



Vision for the Future:

Jack Cioffi Begins Appointment as New Chair of Ophthalmology

“Do real and permanent good in this world.” This famous declaration by Andrew Carnegie motivates George A. (Jack) Cioffi, MD, as he assumes his new role as Chairman of the Department of Ophthalmology at Columbia University College of Physicians and Surgeons as well as Ophthalmologist-in-Chief at New York-Presbyterian Hospital.

Dr. Cioffi brings to these positions a broad background of skills and experience in clinical and research ophthalmology, as well as a proven academic and administrative background. His immediate past positions were as chief medical officer and senior vice president at Legacy Health, R.G. Chenoweth Endowed Chair of Ophthalmology and Chairman of Ophthalmology at Devers Eye Institute, and Professor of Ophthalmology at Oregon Health and Science University in Portland, Oregon.

An active and internationally recognized glaucoma clinician and researcher, Dr. Cioffi was responsible for developing the Devers Eye Institute’s research department. With his primary interest in glaucoma, Dr. Cioffi has presented lectures throughout the world. He has been the recipient of numerous honors, including the Clinician-Scientist Award from the American Glaucoma Society, the Senior Achievement Award from the American Academy of Ophthalmology, and the 2010 Shaffer-Hetherington-Hoskins



George A. (Jack) Cioffi, MD

Award from the Glaucoma Research Foundation in San Francisco. Dr. Cioffi has also been listed among America’s Top Doctors since 2002.

In addition to having authored over 150 peer-reviewed articles, three review articles, one book, 30 book chapters, and 100 published abstracts, Dr. Cioffi’s scholarly rigor is kept in sharp focus as editor-in-chief of the *Journal of Glaucoma*. He has served in leadership positions for many professional societies, including chairman of the Scientific Advisory Committee for the Glaucoma Research Foundation in San Francisco.

Dr. Cioffi excelled scholastically, receiving his undergraduate degree in zoology *magna cum laude* and Phi Beta Kappa from the University of Vermont and his medical degree *cum laude* from the University of South Carolina. He completed his residency at the University of Maryland, where he was chief resident, a position that attests to future leadership and calls upon that person to be a teacher, manager, and problem solver in addition to physician.

A Proven Leader

To direct a department the caliber of the Harkness Eye Institute requires a leader well versed in a multitude of arenas,

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National Eye Institute Awards Major Grant to the Department of Ophthalmology

The National Eye Institute (NEI) has awarded a multi-million dollar five-year grant

for a collaborative study at five institutes led by researchers at Columbia University’s Department of Ophthalmology to find treatment options for any or all ABCA4-associated genetic diseases. Stargardt disease is a genetic form of juvenile macular degeneration that causes progressive vision loss and is the primary disorder caused by mutations in the ABCA4 gene. This gene also contributes to a wide variety of other retinal degenerative disorders, including cone-rod dystrophy, retinitis pigmentosa, and age-related macular degeneration.

The Columbia team, led by Rando Allikmets, PhD, includes Janet Sparrow,

PhD, Peter Gouras, MD, Konstantin Petrukhin, PhD, and Stephen Tsang, MD, PhD, co-investigators who have collaborated together in various combinations on gene therapy and small molecule therapy of Stargardt disease for the past ten years. The NEI grant provides a substantial increase in research funding, which had previously been extremely limited, raising the possibility of finding treatment options for Stargardt disease to a whole new level. The objective of the multicenter grant, Therapeutic Applications for ABCA4-Associated Diseases, is to develop therapies by both gene therapy and small molecule-mediated approaches.

The principal investigator of the NEI grant, Dr. Allikmets, is also the geneticist responsible for first identifying and cloning the ABCA4 gene in 1997. Dr. Allikmets’ discovery of the role of ABCA4 in retinal degenerative diseases has directly led to investigations into possible treatments for Stargardt disease. “The goal of every geneticist is not to find the gene, but through that discovery, help to find treatment for the disease,” affirms Dr. Allikmets. And as our understanding of the genetic basis of eye disease grows, so does our capacity to treat these diseases.

Dr. Allikmets and his colleagues at Columbia will be working in tandem

with four other centers. They will be joining forces with Joan Bennett, MD, PhD, at the University of Pennsylvania, a pioneer of gene therapy for retinal diseases; Richard A. Lewis, MD, MS, and James R. Lupski, MD, PhD, at Houston’s Baylor College of Medicine. In 1977 in conjunction with Dr. Allikmets, they were the first to clone the ABCA4 gene. The third center is the Telethon Institute and the Federico II University in Naples, Italy, with Alberto Auricchio, MD, and Francesca Simonelli, MD, who had previously collaborated with Dr. Allikmets on Stargardt patient characterization and genetic research. The fourth center is the University of Illinois, where the well-respected ophthalmologist, Gerald A. Fishman, MD, has been clinically researching Stargardt disease for decades.

“Rather than competing with each other and doing things in parallel,” explains Dr. Allikmets, “I thought the best way to advance the entire field was to join forces in a multicenter study and work together to find the best therapeutic method to treat Stargardt disease.”

Stargardt therapy can be conducted by many different means, including gene therapy with lentiviral or adeno-associated vectors, model organism research,

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Principal Investigators on the grant from L. to R.: Peter Gouras, MD, Stephen Tsang, MD, PhD, Janet Sparrow, PhD, Konstantin Petrukhin, PhD, Rando Allikmets, PhD.



Dear Friends,

This is my first letter to you as the new chair of the Columbia University Medical Center Department of Ophthalmology, and I could not be more thrilled. I sincerely thank the Harkness Eye Institute's physicians, research scientists, nurses, administrative staff, and patients for being so incredibly welcoming. In this, my inaugural issue of the *Viewpoint*, I am pleased to share my background with you and present my vision for the future of this prestigious institution.

I would like to extend a special note of gratitude to Stanley Chang who is stepping down in his role as chairman, but who will continue to actively see patients, conduct research, and teach at Harkness. Stanley has led this Department with exemplary skill and vision, and I look forward to working closely with him in the months and years ahead.



We are proud to announce that Columbia researchers have been awarded a multi-million dollar grant by the National Eye Institute for a multicenter project to find treatment options for ABCA4-associated genetic diseases, including Stargardt disease and retinitis pigmentosa (RP). The grant provides a substantial increase in our research funding and presents the opportunity to find novel treatment options for the future.

Researchers at Columbia are on the threshold of unearthing critical information about the eye's photoreceptor microstructure by using space telescope technology. Adaptive optics (AO) allows researchers to noninvasively examine patients and gain valuable information that previously could only be obtained by looking at autopsy eyes. AO technology is used at just a handful of sites around the world, and we are excited to be obtaining such detailed cellular level information here at Columbia.

