UH Eye Institute/Year in Review /partial draft
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Rick Middleton

Story #1: VSRC - Pearlman

HEAD: Expanding the Boundaries of Visual Science

COPY: University Hospitals Eye Institute is helping to blaze new trails in the visual sciences. And an essential part of that effort is our commitment to research.

Within the Visual Sciences Research Center (VSRC), our vision is to carry out the most far-reaching, high-impact, and relevant research in the visual sciences. It is divided into three major areas:

1. Visual impairment and blindness due to retinal function disorders.
2. Visual impairment and blindness associated with aging and diabetes.
3. Visual impairment and blindness due to infectious diseases, immune responses and inflammation.

This year, we've made great strides in several areas. Our recruitment efforts have been strong, and we've brought exceptional researchers to VSRC. We now have seven full-time faculty members, and will have eight by the end of the year. In addition, we work with 20-to-30 investigators who interact with us in related areas like immunology, pharmacology, molecular biology, genetics and pathology.

We've cultivated a highly collaborative environment, where we foster interactions between physicians and scientists who have expertise in many key areas. Our goal is to grow and expand all of our research programs and continue to attract grant funding over the next 3-5 years. The university is highly supportive of our work and they've given us an excellent space for research.

SUBHEAD: VSRC Specifics

COPY: VSRC researchers are located in the newly renovated Department of Pharmacology in the Wood Building, and the Department of Ophthalmology and Visual Sciences on the first and third floors of the Institute of Pathology building.

VSRC investigators at CWRU have over 20 National Eye Institute (NEI) grants, which allowed us to apply for the maximum $2.5 million NEI funding for Core Grants, awarded in 2007. This grant has been invaluable to vision researchers since the first successful submission in 1997. The

recent renewal includes Molecular Biology, Tissue Culture and Hybridoma, and Histology, Microscopy and Imaging modules.

We have also received the T-32 Training Grant from the National Institutes of Health. The T-32 grant was renewed in 2005 by Dr. Susann Brady-Kalnay in the Department of Molecular Biology and covers post-doctoral salaries in addition to graduate student stipend and tuition. The T32 grant has supported numerous students, and we propose to expand the role of the visual sciences using the attraction of the T32 grant and blindness foundation fellowships to encourage graduate education in this area.

The VSRC also offers a graduate course (Pharm 432) on the Biology of Vision. The course is offered to students in the Pharmacology, Pathology and Neurosciences programs. We plan to expand this to a two-part course to include clinical diseases, inflammation, and new technologies for vision research including proteomics and imaging.

As you can see, we've fostered a rich environment where we can continue to develop cutting-edge research and findings that lead the discipline.

This past year, 2008, represents a significant step forward in our visual science research efforts. And the coming years hold the potential for even more discoveries and new findings that will add to our knowledge – helping us unlock the mysteries of eye disease and develop hopeful new treatments for our patients.

Eric Pearlman, Ph.D.
Professor and Director of Research
Department of Ophthalmology and Visual Sciences

Story #2 – Eye Institute Centers of Excellence

HEAD: Centers of Excellence

COPY: The University Hospitals Eye Institute, inaugurated in 2008, is the culmination of the impressive growth and development of the Department of Ophthalmology and Visual Sciences over the past 15 years.

The Eye Institute is comprised of three Centers of Excellence:

- The Center for Anterior Segment Diseases and Surgery
- The Center for Pediatric Ophthalmology and Adult Strabismus
- The Center for Retinal and Macula Diseases and Surgery

Together, these Centers of Excellence meet a variety of growing needs in the community, offering the latest treatments to patients while remaining accessible to all individuals who need a high level of care. The Centers of Excellence embody University Hospitals' model of translational medicine by providing superior care in an academic environment, as well as ample opportunities for caregivers to educate patients and the community at large about important issues related to vision care.

Eye Institute physicians are actively engaged in vision research through the multi-departmental activities of the Visual Sciences Research Center (VSRC).

Story #3 - Naomi Singer

HEAD: Naomi Singer: A Passion for Vision

COPY: Naomi Singer will never forget her first glimpse of the pediatric ophthalmology program at University Hospitals Rainbow Babies & Children's Hospital.

"They brought me to a room where a woman was standing over a five-month-old infant, placing contact lenses on the baby's eyes," she says. "It was such delicate work. Later I found out the woman was Dr. Loretta Sczcotka-Flynn. I also learned how important her work is, and that she is helping children who otherwise would lose their ability to see."

For Mrs. Singer, this important work struck a deep nerve. As a child growing up in Akron, Ohio, she struggled with her own vision problems – a disability that often left her feeling like an outsider.

"I was myopic – in other words, near-sighted. They told me my vision was 20/200," she recalls. "The Akron Public Schools had a special program, called 'Sight-Saving Classes,' for visually impaired children. The idea was, if the children were not required to do challenging things, they could 'save' their vision. So we did not write in cursive or attend gym class or read music."

