. Photoreceptors are the cells in the retina that perceive light and that carry the gene defect that causes retinitis pigmentosa. Dr. Tsang uses adeno-associated viruses as a medium to carry healthy copies of the *Pde6* gene to the retina. Viruses can be rendered harmless and can act as delivery systems for genes. He injects this gene therapy virus into a mouse eye, in between the photoreceptor cells and an outer layer of the eye called the retinal pigment epithelium. Providing photoreceptor cells with a functional copy of the *Pde6* gene allows the retina to respond to light and, in turn, to signal the brain to produce a visual response.

In one experiment, Dr. Tsang injected a healthy *Pde6* gene into one eye of several five-day-old mice. He left their other eye untreated. At six



Stephen Tsang, M.D., Ph.D.

months old, the treated eyes revealed healthy photoreceptor cells and normal visual responses; their untreated eyes had no photoreceptor cells and had lost all vision. The treated mice experienced no harmful side effects, indicating that this form of gene therapy is most likely a safe treatment for patients with retinitis pigmentosa. Moreover, the mice that received a single delivery of the gene therapy virus had vision through at least a quarter of their lifespan. “This may be a long-term and exciting result that leads to a human clinical trial to treat patients with retinitis pigmentosa caused by defects in the *PDE6* gene,” Dr. Tsang said.

In other research, Dr. Tsang is working on stem cell transplantation in mouse models. In 2010, he successfully used mouse embryonic stem

cells to replace diseased retinal cells and restore sight in mice with retinitis pigmentosa. Of the mice that received the stem cell transplants, one-quarter experienced restored sight; however, some also developed benign tumors and retinal detachments.

Dr. Tsang’s latest research breakthrough features the cultivation of healthy retinal cells that have been reprogrammed from patients’ skin, and the transplantation of these cells into the retinas of mice with retinitis pigmentosa. Similar to embryonic stem cells, stem cells derived from adult human skin cells can develop into any type of cell in the human body.

In one experiment, Dr. Tsang grew retinal cells from the skin of a 53-year-old donor. He injected the healthy retinal cells into the right eyes of 34 mice. No tumors had been found. Afterward, many of the treated mice enjoyed normal vision, while the control mice—who had received injections of saline or inactive cells—experienced no visual improvement.

Reprogramming cells from a person’s skin and transplanting them as retinal cells back into the same person minimizes the chance of cell rejection that would likely occur if the cells came from a donor. “It’s not like a transplant that’s going to put

you in a circumstance of immediate rejection,” Dr. Tsang explained. “They are your cells. You’ve just reprogrammed them in a way that ought to provide what’s missing. You could imagine doing that for blood diseases, sickle cell anemia, or eye diseases. It’s an appealing possibility.”

Ultimately, Dr. Tsang plans to transplant these personalized stem cells to treat advanced stages of retinal degeneration autologously. “Using patient-specific cells as therapy will pave the way to personalized and precision medicine,” he said.

The philanthropist Donald Jonas has been particularly important to Dr. Tsang’s stem cell research, both as a patient and as a funder (see page 1). Support from Mr. Jonas and his wife Barbara will allow Dr. Tsang to prepare data for human trials, which are about four years away. ■

Basic Science Research: Another Way of Improving Patient Care

In ophthalmology, as in most medical specialties, research and training traditionally have occupied two distinct realms: basic science and clinical medicine. Researchers learn about eye disease in the lab, while clinicians learn at the bedside. But, the growth of translational medicine—bringing the bedside to the bench and back—is bridging the gap between the two. Today, more than ever, Columbia Ophthalmology’s scientists and clinicians are working side by side to improve patient care.

Thus, clinicians see patients with eye disease, while basic science researchers study the disease. Collaborations between physicians in the clinic and scientists in the lab will foster greater understanding of eye diseases and provide the best chance for cures in the future. Scientists conduct molecular explorations of the disease and the mechanisms behind its clinical symptoms. They also develop potential therapies, which they test in cellular and animal models of the disease. Then, they test these therapies in human clinical trials, which involve the patients suffering from the disease.