With the explosion of new information related to genetic science, we offer our patients genetic counseling services to offset the confusion and fear a diagnosis like Stargardt's or RP might cause by providing much-needed information in its place. In this issue, we highlight the invaluable role of the genetic counselor.

An amazing story of an ophthalmologist's journey from Nazi Germany to the halls of Columbia where a lectureship has been named in his honor is a testament to the spirit of determination a whole generation of immigrants brought to our shores. We are pleased to share the bittersweet history of Ulrich Ollendorff, MD, in the pages of the *Viewpoint*.

Finally, it is truly my honor to be asked to guide this celebrated institution. I look forward to earning your trust and partnership so that we may continue the fine work of advancing research and preserving vision.

Sincerely,

George A. (Jack) Cioffi, MD
Jean and Richard Deems Professor
Edward S. Harkness Professor
Chairman, Department of Ophthalmology

NEI Grant *continued from page 1*

or small molecule treatment. With the centers concurrently working towards the same goal by testing different methodologies, the scientists can better determine which treatment, or a combination thereof, is the most effective.

"I honestly don't care if lentiviral gene therapy, which is done at Columbia, is better than that based on adeno-associated viral delivery," emphasizes Dr. Allikmets. "What I care about is finding the best method out there for patients."

To tackle the large assignment of finding therapeutic applications for ABCA4-associated diseases, the grant has been divided into four modular components:

- **Module 1** is designed to capture a thorough and precise clinical and genetic analysis of Stargardt patients to gain a better understanding of the disease. The Stargardt gene has more than 800 known mutations, meaning only a few affected individuals actually share the same two disease-causing variations. The goal of Module 1 is two-fold: first, to gain a better understanding of Stargardt disease development and progression, and second, to define specific patient subpopulations for most efficient clinical trials.

A clinical evaluation method unique to Columbia is quantitative fundus autofluorescence, which was established through collaborative research with Columbia scientists and François Delori, PhD, at Harvard Medical School. "This evaluation method, applied at Columbia, is extremely valuable to researchers and patients because you can precisely measure and quantify the disease progression through an increase or decrease in the autofluorescence," emphasizes Dr. Sparrow.

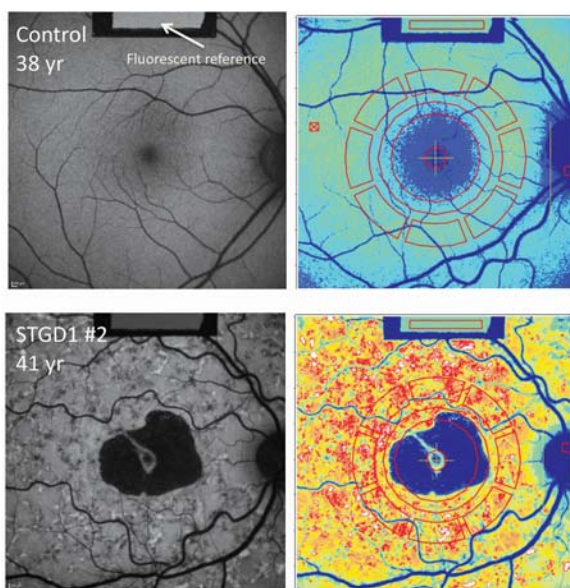
The rate of progression for Stargardt disease is currently unknown. Ideally in future clinical trials, researchers will be able to compare the rate of progression against the disease's natural history and from that determine how well a specific treatment is working.

- **Module 2** utilizes animal models as a tool to evaluate the effectiveness of various treatments.

Based on the work of Dr. Sparrow, a cell biologist, we know the ABCA4 gene transports a form of vitamin A from the photoreceptor membranes so that it can re-enter the visual cycle, and it is the visual cycle that allows us to see. In Stargardt's, the ABCA4 transporter is defective, the consequence of which is an accumulation of a compound called A2E, which is two vitamin A molecules joined together. A2E accumulation in the retinal pigment epithelium kills the cells and leads to many of the characteristics of Stargardt disease.

Fundus autofluorescence imaging in a healthy eye (top) and in an age-matched patient with recessive Stargardt disease (bottom). These images allow measurement of retinal pigment epithelium (RPE) lipofuscin accumulation by an approach (quantitative autofluorescence, qAF) developed at Columbia University.

The images on the right are color coded maps of qAF, with red being indicative of high AF levels. The latter reflects elevated lipofuscin in RPE, a feature of recessive Stargardt disease.



The main measure of Stargardt disease is A2E accumulation, so a lack of increase or a decrease of this compound is one measure of a successful therapeutic outcome. As accumulation of A2E is extremely similar in both mice and humans, researchers use mouse models as a way to investigate if a specific treatment is working or not. Dr. Sparrow and her team are developing methods to transfer the quantitative fundus autofluorescence technology, which is used in the clinic, to their mouse model.

"Currently we need whole eyes to do A2E measurements by high-performance liquid chromatography, so we have to sacrifice the mouse. The advantage of quantitative fundus autofluorescence is that it's a non-invasive imaging approach that does not harm the

animal and enables us to follow the mice over time. In addition, we could model the type of approach that would actually be used in humans to evaluate the success of therapy, meaning that through the mouse model, we would be obtaining information immediately relevant to the human patient," explains Dr. Sparrow.

In the Stargardt mouse model the ABCA4 gene is "knocked out" or made inactive. These "knockout" mice are important animal models for studying the

role of genes in normal physiology and disease. More importantly for these studies, the ABCA4-deficient mice are invaluable models to test therapies and generate treatments, necessary steps prior to establishing human clinical trials.

For example, ABCA4 "knockout" mice are used for gene therapy experiments, which are primarily done with viruses that carry the therapeutic or curative gene to the desired cells. The genes that cause disease within the virus are

deleted, so the virus genes instead act as a delivery vehicle or "vector." In 2008, Drs. Allikmets, Sparrow, and Gouras cloned the normal working human ABCA4 gene into a lentiviral vector and injected it into mouse eyes. The mice were then followed to see if their eyes improved, and they did.

- **Module 3** directly compares two methods of gene therapy: lentiviral versus adeno-associated viral delivery, to determine which method is more efficient.

Lentiviral therapy, which has been developed at Columbia Ophthalmology, entered Phase I clinical trials last year. Now Dr. Allikmets and colleagues are looking to further improve the delivery vectors to

► *continued on page 8*

Clinical Spotlight: Genetic Counselor: A Critical Connection Between the Physician, Patient, and Scientist

Imagine for a moment you were just told that you, your spouse, or your child had an inherited eye disorder where vision would seriously worsen over time and for which there is no known cure. What would you do? Where would you turn? How would you cope? Receiving such a diagnosis would be understandably overwhelming. Add to that a genetic component, and questions arise as to how this will impact your immediate and extended family going forward. In the uncharted waters of genetic testing, a genetic counselor takes on a critical role in communicating to the patient and the patient's family what the diagnosis means and helping them to navigate the challenging course ahead.