For most of her life, Mrs. Singer wore thick glasses. And she was determined to overcome her limitations. After leaving Sight-Saving Class in the eighth grade, she enrolled in high school but refused help from a state-provided tutor.

"The tutor's job was to go to classes with me and read my assignments aloud," she says. "I refused. I wanted to be like the other kids. So I told my mother and our doctor that I was going to read all of my work. They were skeptical but let me try. And I did it!"

Internalizing the advice of Sight-Saving teachers who taught the children to "never feel sorry for yourselves," Mrs. Singer has worked hard to ensure that vision problems are not a disability. She graduated from Ursuline College, taught herself to play tennis (after age 40), and eight years ago had cataract surgery. "I can see things that I never could before," she says.

SUBHEAD: Advocate and Philanthropist

COPY: Today, Mrs. Singer is a champion for those whose vision problems are jeopardized by disease or dysfunctions. And she is an avid supporter of the work of Dr. Sczcotka-Flynn.

"She works with corrective contact lenses that help a child retain vision until he or she is done growing. At that point, corrective surgery becomes an option," she says. "But the lenses are necessary so the child does not go blind. And what frustrated me was learning that people were unable to afford these lenses. It's not only uninsured people, but many people with insurance find out that the lenses are not covered. I could not believe that when I heard it."

Naomi and her husband, Ed Singer, along with several friends, started a unique endowment fund at Rainbow Babies & Children's Hospital which helps many families pay for the corrective lenses. And the Singers have also hosted fundraisers at their Pepper Pike home for Dr. Sczcotka-Flynn's work.

"I hope the Eye Institute will grow and expand its reach," she says. "People need to know that there is a place where they can get excellent care."

Story #4: Irina Pikuleva

HEAD: Cholesterol and Vision: Understanding a Key Connection

COPY: Irina Pikuleva, Ph.D., arrived in Cleveland a month later than she expected.

The distinguished researcher was supposed to leave her post at the University of Texas Medical Branch in Galveston at the end of September, 2008, and begin work at Case Western Reserve University on October 1. However, Hurricane Ike changed those plans – and impacted her research.

"When the hurricane was approaching, everyone in Galveston was told to evacuate," she recalls. "We shut down our lab and left the island. The hurricane hit on September 13 and Galveston was flooded for 10 days."

The hurricane damaged Pikuleva's lab. "Electrical power was lost, and everything in our freezer was ruined," she says. "We had to wait several days for our supplies to dry out. We salvaged what we could, but in some areas we are starting over."

Pikuleva finally arrived in Cleveland at the end of October, continuing her groundbreaking research into cholesterol metabolism and how it relates to age-related macular degeneration (AMD). Her research is critically important for understanding the development of certain eye diseases that reduce vision. Cytochrome P450 (P450 or CYP) enzymes metabolize a wide variety of substrates and play key roles in many biological processes.

SUBHEAD: A Rich Environment for Research

COPY: Pikuleva is pleased to bring her research to CWRU, which provides an ideal base for collaboration and analysis.

"Case Western is highly ranked and offers the opportunity to collaborate with great people," she says. "There is tremendous expertise in so many areas, and this allows a researcher to bounce ideas off people who have great expertise."

While Pikuleva has studied the impact of cholesterol for many years, it is only in the past few years that she has studied its effect on vision.

"Cholesterol is a key area for all types of health research," she says. "We know it is important to cardiovascular health. It is a factor in the development of Alzheimer's disease. And now, we are seeing a link to adult macular degeneration."

Pikuleva's research examines the foods that individuals eat, and how those foods impact how cholesterol is synthesized and eliminated in the human body. Enzymes in the body determine how cholesterol is catalyzed. As Pikuleva says, her research asks, "Can we increase the efficiency of those enzymes? Can we do anything to make enzymes work more effectively?"

SUBHEAD: Diet and Drugs Show Promise

COPY: Pikuleva is exploring specific areas where nutrition can make a difference in the body's ability to regulate cholesterol.

"We know that people do not get enough fish oil in their diets," she says. "We are investigating whether fish oil will make the enzyme more effective in regulating cholesterol. The average person needs two 'oily fish' meals per week to achieve an optimum level, but most people don't eat fish that often. So we're looking into the viability of using supplements to compensate for that."

In addition, pharmacological advances are offering promising solutions. Drugs are being developed which will help enzymes work more efficiently so that cholesterol can be brought under control. However, Pikuleva notes the key link in this process has not been firmly established.

"We're exploring an interesting hypothesis," says Pikuleva. "If we see a deficiency in the body's ability to process cholesterol, we know the metabolism is impaired or degraded. It can be compared to a fracture, if you will. The question is: how can we repair this fracture?"