Training for a career in scientific research takes approximately five to seven years, depending on the academic program. It begins with a year or two of coursework, exposure to different sciences and research techniques, and rotations through various labs to help students choose a specialty. At the end of their second year, students take a qualifying exam, which typically includes a mini thesis dissertation and defense of their proposed research project. Provided that they pass, they earn a Master of Philosophy degree and begin their Ph.D. research.

In the third year, doctoral candidates work in the lab that they have chosen and develop a research project, under the guidance of a principal investigator, who serves as a mentor. They also take classes or seminars, and participate in journal clubs, where they discuss their research and other research in the field. They meet with a committee of experts in their field of research at least once a year to report on their progress and receive feedback. “As a Ph.D. candidate, you learn how to think like a researcher, carry out experiments, and work on a novel research project, which you follow all the way through to publication,” explained Katherine Wert, Ph.D., who recently earned her doctorate in nutritional and metabolic biology from Columbia’s Institute of Human Nutrition.

Under the guidance of Stephen Tsang, M.D., Ph.D., Dr. Wert researched retinal degenerative eye diseases, specifically retinitis pigmentosa. She created a gene therapy virus that could slow the progression of retinitis pigmentosa, which is caused by a mutation in the alpha subunit of a gene called phosphodiesterase 6 (*PDE6A*). Using mouse models, she tested the efficacy of this gene therapy virus before and after the onset of retinal degeneration. Dr. Wert’s research is now being developed for a potential human clinical trial for patients with retinitis pigmentosa caused by mutations in *PDE6A*.

Although Dr. Wert has completed her doctoral studies, her basic science research training will continue

in January, when she begins a postdoctoral fellowship at the Massachusetts Institute of Technology in Cambridge, MA. “As a postdoctoral researcher, I will be learning how to be independent, expand my knowledge, train others, and become an expert in a specific field of research.”

Postdoctoral fellowships give new scholars valuable time to transition from being students to professionals. The fellowships last approximately three to six years and help young scientists establish independent research careers and develop expertise in their fields. They provide the experience that can help researchers qualify for faculty positions and government funding.

“As a postdoctoral researcher, you learn research under the supervision a new mentor and follow through on your own ideas,” Dr. Wert said. “You undergo training that prepares you to lead your own lab, and find new ways to treat diseases and help people.”

Unlike Dr. Wert, Yao Li, M.D. began her training on the clinical side of ophthalmology, with the goal of treating patients in her native China. In 2010, Dr. Li came to Columbia to finish a research paper required to complete her medical degree. However, conducting basic science research convinced Dr. Li that having a more thorough understanding of the molecular mechanisms of eye disease would make her a better physician.

For the past three years, she has been a postdoctoral fellow in Dr. Tsang’s laboratory, where she is creating induced pluripotent stem (iPS) cell lines from human skin cells, and using them to produce healthy retinal cells that are currently being injected into genetically engineered mice with eye disease. Although she earned her medical degree in 2011, she plans to continue her postdoctoral studies for the next few years, so she can help move the research into human clinical trials.

As a clinician and now a basic scientist, Dr. Li is uniquely positioned to bridge the realms of medicine and basic research. “Currently, my major work in the lab is running experiments and trying to discover new treatments for clinical disease,” she said. When she returns to China, she will begin practicing ophthalmology with a deeper understanding of eye disease, and the therapies that are being developed to treat it. “It’s a perfect match.” ■



Katherine Wert, Ph.D.



Yao Li, M.D.

Promotions and Announcements

Robert Catalano, M.D., promoted to Associate Clinical Professor of Ophthalmology, effective March 1, 2012

Dan Kauffman-Jokl, M.D., promoted to Associate Clinical Professor of Ophthalmology, effective May 1, 2012

Lama Al-Aswad, M.D., promoted to Associate Professor of Clinical Ophthalmology, effective May 1, 2012

Leejee Suh, M.D., promoted to Associate Professor of Clinical Ophthalmology, effective March 13, 2013

Stephen H. Tsang, M.D., Ph.D., appointed Lázló Bitó Associate Professor of Ophthalmology, effective July 1, 2013

Faculty Spotlight:

Ophthalmological Research in the Era of Sequestration

Yao Li, M.D.
(foreground)
and Stephen
Tsang, M.D., Ph.D.