Inherited Eye Diseases

Currently 180 retinal disease genes have been identified. Stargardt disease, as one example, is an inherited eye disorder that causes progressive vision loss. It is estimated that up to 1:20 people carry a mutation in the ABCA4 gene, the gene responsible for Stargardt disease. To manifest the disorder a person must have two mutations by receiving one defective copy of the gene from each parent.

Retinitis Pigmentosa (RP) is another hereditary eye disorder that affects approximately one in 3,000 people worldwide and which also causes incurable vision loss.

Like Stargardt disease, RP often first appears in childhood, but severe vision problems usually develop in early adulthood.

(To learn more about Stargardt disease and the studies being conducted at Columbia University's Department of Ophthalmology to find treatment options for any or all ABCA4-associated genetic diseases, please refer to the Stargardt grant article on page 1.)

Genetic Counseling

With the explosion of new information related to genetic science, researchers at Columbia are aggressively pursuing answers to better understand hereditary eye disorders and to ultimately find treatments, but genetic eye disease is extremely complicated both in the lab and to the patient trying to comprehend all of its implications.

Rando Allikmets, PhD, Columbia University Medical Center's Director of Research for the Department of Ophthalmology, and his team work together with the Clinical Laboratory Improvement

Amendments (CLIA)-certified Molecular Pathology Diagnostics Laboratory, to offer their patients genetic counseling services to offset the confusion and fear a diagnosis like Stargardt's or RP might cause by providing much-needed information in its place.

Carolyn Brown, MSc, has been Columbia's on-staff, American Board of Genetic Counseling-certified genetic counselor for one and a half years and is a valued asset for her work with patients and the community. Due to the medical implications for family members as well as the affected individual, counseling is an important part of managing genetic disorders. Ms. Brown offers an immediate benefit by providing facts, support, and resources.

While some physicians may feel they can provide genetic counseling services themselves, or may not see the value in it, inclusion of a genetic counselor is a major added-on benefit

to the patient. In many cases, the physician might have the best of intentions but simply doesn't have the time or necessary expertise in human molecular genetics to educate the patient following diagnosis.

Dr. Allikmets explains, "It is important to understand that genetic counseling is conducted by a person with specific training and education. I direct the molecular genetics lab at Columbia and have conducted basic genetic research to find the genes that cause eye disease for 15 years now, but even someone with my background and experience often does not have the proper skills to be a genetic counselor. It is a specialized and valuable professional service."

Learning that a disease is genetic often has a practical and psychological impact on the wellbeing of individuals and their families that extend far beyond the medical component. When a genetic diagnosis is suspected, Ms. Brown works with the medical team to determine possible genes involved, inheritance patterns, and logical next steps, such as examining family members and genetic testing. Perhaps more importantly, with her training in psychological counseling, Ms. Brown can help the patient adapt to the diagnosis and provide tangible information, giving patients a greater sense of control at times that may be highly emotional or filled with uncertainty. Ms. Brown elaborates, "My goal is to present complicated medical and genetic information in an understandable way so people can make informed medical decisions, and, hopefully, to allay what could be a frightening diagnosis. I try to create a space where people can express concerns and ask questions that might not be brought up during a typical doctor's appointment. While each situation is unique, issues often arise like family planning or how to tell relatives they are at risk for a genetic disease."

Genetic Testing

Scientists' knowledge about inherited eye diseases is growing at an unprecedented rate, and there is great hope that scientists will someday develop a reliable treatment option. Hence, another key aspect of Ms. Brown's position has become the recruitment of patients for ongoing research. By undergoing genetic testing and being included in a database, patients with hereditary eye disorders can be matched to

those who share the same combination of genetic variants and to whom later treatments would be of most benefit.

There are more than 50 known RP genes and many more unknown that are clinically similar. Variations in genes play a significant role in determining if gene therapy or a more general therapy can be scientifically recom-

mended. Dependent on the RP-causing gene, for example, vitamin A supplements might be beneficial for one patient while detrimental to another.

"With all the variations in the Stargardt gene, ABCA4, it is challenging because we need a large number of people with the same genetic combination as their disease progression and response to treatment would likely be similar," points out Dr. Allikmets. "We have more than 600 Stargardt study subjects at Columbia in our database, and we are a center within the National Ophthalmic Disease Genotyping Network, eyeGENE®, which is the National Eye Institute's central depository. We work with other CLIA-certified centers, providing official diagnostic screening and results to patients at no cost. Being part of the eyeGENE® is also beneficial scientifically since we have access to de-identified genetic and clinical results of all patients enrolled at more than 12 centers around the United States, so the numbers alone provide a substantially increased statistical power to our studies."

Gathering information on a patient for inclusion in a database has a long-term benefit, though not an immediate direct benefit to the patient. Patients' participation in genetic studies helps scientists find new disease-causing genes and develop a better understanding of the disorder. Information can then be used to produce treatments and ultimately a cure. Studies of family members are also considered useful in identifying disease-causing genes.

Major strides have been made in gaining an understanding of genetic eye diseases, which were once thought to be untreatable. While researchers continue their search for a cure, genetic counselors are the critical connection between the physician, patient, and scientist: empowering patients through knowledge. ■



Carolyn Brown, MSc



Ms. Brown is counseling family members from L. to R.: Tom Wolf, James Wolf, and Mary Russotti.

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The Department Observes the Fifteenth Anniversary of the Ulrich Ollendorff Lectureship

The winds of fate blow a different course for each traveler. For Ulrich Ollendorff, MD, they carried a practicing ophthalmologist and academician from Nazi Germany to the esteemed halls of Columbia University's Department



L. to R.: Stanley Chang, MD, Jack Cioffi, MD, Bjorg and Stephen Ollendorff.

of Ophthalmology, where a prestigious lecture is presented every year in his honor.

Ulrich Ollendorff Lectureship

This March, the Department of Ophthalmology at Columbia University marked the fifteenth annual Ulrich Ollendorff Lectureship. Paul L. Kaufman, MD, professor and chair of ophthalmology and visual sciences at the University of Wisconsin Clinical Science Center, presented the talk, "Presbyopia: Up Close."

The Ulrich Ollendorff Lectureship was established in 1997, the year before Dr. Ollendorff's death, to honor his long and renowned career as an eye doctor. The annual lectureship was endowed by a gift from his son, Stephen and his daughter-in law, Bjorg.

"The Ollendorff Lectureship is a standout for many reasons," notes John T. Flynn, MD, special lecturer in the Department of Ophthalmology who has been involved with this program since its inception. "It is a rarity in American ophthalmology because it includes presentations on every subspecialty, given by experts on that subject. The lectures focus on innovative research in the field."