Her lab is currently conducting several investigations to answer this question. Researchers are exploring whether the enzymes' processes can be stimulated, either through dietary supplements or other interventions. Pikuleva realizes that patience is a virtue in her line of research.

"We have to wait a long while to understand what happens to the enzyme process," she explains. "We look at cholesterol levels for people in middle age, and we explore how those levels eventually result in Alzheimers or macular degeneration when those same people reach their later years. It's a long process."

Pikuleva appreciates the rich collaborative environment of UH Case Medical System, where physicians and researchers can share their knowledge.

"I'm in basic research, but I collaborate very closely with physicians who see patients all day," she says. "This relationship has tremendous benefits for research. For example, when we are developing a research project, we

might receive some extremely valuable input from a physician who can describe the trends he is seeing. That's critically important to our research efforts."

Story #5 – Eileen Butler

HEAD: The Gift of Vision: Eileen Butler is the "Perfect Patient"

COPY: Ask a group of people if they'd ever consider participating in a clinical trial and many will reply with a quick "no." Thankfully, however, enough brave people answer "yes," and their contributions are helping many of the finest research institutions in the world unlock medical mysteries and develop new procedures to enhance human health.

Berea resident Eileen Butler is one of those who answered the call. Her participation as a research volunteer is helping the Vision Research Coordinating Center at University Hospitals Case Medical Center (UHCMC) conduct one of the largest (and most advanced) long-term clinical trials in the study of visual health. Sponsored by the National Institutes of Health/National Eye Institute, the Cornea Donor Study (CDS) is a nationwide effort – and Butler has proved to be the "perfect patient" for this investigation.

Diagnosed with cataracts many years ago, the now 81-year-old Butler knew she was faced with continued vision loss and possibly blindness. What this spry woman didn't know was that she also had Fuchs' Dystrophy in both eyes. Fuchs' Dystrophy is a suspected genetic vision disease affecting the corneal endothelium, the delicate back cell layer of the cornea that keeps the cornea clear. As her vision worsened, Butler was treated by Dr. Jonathan Lass, Professor and Chair of the Department of Ophthalmology and Visual Sciences at UHCMC and Case Western Reserve University. According to Lass, the only realistic treatment was to receive corneal transplants on each eye.

The surgeries were successful, and Butler was pleased with her improved vision. And in the spirit of gratitude, she eagerly enrolled in the Cornea Donor Study, a trial that has the potential to restore vision to thousands of people every year.

"I really didn't have an expectation of anything at all by participating in the study. I just knew I liked to help people; I have long donated blood, and if this would help too, I wanted to be part of it," says Butler.

SUBHEAD: National Study Provides Key Insights

COPY: The CDS is a long-term study that began in 2000. It was designed to determine whether the graft success rate (over a 5-year period) of corneal tissue from donors older than 65 years of age is equivalent to tissue from younger donors less than 65 years of age. The study recruited 1101 patients across 80 sites and 31 eye banks nationally; UHCMC enrolled 33 of those patients, including Eileen Butler. The study is led by Dr. William

Reinhart, Professor in the Department and head of the Cornea Service at UHCMC. Reinhart is also Medical Director of the Cleveland Eye Bank.

The CDS study produced startling results, demonstrating that cornea transplants from older donors have similar rates of survival as transplants which use tissue from younger donors. The five-year transplant success rate was 86% for donors 66-75 years of age – the same success rate reported for those donors in the 12-65 year age group.

More than 33,000 corneal transplants are performed each year in the United States. Locally, northeastern Ohio averages 600 transplants per year, but meeting the demand for organ donation continues to be a struggle. However, by showing that "age doesn't matter," the study gives health care providers hope that a greater number of donations will be possible.

"The study outcome plays an important role in the future of corneal transplants and the ability to increase organ donor participation nationwide," said Lass. "By validating the health of the cornea regardless of the chronological age of the donor, we have a greater capacity to treat patients who would otherwise have to wait longer for transplant due to an insufficient supply of cornea donations."

SUBHEAD: Transplant Restores Vision and Vitality

COPY: For Butler, one of the first to enroll in the CDS, the corneal transplants have meant a return to business as usual. This energetic, self-described "someone-who-doesn't-like-to-sit-around" woman has no use for idle time. Her first love as a draftsperson led her in 1996 to study AutoCad, where her skill has allowed her to develop a flair for kitchen design along with her other hobbies of sewing, knitting and woodworking.

This grandmother of three and great-grandmother of two designed and built her own custom cabinetry, and in 2008 she partnered with a friend to showcase her talents at a Holiday Bazaar. "I couldn't imagine having the same quality of life without my hobbies," she says. "I now have excellent vision, but the important thing is that I am helping other people, not just myself."