Scientific research is the engine that drives academic medicine, while government financing—particularly from the National Institutes of Health (NIH)—provides much of the fuel. Unfortunately, sequestration and the subsequent \$1.7 billion cut to the NIH budget could leave some research engines sputtering.

Fortunately, the Research Division of the Department of Ophthalmology, with more than \$7 million in total grant funding (including a core grant from the NIH's National Eye Institute [NEI]) and a renowned faculty, is thriving. Yet, as sequestration squeezes federal dollars, the Department's researchers—from its director to its most junior scientist—know that securing future financial support could become increasingly difficult.

“When I came to Columbia 15 years ago, the funding rate for grants from the NEI was 40%,” said Rando Allikmets, Ph.D., Research Director of the Harkness Eye Institute, and William and Donna Acquavella Professor of Ophthalmology, and Pathology & Cell Biology. This means that for every 10 submitted grant applications, four received funding to allow researchers to conduct their investigations. It was the late 1990s. The United States had a budget surplus. Funding was generous. Then the economy plummeted. “Now, funding rates are below 10%, although a bit higher at the NEI—about 15%,” Dr. Allikmets continued. “This means that only one in 10 grant applications get funded. It's a tough situation.”

Financing their research—including equipment and staff salaries—is a constant and time-consuming chore for senior scientists like Janet Sparrow, Ph.D., the Anthony Donn Professor of Ophthalmic Science in the departments of Ophthalmology, and Pathology & Cell Biology, whose only revenue comes from grants. Grant writing is not only arduous; its outcome is unpredictable. “The difference between a grant that gets funded and one that does not could be miniscule,” said Dr. Sparrow, who serves on NEI grant review panels. “It's a roll of the dice.”

During her 16 years at Columbia, Dr. Sparrow has been researching retinal disease and various forms of macular degeneration. She has received support from Foundation Fighting Blindness, Fight for Sight, and the Macular Vision Foundation. But, her major—and steadiest—funding has come from the NEI, which recently reduced her award. The NEI is a particularly important resource, because its grants last up to five years. “You need a block of time when you're not writing grants, to be able to focus and be creative and make progress on the work,” she commented.

When funding doesn't come through, research suffers. Principal investigators scale back experiments and sometimes lay off staff. “If you can't continue to support your research program, you have to shut things down,” Dr. Sparrow said. This may mean losing highly trained postdocs, who

conduct the intricate procedures that senior scientists are too busy to do.

To Associate Professor Konstantin Petrukhin, Ph.D., who dedicates 30–40% of his time to grant writing, postdocs are the driving force behind experiments. “They define the shape of research,” Dr. Petrukhin said. He knows that if he loses the funding supporting his investigation of drug treatments for age-related macular degeneration (AMD), he will likely lose his postdocs too.

Dr. Petrukhin is a member of the NIH's Blueprint Neurotherapeutics Network, a \$50 million, five-year program that helps investigators develop new drugs. In addition to a grant, the Blueprint Network provides Dr. Petrukhin with millions of dollars in services typically available only to pharmaceutical companies. Besides one postdoc and a part-time technician supported by the grant, he has several NIH consultants on his team. He worries that reduced funding will slow, if not stall, his research, delaying his ability to move experimental drugs into human clinical trials by 2015. “Sequestration affects the amount of money the NIH can spend on this project,” he said. “It will not allow as many experiments as are required, and we may not be able to proceed as fast as we could.” If he loses his funding, he will have to stop certain projects and let people go. As Dr. Sparrow stressed, “To keep a research program moving forward, you have to have personnel in your lab who have the talents and expertise to conduct experiments.”