Open to the entire ophthalmology community, the Ollendorff Lectureship has an appeal to physicians in Manhattan and beyond. "We identify individuals who have made significant contributions to the development of ophthalmology both clinically and scientifically," describes Stanley Chang, MD, former departmental chair. "As ophthalmic leaders, our presenters are an inspiration to young trainees, fellows, and residents, and we want to honor them for their contributions." A feature unique to this lectureship is that the Department's young ophthalmologists join the guest speaker for dinner, an occasion that provides an opportunity for young clinicians to interact with ophthalmologic luminaries in a more casual atmosphere.

Establishment of the Lectureship

It is impossible to discuss the Ollendorff Lectureship without talking about the man behind the name. As Dr. Flynn keenly states, "The Ollendorff Lectureship has a shine unlike any other because no other lecture

has such a unique background of triumph over tragedy."

Stanley Chang, MD, was the newly minted chair of the Department of Ophthalmology in 1996 when, over the long Fourth of July weekend, he successfully treated Stephen Ollendorff's eye problem. In return, Mr. Ollendorff wanted to do something special for the Department. "While discussing various options, I mentioned to Dr. Chang that though my father had one of the largest ophthalmology practices in Washington Heights, he was denied privileges to practice at Columbia's Department of Ophthalmology solely because he was Jewish."

Mr. Ollendorff was referring to a time in history when America, in all her infinite promise, was still a land of quotas and restrictions. In that era, Columbia held to a policy of not hiring Jewish physicians. In a gesture both compassionate and ironic, Mr. Ollendorff and Dr. Chang decided to establish a lectureship series in Dr. Ollendorff's name at the Harkness Eye

Institute. Reflecting that Columbia had once turned its back on his father, Mr. Ollendorff summarizes the emotion behind the decision, "It felt like a redemption of sorts."

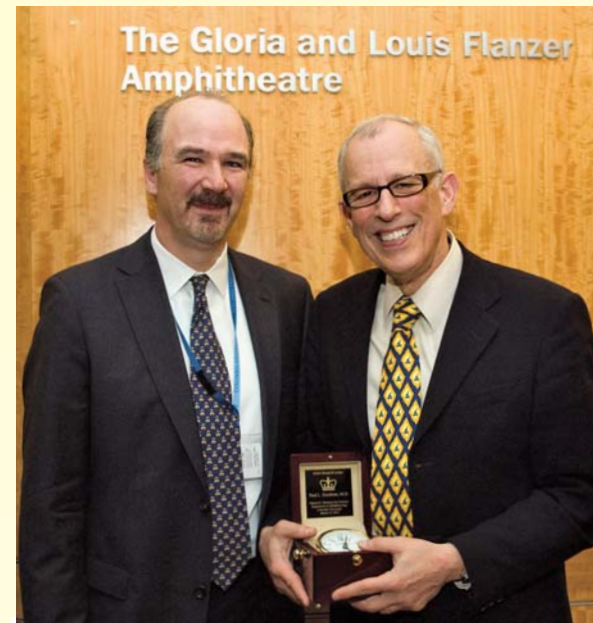
"Steve and I thought an annual lectureship would greatly honor his father," explains Dr. Chang. "We wanted to make people at the eye institute and in the community aware of Dr. Ollendorff's contributions to New York's Upper West Side, the neighborhood that houses Columbia University Medical Center. I also recognized that this lectureship would contribute to Columbia's intellectual environment by bringing outstanding academic ophthalmologists from throughout the country to the Harkness Eye Institute."

The lecture is also an opportunity to reflect on the entire movement of well-trained professionals, doctors, scientists, artists, and musicians who escaped the Holocaust and successfully integrated into American life. "Their story is very inspiring," emphasizes Dr. Chang. "Dr. Ollendorff, for example, gave up everything in his home country, yet still built a successful practice in the United States, raised a wonderful family, and gave back to the community."

The Ollendorffs have also established a Diagnostic Center for the Harkness Eye Institute. Dr. Chang acknowledges, "The faculty has come to know Steve and Bjorg. They are a family interested in helping others, and they are incredibly supportive of the whole Institute, both as members of the Advisory Board and as generous donors."

Ulrich Ollendorff, MD

The marking of the fifteenth anniversary of a highly respected named lectureship is a proud achievement, but the journey of the man behind the name is the true testament to this accomplishment. It is Dr. Ollendorff's story, steeped in history, which creates the special aura surrounding the lecture program.



Jack Cioffi, MD and Paul L. Kaufman, MD

Ulrich Ollendorff was born in Breslau, Germany in 1906. After graduating from medical school at the top of his class, he became a professor of ophthalmology. The mood in Europe, however, was darkening. In November 1938, the day before Kristallnacht ("The Night of Broken Glass"), Dr. and Mrs. Ollendorff were cautioned by their landlord that the Nazis were going to raid their Berlin apartment. Believing the warning was a harbinger of worse things to come, Ulrich, his wife Anne, and their four-month old son Stephen immediately went to stay with Anne's parents. They secured visas, and the day following the vicious series of planned attacks against the Jews, the three safely arrived in England; shortly thereafter, Anne's family relocated to Chile.

Ulrich's parents Valli and Arthur, his brothers Wolfgang and Gerhard, and his aunt Ella stayed behind in Breslau, as Arthur was convinced they were safe due to his service as a colonel in the German army during the First World War. To a degree he was correct, but in 1940, Arthur died of a heart attack and the family's security was suddenly less sure. In 1941, Wolfgang, a member of the resistance, was captured in Holland, tortured, and ultimately killed while trying to



escape from the Mauthausen concentration camp. Around that same period, Gerhard was abducted and killed by the Nazi's for "medical reasons." On August 24, 1942, the Nazis arrested Valli and her sister Ella. Certain of their bleak destiny, Valli realized that Ulrich, safe in New York, would be the only family member to survive, and she wrote her beloved son a letter of farewell while on her way to the Theresienstadt concentration camp. On October 16 Valli died and on December 2, her sister Ella followed.

On his arrival to the United States, Dr. Ollendorff and his family began building a new life. He learned English, re-established his professional credentials, and opened an ophthalmology practice in the northern Manhattan neighborhood of Washington Heights, an enclave of German Jewish immigrants. Dr. Ollendorff quickly became known throughout the community, building a wonderful reputation based on his great skill and care. He is remembered for his compassionate medical ideals—he would knowingly operate on patients who could not afford his services in exchange

for an apple pie. He made regular house calls, climbing countless flights of stairs for a payment of \$6 a visit. After his evening rounds he made sure to stop and read poetry each night to a patient whose eyes had to remain bandaged for thirty days, an act of simple kindness in his daily life.