Story #6: Johnny Tang

HEAD: Mapping New Pathways for Vision

COPY: Johnny Tang, M.D. sees an important common theme in many retinal diseases. And finding those common links is something that comes naturally to Dr. Tang, a physician-researcher who embodies the collaborative philosophy of UHCMC.

Tang joined the Case School of Medicine Ophthalmology Department in 2007 after a research fellowship at Harvard Medical School. He is trained as a vitreoretinal surgeon, uveitis specialist and retinal electrophysiologist. His research on age-related macular degeneration (AMD) has led to his hypothesis that a majority of common retinal diseases – retinitis pigmentosa, Stargardt's Disease, Leber's hereditary optic neuropathy and AMD – share common problems in their pathways of retinoid flow and rhodopsin metabolism.

"If we can understand the pathways, the results may be universally applicable to the entire group of retinal diseases," says Tang. His research focuses on the role that retinoid flow has on a wide variety of retinal diseases including inherited retinal dystrophies and age-related macular degeneration.

"Retinoid flow is the most fundamental aspect of human vision, and without it, sight cannot take place," he explains. "Looking at this retinoid cycle is a wonderful place to look for answers to solve our most challenging questions regarding disease mechanisms and to look for treatments."

As Tang explains, cone function is important in daytime vision and illuminated environments. However, there is greater understanding of rod function, due to extensive research on animals that primarily rely on their night-time vision.

"There is a generalized deficit in the knowledge of cone physiology and pathophysiology compared to rod physiology," he says. "But in modern-day living, humans are more reliant on cone function than rod function."

SUBHEAD: Slowing the Spread of Disease

COPY: Tang's research is looking into the possibility of a pharmaceutical solution to macular degeneration. As Tang explains, drugs can help reverse the mutations that lead to macular degeneration.

“The mutation generates an amount of what I refer to as ‘garbage,’ or waste product,” he explains. “If the body can’t regulate it, the waste will build up and kill healthy material. Now, if we can slow that development with the right pharmacologic interventions, we can prolong healthy function.”

As a practicing physician, Tang experiences the frustration of seeing patients with vision problems but having no solutions to offer. “That’s what got me interested in research,” he explains. “I thought there’s got to be something we can do to learn about these conditions and hopefully find effective treatments.”

Not surprisingly, he is a great proponent of the Eye Institute’s model of translational research.

“It’s another great reason for patients to come to University Hospitals,” he says. “This model of patient care helps us excel as physicians and as researchers.”

Story #7 – Paul Park, Ph.D.

HEAD: Paul Park Unlocks Medical Mysteries

COPY: For Paul Park, Ph.D., vision research is similar to detective work: a never-ending quest for more information, continually asking questions, and seeking to understand the mysteries of human vision.

The Canadian-born researcher is Assistant Professor in the Department of Ophthalmology and Visual Sciences at CWRU. His work is centered on understanding the mechanism of action of rhodopsin and other G protein-coupled receptors. Rhodopsin is a pigment of the retina that is responsible for both the formation of the photoreceptor cells and the first events in the perception of light. Rhodopsins belong to the G-protein coupled receptor family and are extremely sensitive to light, enabling vision in low-light conditions.

"Rhodopsin is found in the rod outer segments of the retina," he says. "It initiates transduction, which is a set of biochemical events that occurs in the initial stage of vision."

According to Park, small details are all-important.

"If you don't know the details at the molecular level, you won't understand how the entire system works," he explains. "In the 1980s and 90s, much of our research was in the genetic area. That helped us learn who the players are. Now, we are asking deeper questions. For instance, we want to know how things come together and create the mechanisms that provide vision. And once we understand the system, we can see the ways in which disease disrupts the system. We ask, 'What goes wrong?' And that helps lead us to effective treatments."

Park is working to develop an accurate molecular description of the action of G protein-coupled receptors (GPCRs). GPCRs represent the largest class of cell surface proteins.

"This family of proteins is involved in virtually every physiological process," he says. "Dysfunctions in these systems can lead to diseases such as blindness, addiction, diabetes and heart disease. Understanding the molecular mysteries of these systems will lead to the development of more effective therapeutic solutions."

Park's lab is also focused on the mechanism of receptor action. "The goal is to unravel the molecular and temporal mysteries of GPCR-mediated signaling events, which will allow us to better understand the mechanism by which the receptor carries out its activities," he explains.

New technology has greatly enhanced research in this area, Park notes. “A hundred years ago, they were asking the same questions. But the resources limited what they were able to do. Today, we have advanced technology like light microscopy with incredible resolutions. We can revisit these classical experiments and come up with better data and much finer detail than was possible in the past.”

Story #8 – Blake story (still needed?)

Story #9 – Dr. Reinhart retirement / Dr. Burney celebrates 25 years (still needed?)