Researchers who may suffer the most from funding cuts are those who are beginning their careers, like Assistant Professor Quan ‘Donny’ Hoang, M.D., Ph.D., who joined the Department a little more than a year ago. “In order to apply for your first grant, you need experimental proof of principle. Conversely, in order to run experiments, you need funding,” Dr. Hoang explained. Dr. Hoang, who studies extreme nearsightedness,

has been fortunate with funding from sources other than the NIH. He shares a philanthropic gift with his mentor, Stanley Chang, M.D., the K.K. Tse and Ku Teh Ying Professor of Ophthalmology. He also has two grants from Columbia University: a 2013–2016 Louis V. Gerstner, Jr. Scholar award, which supports early stage physician–scientists, and an institutional NIH KL2 clinical translational sciences award from the Irving Institute for Clinical Translational Research. These grants were among *nine* that Dr. Hoang sought last year. They afford him one paid technician, but not a postdoc. Given his limited staff and his teaching and clinical obligations, he has had to curtail the scope of his research. “It is easier to test multiple new ideas concurrently with more people power,” he said. “I would love to have a technician *and* a postdoc *and* one or two graduate students. Hopefully I'll have this kind of staffing in five years or so, when I'm more established.”

Like his senior colleagues, Dr. Hoang knows that surviving sequestration will require applying to major funding agencies, like the NEI, as well as small, non-governmental organizations and foundations. Indeed, Columbia Ophthalmology faculty already cast a wide net when soliciting support, submitting high-quality proposals that are tailored to meet funders' specific goals. Currently, eight of the Department's 11 principal investigators are funded by NIH grants: four have two R01 grants from the NIH, three have one R01 grant, and, one has a U01 grant.

The Department's fundraising ability only partially accounts for its success. The Department consistently attracts and retains scientists with world-class training, whose cutting-edge, translational research is closing the gap between bench science and patient care. “We are strengthening our programs with internal and external

Giving Back for the Gift of Sight *continued from page 3*

care arena, particularly in nursing and mental health.

Among the couple's most noted programs is *The Jonas Center for Nursing Excellence*, founded in 2006, during the country's unprecedented nursing shortage. The Center is one of three initiatives of The Barbara and Donald Jonas Family Fund, which was created with more than \$44 million, raised through an auction of a portion of the family's noted contemporary art collection. Columbia University's School of Nursing and NewYork-Presbyterian Hospital were among the Center's founding partner-recipients. In 2008, the Jonas Center turned its attention to the need for qualified faculty to train the next generation of nurses. It launched the *Jonas Nurse Leaders Scholars Program*, a groundbreaking national initiative, supporting nursing faculty and clinical leader training of

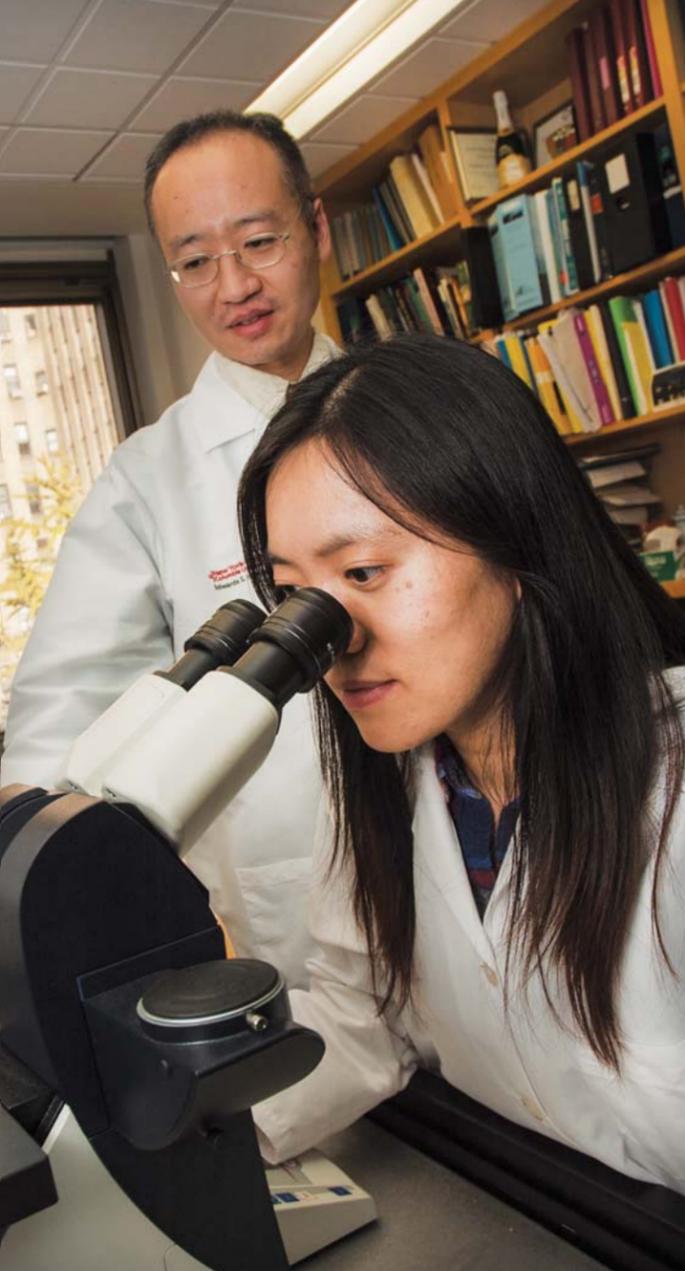
doctoral level nursing candidates. The program now includes more than 200 scholars in all 50 states through partnerships with nearly 90 schools of nursing.