"Everyone in Washington Heights knew Dr. Ollendorff, and it was common for people to wait for three to four hours in order to see him," recalls his daughter-in-law Bjorg. "They were willing to wait because he was a wonderful doctor, a beautiful human being. He generated enormous respect within the community." By the time he retired in 1986 at the age of 80, Dr. Ollendorff had treated more than 300,000 grateful patients.

The Letter

Although well established in New York, Dr. Ollendorff had never stopped looking for news from his homeland and ultimately learned the unspeakable fates his family had suffered. In 1985, Dr. Ollendorff was 79 years old and on the eve of his retirement. In the mail,

lying among the bills and advertisements was a hand-addressed letter to Ulrich from South America. It was the farewell letter his mother Valli had written to him in 1942, two months before she died.

Translated from German, her love letter to her son begins, "My beloved, my good boy," and speaks of the dark future Valli knows she will face. In the most gentle of goodbyes, she asks her son to carry the knowledge that through his life he was the source of purest joy for his parents. The letter ends with Valli acknowledging her certain destiny, "I was and I am daily even longing very much for you and your life. However, fate did not let me go."

The letter, a beautiful memento of a mother's undying love for her son, gives substance to the man himself. Dr. Ulrich Ollendorff was a true "gentle man" who served almost 50 years as a beloved ophthalmologist, honoring the spirit of his family every day in his devotion and caring of others. (For more information about Valli Ollendorff's letter to her son, go to: www.fatedidnotletme.org.)



Welcome Reception for Jack Cioffi

On Tuesday, April 17, Lee Goldman, MD, dean of the Faculties of Health Sciences and Medicine, and executive vice president for Health and Biomedical Sciences at Columbia University Medical Center (CUMC), hosted a reception at Le Cirque restaurant to celebrate the appointment of George (Jack) Cioffi, MD, as the Edward S. Harkness professor and chairman of the Department of Ophthalmology at CUMC.

The evening event was an excellent opportunity to introduce Dr. Cioffi to our constituency. Invited guests included ophthalmology faculty, CUMC departmental chairmen, members of the CUMC Board of Visitors, members of the ophthalmology Board of Advisors, and friends of the Department. The 125 people in attendance enjoyed the Dean's welcoming remarks about Dr. Jack Cioffi followed by Dr. Cioffi's presentation on his vision for the Department's future.

Both the dean and Dr. Cioffi thanked Stanley Chang, MD, the outgoing chair, for his inspiring leadership for the past 17 years and for his extraordinary counsel facilitating Dr. Cioffi's transition to his new position. Everyone had a wonderful time and left the restaurant with a clear understanding of Dr. Cioffi's mission to elevate the Department to even greater heights.



Left: Lee Goldman, MD introduces the new Chair.

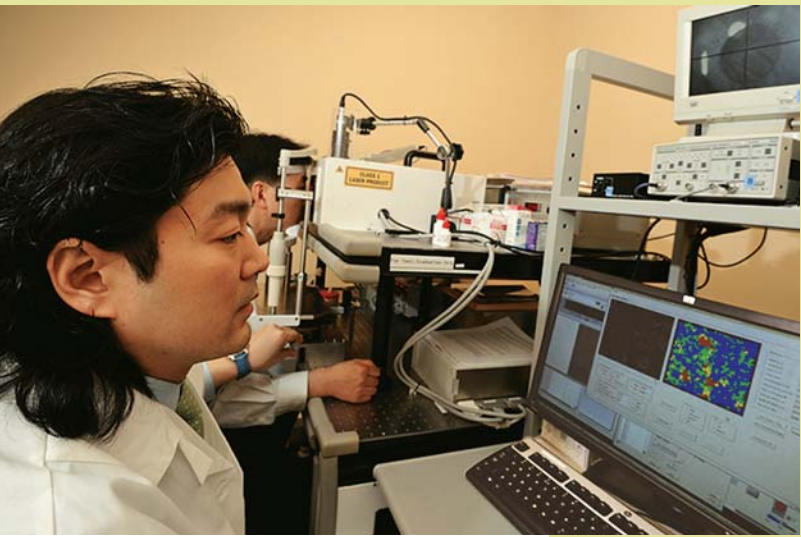
Clockwise from top L. to R.: Stanley Chang, MD, Jack Cioffi, MD, and Lee Goldman, MD; Bernard and Shirlee Brown; Jane Heffner, Ned and Emily Sherwood; John and Margot Catsimatidis, Jack Cioffi, MD, and Stanley Zabar; Dukes and Kay Wooters and Jack Cioffi, MD; E. Virgil and Elaine Conway and Stanley Chang, MD; Carl Frischling, Jack and Linda Cioffi; Lama Al-Aswad, MD, Louis Chang, MD, PhD, Courtney Chang, and Dana Blumberg, MD; Lee Goldman, MD, Donna Acquavella, Jill Goldman, and William Acquavella; Nicholas Mezitis, MD and Peter Michalos, MD; David and Julie Tobey; Stephen Trokel, MD, Cynthia Conigliaro, John Espy, MD and Polly Espy.



Science Insight:

Space Telescope Technology Used to Better See the Back of the Eye

The same tools used by astronomers to examine the far off reaches of the universe are being employed by researchers in the Department of Ophthalmology so that ophthalmologists can better see the back of the eye. Adaptive optics (AO) is an imaging technology originally developed as an astronomy tool to adjust for atmospheric turbulence when using ground telescopes.



Sungpyo Park, MD looking at the images from the AO-SLO machine.

Principal Investigators of AO research at Columbia, SungPyo Park, MD, PhD, Stanley Chang, MD, and Stephen Tsang, MD, PhD, are using this technology instead to visualize the retina at the individual cell level.

Ophthalmic Imaging

Ophthalmic imaging is a fundamental tool in the ophthalmologist's arsenal because it enables a retinal physician to

noninvasively diagnose diseases by observing the retina through the natural optics of the human eye.

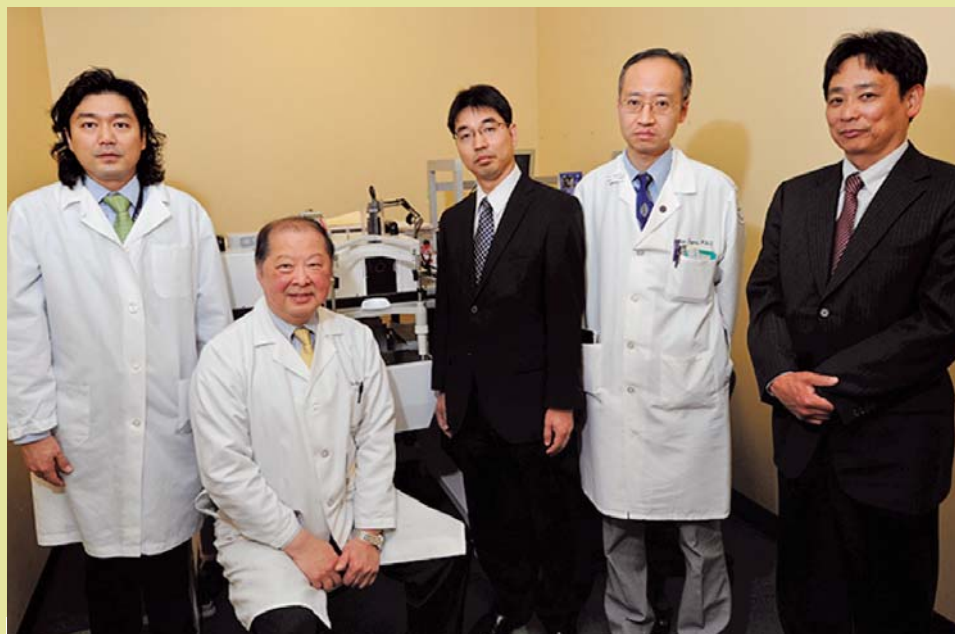
The human eye, however, has an extremely complicated visual system. Due to the blur caused by natural irregularities in the eye's optics, the current retinal imaging methods used in clinical practice are limited in the level of information they are able to provide. For example, while common imaging modalities are able to show different trends or patterns in the retina, such as the behavior of the retinal cells, they are not able to do so at a close distance.

Furthermore, they are unable to provide details about the photoreceptor microstructure, which means that possibly critical information remains hidden.

The retinal specialists at the Harkness Eye Institute are the foremost in the nation and they use these diagnostic tools to look at images of the retina. In 2011, in partnership with the Canon company, Dr. Chang laid the groundwork for a pioneering imaging technique by bringing in an AO machine and combining it with an established system, scanning laser ophthalmoscopy (SLO). The two modalities together create a new imaging system referred to as AS-SLO, which Columbia's Department of Ophthalmology is using to obtain high-resolution retinal images.

With AO-SLO's high magnification, researchers are able to view the retina in an entirely different way, obtaining detailed cellular level information about the retina. The AO-SLO enables physicians to visualize the shape and morphology of each cone cell within the retina. They are able to count how many cells are viable, see how the cells are arranged, note any differences among them, and determine if the packing arrangement of the cells changes throughout the pathology of the disease.

Dr. Park explains, "This ability to count cells is a significant asset of AO-SLO. Since we can see every single cone cell, we can count how many exist and then compare that number to a normal retina. This is a helpful tool, because in some diseases, an increase in cone numbers indicates many different kinds of problems. We can also look at the changes in the shape and orientation of the cones. AO-SLO holds promise of earlier diagnosis because we can observe cone behavior earlier in the disease. In addition, we can monitor disease progression, from when it begins, which will help us uncover how it manifests itself in the earliest of stages and other subtle changes that could not be detected otherwise."



L. to R.: Sungpyo Park, MD, Stanley Chang, MD, Norihiko Utsunomiya, an engineer with Canon based in Tokyo, Stephen Tsang, MD, PhD, and Takeshi Kitamura, an engineer with Canon based in New York.

Features of AO-SLO

The key features of the AO-SLO system include the incorporation of a dual liquid crystal on silicon spatial light modulator (LCOS-SLM) as a wavefront compensation device and sequential processing of aberration measurement/compensation and SLO imaging.

In an AO system, two important implementations are used to compensate for natural irregularities, or aberration, of the eye's optics: a deformable mirror and a LCOS-SLM. Although deformable mirrors are widely used for this purpose, their performance alone is not enough to correct the large amounts of aberration in the human eye, and deformable mirrors are also susceptible to static electricity.

The LCOS-SLM is able to compensate for large amounts of natural aberration by a phase-wrapping method utilizing the continuity of the wavefront of a laser beam, but it corrects only a particular polarization component. To overcome these deficiencies and to counterbalance the two orthogonal polarization components and sequential processing taking the SLO image, Columbia researchers have adopted dual LCOS-SLMs.

The Columbia AO-SLO system sufficiently compensates for optical irregularities in the eye, improves the contrast of the SLO image, and allows for efficient high-speed imaging—a convenient attribute for busy clinics. These improvements pioneered by Columbia's particular system have furthered AO-SLO technology and have provided ophthalmologists, especially retina specialists, a new and effective way of producing high-resolution, cellular level images of retinas in a clinical setting.

AO-SLO in the Clinic

To examine diseased retinas at the cellular level prior to the advent of AO-SLO technology, researchers have been limited to looking at autopsy eyes that have been enucleated from the body. Although a great deal of information has been learned through these types of histologic studies, the stains used during the pathology procedure and the artifacts introduced during preparation of the retina further complicates the interpretation of disease processes at different stages.

In contrast, AO-SLO allows noninvasive, direct observation of the retina at a microscopic resolution comparable to that of histology, but happily for the patient, they are alive and well in the clinic! While the procedure is comfortable, it does require the patient to fixate on a target. Each procedure takes about 20 minutes per eye, and patients are normally in and out in usually less than an hour.

Research Studies

AO technology is currently only used at a handful of sites. For example, only one AO-SLO system is available in all of Europe. As the AO-SLO system is still relatively primitive at this time, it is currently only used in research studies.

For the Department of Ophthalmology's first AO-SLO study, researchers recruited approximately 200 patients of all different age groups, ethnicities, and demographics. Study subjects were scanned by the AO-SLO and a comparative database of normative patients was created. Dr. Tsang comments, "We explain to the patients that by

using the AO-SLO system, we hope to learn more about disease mechanisms, including why they have the disease and their rate of progression. It's up to the patient if they're interested in participating as a study subject and learning more. Once we image the study subject, we have a baseline. It is our hope that AO-SLO can offer earlier detection of disease progression. In addition, when a treatment comes along, this technology will let us know very early on if the treatment works, knowledge which could possibly shorten human clinical treatment trials from five years to one year."

Using the AO-SLO, scientists at Columbia have also looked at enhanced S-cone cells. S-cone syndrome is characterized by S-type cones overpopulating the retina at the

expense of other cone cells. It causes patients to lose vision that they would have otherwise obtained from the rod cells. Through AO, researchers can obtain a detailed visual picture of what is actually occurring in this syndrome.

The Department is considering other possible studies using the AO-SLO. This technology, for instance, could be informative in gaining greater understanding of retinitis pigmentosa (RP). In RP, the visual field constricts from the periphery of the retina. The AO-SLO could ideally be used for looking at the cone cells in the center of the constricting ring to determine if they are normal or not. Dr. Park is also especially interested in learning more about end-stage glaucoma, while Dr. Chang is intrigued by using AO to see the effect of drusen, the small accumulations of hyaline bodies underneath the retina. AO could also possibly provide information related to diabetic retinopathy or age-related macular degeneration.