Extending the Focus to Veterans

In 2012, the Jonases focused their philanthropic efforts on veterans. They created the *Jonas Veterans Healthcare Program*, which is addressing veterans' most pressing health issues by expanding the field of qualified caregivers through scholarships to 54 doctoral-level nursing candidates in 21 states—again, including two at Columbia University.

Spurring Innovation in Mental Health Care

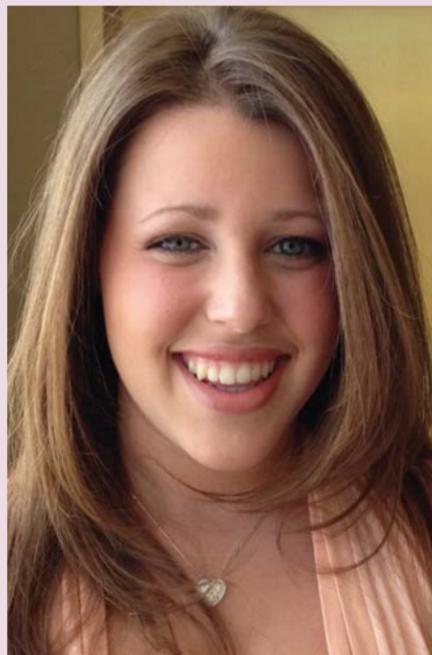
Mental health is a cornerstone of the Jonases' giving, such as through the *Barbara Jonas Psychiatric Hospitalist* at NewYork-Presbyterian Hospital. A longtime mental health advocate and former practicing psychotherapist, Mrs. Jonas recognized that



Colbey Plutzer Turns Tragedy into Triumph

Colbey Plutzer cares deeply about giving back. For the last several years, she has provided meals, clothing, and toys for disadvantaged families on Long Island. She works as a peer helper with elementary school children. And, ever since Stanley Chang, M.D. halted the acute posterior multifocal placoid pigment epitheliopathy (APMPPE) that had abruptly begun destroying Colbey's sight, she has been conducting a steadily growing fundraising campaign to benefit Columbia Ophthalmology.

In 2007, Colbey was a sixth-grader with brand new glasses when her vision suddenly blurred. Her parents blamed the glasses. But in less than three weeks, her vision in both eyes deteriorated from 20/20 to 20/400. With vision of 20/400, one is barely able to see the large E at the top of the eye chart. "It went from bad to worse in seconds," said Ann Plutzer, Colbey's mother. Gary Plutzer, Colbey's father, added, "All of a sudden, our normal, thriving adolescent couldn't walk downstairs or recognize people's faces."



Colbey Plutzer

The Plutzers raced their daughter to a pediatric ophthalmologist, who said the situation was dire. They needed a specialist. Frantic, Mr. Plutzer researched the country's top ophthalmologic centers. He was prepared to travel anywhere to find a doctor who could save his daughter's sight. But he only had to go as far as Washington Heights, where Dr. Chang saw Colbey immediately. "We were given the opportunity to see Dr. Chang, when other doctors said they didn't have time in their schedules," Mrs. Plutzer said. "Without him, I don't know what would have happened."