Researchers at Columbia hope that eventually AO-SLO will become another useful tool in the arsenal of ophthalmic imaging techniques, providing ophthalmologists with greater insight into the cellular workings of the retina. ■

Jack Cioffi Appointment

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and Dr. Cioffi has extensive experience in the laboratory, clinic, operating room, and boardroom. In his role as chief medical officer at Legacy Health, Dr. Cioffi oversaw five hospitals and a children's hospital, which provided an array of health care services.

A cornerstone of Columbia University's Department of Ophthalmology is a medical team made up of globally renowned physicians, who are at the forefront of medical eye research, which is an area familiar to Dr. Cioffi. "I have an established history of having expanded a large research department and an eye institute. As chief medical officer, I was responsible for recruiting hundreds of gifted physicians and researchers with cutting-edge and complementary skill sets to manage and prevent eye disease."

Dr. Cioffi takes over the chairmanship from Stanley Chang, MD. During his time as chairman, Dr. Chang attracted a top-notch team of researchers and clinicians to the department, developed new faculty practices in New York and New Jersey, more than doubled the number of surgical cases in the Harkness Eye Institute, and dramatically increased research funding. Although Dr. Chang is stepping down as chair, he will continue his patient care, research, and teaching commitments. "I am so pleased and happy that Stanley is remaining fully active at Columbia," affirms Dr. Cioffi. "He is a vital member of the faculty and his value here cannot be overstated."

Dr. Cioffi's personality is warm and forthcoming, and he is quick to acknowledge that through the great work of the department's previous chairs, he stands on the shoulders of giants, proclaiming, "Under their leadership, Columbia ophthalmologists and scientists accomplished a series of 'firsts,' including the first use of lasers in medicine, the first human corneal transplantation in the United States, the first human retinal cell transplantation, and the first artificial cornea."

Grateful especially for the legacy left by Dr. Chang, Dr. Cioffi affirms, "A perfect groundwork has been laid for our department to lead ophthalmology training and vision research into the future. Dr. Chang has recruited great talent, both in research and clinical ophthalmology, and he developed a strong philanthropic base, which better secures us going forward."

Dr. Cioffi and Dr. Chang have been working closely together over the past months. "Dr. Chang has been extremely candid throughout this transition, providing insights so I can better interpret the complexities of the department. Thus, I am more effectively able to see the potential for building upon Dr. Chang's achievements and achieving my vision. I look forward to working alongside Dr. Chang to realize these goals." Dr. Chang is confident in his successor's ability. "Jack is a terrific individual with a great vision for further growth of this department, especially in the challenging times medicine is facing today."

Vision for the Future

Dr. Cioffi's overarching goal is for the Harkness Eye Institute to become the foremost department of ophthalmology in the country. "It's not often you get offered the opportunity to guide a celebrated Institute," Dr. Cioffi explains. "I plan to build upon the great foundation that is already in place and then add my vision, which is for us to be the top ophthalmology program in the country. We have that potential."

Dr. Cioffi's vision for the Harkness Eye Institute focuses on four primary areas he plans to address in the upcoming months and years: Clinical Services, Residency Training, Vision Research Growth, and the Aging Infrastructure of the Department.

Clinical Services

Dr. Cioffi supports the "Hub and Spoke" model as a vehicle to provide the highest quality and most efficient health care to more people. For the hub and spoke archetype, one site acts as a centralized principal base supporting connected satellite sites. To expand access to basic clinical services and diagnostics to more patients, Dr. Cioffi sees the opportunity for outreach offices, while high-end services—such as specialized surgery—would remain on the Columbia campus. He will also be exploring the possibility of developing ambulatory surgical centers (ASC) at other sites. In his previous position, Dr. Cioffi opened a highly efficient and successful ASC with outreach to a six-state region

and the Pacific Rim. Dr. Cioffi elaborates, "By recruiting the best physicians and cultivating both high-end and efficient clinical services, I believe the outreach potential for Columbia's Department of Ophthalmology is great, and I look forward to making it a reality."

Residency Training

Agreeing with the words of his mentor, "You will be known by those you train," Dr. Cioffi emphatically believes that one of the Department of Ophthalmology's core missions is to teach the medical leaders of tomorrow. "We have the unique ability to train practicing ophthalmologists, technicians, nurses, and researchers. Skilled clinicians and scientists come to us from around the world seeking the latest ophthalmic education, and our residency program is a focal point for training these future leaders. In order to be in the most elite group of training programs, we need to grow and enhance our educational capabilities, and I will work diligently to enhance the Department of Ophthalmology's residency training program to ensure it is one of the top tier educational platforms in the country."

Vision Research Growth

With his experience and proficiency in research, including having been continuously funded for 18 years by the National Institutes of Health (NIH), Dr. Cioffi wants to build upon Columbia's proud vision research history. "Our collaborations with scientists in other departments, such as neurosciences, biochemistry, and pathology, are critical to our future success, and I would like for us to strengthen and extend these collaborations going forward."

Creating a successful research program requires several key elements, according to Dr. Cioffi. "First, research programs that aim to answer vexing clinical problems are often more successful as they tend to be funded by the NIH, donors contribute to these programs, and patients directly benefit from these programs. Second, by following a 'Clinician-Scientist' model, both clinicians and scientists bring unique perspectives to a project, which is a great advantage and works hand-in-hand with a third important element, collaboration among scientists at Columbia. Finally, I believe in programmatic focus: I would rather the research program be world class in a select number of areas, than be broad based in too many areas. Columbia has been a research leader in retinal disorders and retinal genetics. At a minimum, I would like to add an increased glaucoma research endeavor to Columbia's portfolio, as retinal research and glaucoma research are very complementary, and the addition of glaucoma scientists would be extremely positive."

Aging Infrastructure

The aging infrastructure of the Harkness Eye Institute is a concern voiced by many, including Dr. Cioffi. "In order to attract and retain the best faculty, we must address the infrastructure issue. Due to the amazing fundraising success of the department in the past decade, I am confident that we can raise funds to revive the facility." New York-Presbyterian Hospital and Columbia University Medical Center have committed resources to Dr. Cioffi to renovate space within the Harkness Eye Institute, and they will jointly develop a short-term and long-term facilities plan. Dr. Cioffi has begun a formal space assessment, including current and projected space needs for research, faculty practices, resident clinics, eye surgery, procedural units, meeting and educational facilities, and administrative space. An informed decision too will be made about the advisability of renovating rather than building new space.

Moving Dr. Cioffi's vision forward will take dedicated leadership, and he plans to be as straightforward and transparent as possible. A tenet of Dr. Cioffi's is that a

good leader listens and learns. Since his arrival, he has been interviewing faculty members one-on-one to gain an understanding of their desires and aspirations. He is also conducting a series called "Lunch with the Chair" that enables staff members a chance to meet in a smaller setting and ask any questions that may be on their minds.

Background

At a young age, Dr. Cioffi was given the nickname of Jack, the acronym of his initials, G.A.C. He grew up in New England, and it was his undergraduate study of zoology that first piqued his curiosity in science. "I was intrigued by science, and particularly by genetics during my undergraduate years, and I realized early on that a medical degree would open up a world of possibilities, which I could then explore to the furthest reaches."

He was drawn to ophthalmology and the area of glaucoma for the surgical specialty it offered and for the patient relationships that develop due to the chronic nature of the disease. Dr. Cioffi elaborates, "Glaucoma impacts the entire age spectrum, and you get to know your patients over long periods of time. Treatment may begin in infancy and you are with that patient until they go off to college. In other cases, you treat someone as they are about to retire and stay involved

Department Ranks High in Research Funding

The Columbia Department of Ophthalmology ranked seven out of 65 Departments of Ophthalmology nationwide in dollars awarded by the National Institutes of Health (NIH) for vision research in 2011. This continues a forward trend by our Department. In 2010, Columbia was ranked 16, which was a significant jump from earlier years when our Department of Ophthalmology was ranked in the mid-twenties.

Total NIH funding was \$7,455,200. Additional grant applications are being submitted this year that will further expand our program depth in the research portfolio.

The credit for this substantial increase in ranking goes to our group of brilliant scientists led by Rando Allikmets, PhD, Director of Research. The generosity of our patients provides much of the seed funding for projects and allows our senior scientists, such as Janet Sparrow, PhD, and Carol Mason, PhD, to mentor our younger investigators to success by creating the preliminary body of work necessary to apply and receive research funding. We congratulate all those who made this wonderful news possible, and we look forward to advancing even higher in the future! ■

in their lives through their golden years. Physicians play a privileged role. There aren't many specialties in ophthalmology, nor in medicine for that matter, where you can contribute in all phases of a person's life and interact closely with their family. I feel truly blessed to be entrusted with the long-term care of my patients." Dr. Cioffi's role as a physician will continue at the Harkness Eye Institute, where he will be interacting with glaucoma patients clinically and surgically.

For Dr. Cioffi, several personal factors drew him to Columbia University's Department of Ophthalmology. "First it was the storied history of the Harkness Eye Institute itself. It holds a special place in American and worldwide ophthalmology in terms of the greats who have walked these halls. Second, Columbia University is an academic institution beyond compare. Finally, there is an undeniable combined appeal of being part of a world-class eye institute, at a world-class university, in a world-class city."

Dr. Cioffi, his wife Linda, and their two children, William and Elizabeth, are excited about moving from the Pacific Coast and living in New York. With their extended families scattered up and down the Eastern Seaboard, they are looking forward to being closer to home.

With the roadmap he has laid out, Dr. Cioffi reflects on the upcoming months and years ahead, "We truly have the opportunity here to do real and permanent good, which is an awe inspiring and humbling thought. I am honored to be at this celebrated institution, and I look forward to working together with this fine community to accomplish many great things." ■

Columbia Ophthalmology Consultants Opens New Satellite Office in New Jersey

Bryan J. Winn, MD, has opened a satellite office in Ridgewood, New Jersey, to offer a convenient alternative to patients. This move signifies a new presence for Columbia Ophthalmology Consultants outside of Manhattan.

Specializing in ophthalmic plastic and reconstructive surgery, Dr. Winn performs critical reconstructive procedures that positively impact on both the physical and emotional well-being of a patient, such as rebuilding areas of the face after trauma or skin cancer removal, eyelid surgery to resolve congenital or age-related changes, and tear duct and orbital surgery. In addition, Dr. Winn offers a wide array of aesthetic procedures, including brow, cheek, and lid lifts in addition to Botox and dermal fillers.

Having grown up in northern New Jersey, Dr. Winn is excited to work in a location that he describes as close to his heart. He also feels that his specialty and choice of location will be of benefit to his patients. "It turns out that a third of my patients who see me in Manhattan actually come in from New Jersey, so it's a natural place to go. The area has also been underserved for the particular treatments I offer," notes Dr. Winn.



Bryan J. Winn, MD

Dr. Winn is an Assistant Professor of Clinical Ophthalmology at Columbia University Medical Center, board certified in ophthalmology, fellowship trained in oculofacial plastic surgery, and a fellow of the American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS). Dr. Winn graduated *summa cum laude* from Amherst College where he was elected to the Phi Beta Kappa honor society. He received his medical education at the Columbia University College of Physicians and Surgeons, where he graduated at the top of his class and was elected to the Alpha Omega Alpha honor society.

In addition to tending to his practice, Dr. Winn is the Associate Residency Program Director and Director of Medical Student Education for the Department of Ophthalmology at Columbia University College of Physicians and Surgeons, and he is responsible for teaching the ophthalmology residents oculofacial plastic surgery.

Dr. Winn's New Jersey office is located at 119 Prospect Street, Suite 1, Ridgewood, New Jersey, 07450; the office telephone number 201-445-0444. Dr. Winn continues to see patients at the Harkness Eye Institute and Columbia's midtown Manhattan east side office located at 880 Third Street. For more information about Dr. Winn, please go to www.ColumbiaEyelidSurgery.com.

NEI Grant

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provide more efficient treatment to patients. The University of Pennsylvania and the Telethon Institute centers are working on the adeno-associated virus delivery systems.

"Gene therapy is likely the cure for recessive diseases," notes Dr. Allikmets. "In recessive diseases there is not enough gene activity, so the gene is not working properly. If you give the patient the working gene, that should, theoretically, alleviate the problem and resolve the disease."

Gene therapy works especially well in early stages of a disease where a large number of cells are still alive. In severe late cases, gene therapy would likely not be successful because there are fewer cells or possibly no cells available in which to insert the normal gene.

• **Module 4** addresses small molecule therapy, which is performed primarily by Dr. Petrukhin in collaboration with Drs. Sparrow and Allikmets. Dr. Petrukhin, who brings 10 years of drug development from Merck & Co., Inc., and colleagues are working on compounds that can modulate the visual cycle by slowing down the uptake of vitamin A or by interacting with key proteins in the cycle. These molecules are identified by three complementary strategies: high throughput screening of large libraries of small molecules, optimization of known leads derived from chemical structures, and in silico screening of virtual compound libraries.

While small molecule therapy is not a cure for Stargardt's, its critical role would be in slowing down the progression of disease. Theoretically, gene therapy and small molecule therapy could be used concurrently. Small molecule therapy would be used to slow the disease progression so gene therapy could be introduced to treat the disease even at later stages.

Through the focused work of the many gifted researchers at Columbia University, and their talented and dedicated partners involved in this multicenter study, treatment for Stargardt disease and other genetic retinal disorders, which was once thought to be unattainable, is now closer at hand than ever before.

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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