APMPPE is a rare inflammatory eye disease that causes lesions and scarring of the choriocapillaris, retinal pigment epithelium, and outer retina of young adults. It is considered an autoimmune disorder, whose onset has been associated with viruses and fevers. Diagnosed at age 11, Colbey was the second youngest recorded case of the disease in the world.

Dr. Chang prescribed swift, intensive treatment: huge doses of steroids and anti-inflammatory medications, injected every other day, for 18 months. The regiment was grueling. Three times a week, Colbey's mother drove her from Syosset to Columbia for treatment and testing. Colbey fell behind in school. The injections left scars. She suffered side effects from the medicines; she gained 25% of her body weight in three weeks, her height capped at five feet, and her hands began—and continue—to shake. However, the treatment stabilized the disease. Gradually, her vision returned to 20/40 in her

right eye, where the most serious damage had occurred, and to 20/30 in her left eye. "I call Dr. Chang my God," Ann Plutzer said. "He did an unbelievable job in stopping the disease." Gary Plutzer said, "Without the skill and treatment Colbey received at Columbia, she would have already lost her vision."

In 2008, with the crisis abated, Colbey turned her attention toward her upcoming bat

mitzvah—and finding a way to thank Dr. Chang and Columbia Ophthalmology. She decided to dedicate her bat mitzvah project to raising money for the Department. "I always knew I would give something back," she said.

Her project started small: redeeming bottles and cans for cash, and matching whatever she earned with her own money. Her efforts gained momentum after she had her bat mitzvah. She asked family members for contributions. Then, her father became involved, adding her campaign to the charities his business supports. "We've attracted a

sizeable group of people," Gary Plutzer said. Noted Mrs. Plutzer, "It's something we've all become passionate about."

Today, Colbey is a senior at Syosset High School, working on college applications and dreaming of becoming an elementary school teacher or speech pathologist. With the help of tutors, extra-large print materials, special computer software, magnifying glasses, and additional time to take tests, she has caught up in school, and carries a 94 grade point average. "I need my glasses to read or the words look like mush," she explained. Indeed, she needs her glasses all the time. "I can't see too far in front of me without glasses."

Colbey's road to recovery has been long and winding. She has sustained irreversible retinal damage. And, she lives knowing that APMPPE may reoccur, or that she ultimately may develop advanced macular degeneration. Thus, her parents' relief is cautious: Ann Plutzer keeps a notebook in which she records the slightest changes in Colbey's reading ability, eye pressure, or overall health, so she can correlate identifiable markers with the disease's potential re-emergence. "It's something that never leaves your mind," Gary Plutzer said.

What never leaves Colbey's mind is the gratitude she feels toward Dr. Chang and Columbia Ophthalmology, and her resolve to continue raising money to help patients with APMPPE or other eye diseases. "It makes me feel good to know I am helping someone else," she said. "I like the feeling of saying, 'Here, do the research, do what you have to do. If there's someone else like me, God forbid, you'll have the resources you need.'"

collaborations, a synergy of good new ideas, and translational research," Dr. Allikmets said. Principal investigators commonly collaborate on projects, whether exploring therapy for Stargardt disease and AMD, or quantifying retinal autofluorescence (see page 2), to name just a few examples. "If you have many strong components in the same project, the proposal has more chances for success."

Clinical trials also have emerged from the Department, and some are in the pipeline for the future. "We have a relatively small but coherent group of researchers who work together well and are driven by the same goal, which is to determine the cause and provide treatment options for eye disease," Dr. Allikmets said.

This is the goal that will continue to fuel the groundbreaking research of the Department, no matter how tough times get. ■

overlooked mental health needs complicate care in many hospitals, worsening response to treatment, lengthening stays or affecting recovery. Herbert Pardes, M.D., Vice Chairman and CEO of the hospital when the position was created, said, "Adding a dedicated psychiatric hospitalist has helped further ensure that we can appropriately address all patient needs." Additionally, the Jonases have funded the *Barbara Jonas Institute for the Study and Treatment of Children at Risk* at NewYork-Presbyterian, and the Columbia University *TeenScreen Program*.

Columbia University has been at the center of many of the Jonases' philanthropic initiatives—all designed to improve health by supporting faculty, investigators and students. "We are immensely proud to partner with Columbia as we advance our shared passions and vision to improve health care, especially for the most underserved populations." ■

In Memoriam:

Columbia Mourns the Loss of Louis Flanzer, Friend and Benefactor

Louis Flanzer, who with his wife Gloria, was a major benefactor of the Columbia University Medical Center and a staunch supporter of the Department of Ophthalmology, died on June 30, 2013.

Mr. Flanzer, a retired real estate investor, was a dedicated philanthropist who was strongly committed to improving hospitals and health care. Starting in 1997, his wife and he made generous gifts in support of the creation of many of Columbia's state-of-the-art facilities, including the Flanzer Eye Center, the Gloria and Louis Flanzer Cardiac Center, and the Flanzer Vision Care Center in midtown.

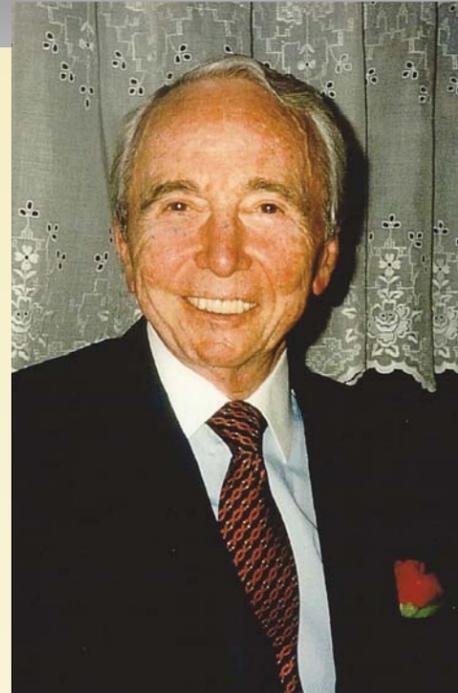
The couple led a consortium of donors who brought about the complete revitalization of the Harkness Eye Institute's first floor, turning it into the Flanzer Eye Center, which opened in 1998. The pledge that the consortium made in 1995 to construct the modern, comprehensive and patient-friendly care facility was instrumental in drawing Stanley Chang, M.D. to the Department as its new Chairman. During that same year, the Flanzers began their longtime membership on the Department's Board of Advisors; they also funded a fellowship in their name that supported young vitreoretinal surgeons working under the aegis of Dr. Chang to hone their diagnostic and surgical skills. "From the beginning of my tenure, Louis and Gloria Flanzer supported me and all the projects I undertook," Dr. Chang said. "They were always there to help."

In 2004, the Eye Institute opened the doors of its newly refurbished and equipped Gloria and Louis Flanzer Amphitheater, named for its sponsors. Through their generous philanthropy, the Flanzers also supported the Gloria and Louis Flanzer Vision Care Center at Third Avenue and East 53rd Street,

making state-of-the-art eye care easily accessible to patients living and working on Manhattan's east side, and those traveling from all directions of the tri-state region. The 8,000 square foot facility, which occupies the entire second floor at 880 Third Avenue, opened in 2010 and provides care in all subspecialties of ophthalmology.

Louis Flanzer was a soft spoken, elegant gentleman known for his sense of humor, passion for the Brooklyn Dodgers, and love of learning. He was a United States Army and World War II veteran, who overcame his fear of flying by becoming a licensed pilot. He lived with his wife in Westchester and Florida. Together, they had diverse philanthropic interests and participated in many charities. They were major donors to White Plains Hospital, board members of the Flanzer Jewish Community Center in Sarasota, and supporters of the Sarasota Ear Research Foundation.

Jack Cioffi, M.D., Chairman, Department of Ophthalmology, lauded the Flanzers for funding projects that have laid the critical groundwork for the Department's success. "While I never had the good fortune to meet Mr. Flanzer, I appreciate the important contributions he made to our Department," Dr. Cioffi said. "The Flanzers have played a major role in the Department's prominence as a world-class resource for vision care." ■



Louis Flanzer

Important Patient Care Information

Specialties: Cornea/External Ocular Disease
Glaucoma
Pediatric Ophthalmology and Strabismus
Refractive Surgery/LASIK
Vitreoretinal and Uveitis

For inquiries and appointments, please call 212.305.9535



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