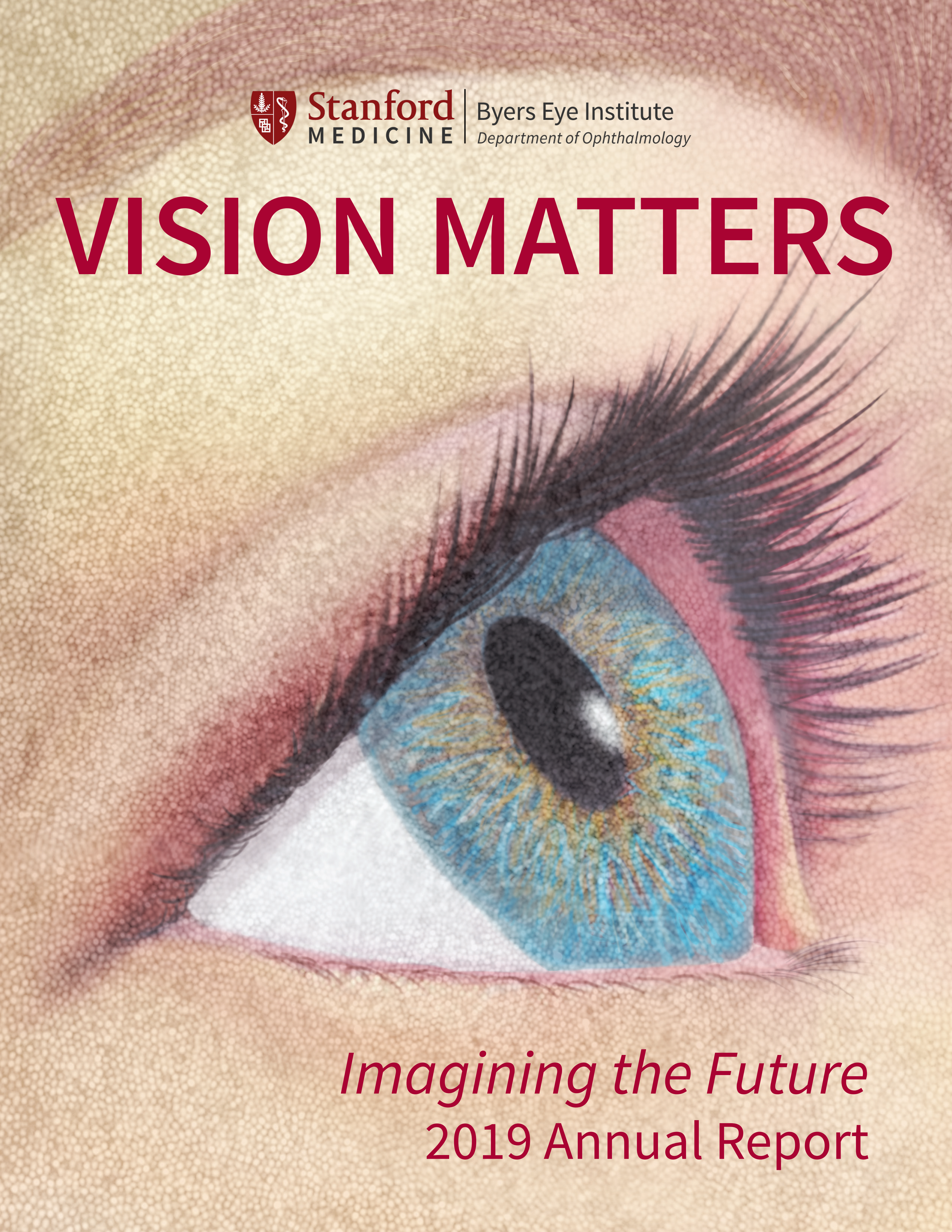
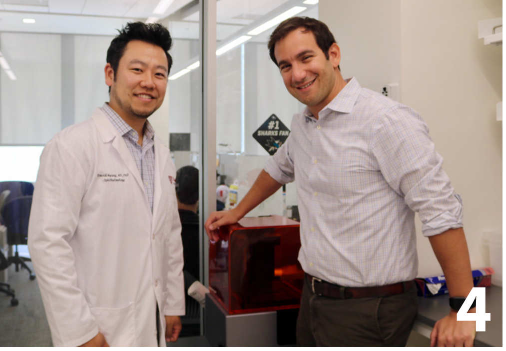


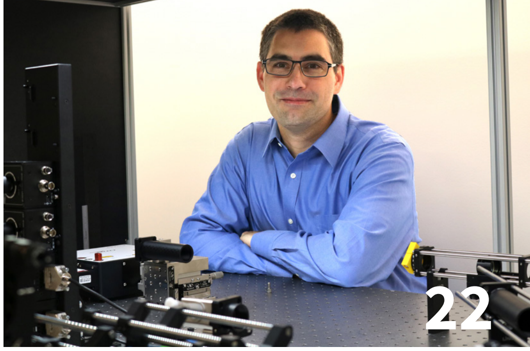
Stanford MEDICINE | Byers Eye Institute
Department of Ophthalmology

VISION MATTERS

Imagining the Future

2019 Annual Report





VISION MATTERS: *2019 ANNUAL REPORT*

On the cover: Adaptive optics imaging of the photoreceptor mosaic forms the background for this illustration by Alton Szeto, MFA, © 2019. See cover story, page 22.

Editor-in-chief Kathryn Sill

We gratefully acknowledge additional writing by MaryAnn Mahajan; copy editing by Susan Monroe of Written Right; additional photography from department faculty and residents; Carmel Mercado, MD; Janelle Silva; @JaseKellyMaui Photography; Lifeline Express; Oculeve; Lopa Y. Gupta, MD; Paul Keitz Photography; Peggy Kixmoeller; Stanford Medical History Center; Himalayan Cataract Project: Michael Amendolia, Amanda Conde, and Ace Kvale.

A note from our Chair

Every day I count it a privilege to work alongside such incredible colleagues here at Stanford. I witness our faculty, residents, fellows, and staff going above and beyond in pursuit of vision restoration and comprehensive vision care. This is displayed in their advancement of groundbreaking research in genetics, stem cell medicine, imaging, neuroscience, and engineering, to education of the next generation of clinicians and vision scientists, to development of eye care programs globally.

A few recent steps to be proud of include Dr. Daniel Palanker's photovoltaic retinal prosthesis for restoring sight in retinal degeneration that reported positive results in a clinical feasibility trial (page 6); our new educational initiatives including the Ophthalmic Innovation Fellowship (page 5) and the Stanford Ophthalmology Advanced Research (SOAR) Residency Program (page 18); developing novel instrumentation for advanced diagnostics (pages 4, 22, 24, and 26); and opening the Mary M. and Sash A. Spencer Center for Vision Research at the Byers Eye Institute (page 13).

While I have the honor of witnessing such accomplishments daily, my hope is that this inaugural department report gives you a glimpse into our department's vision and recent achievements, and in what ways everyone is participating in imagining the future of eye care, and then working diligently to bring creative ideas into reality.

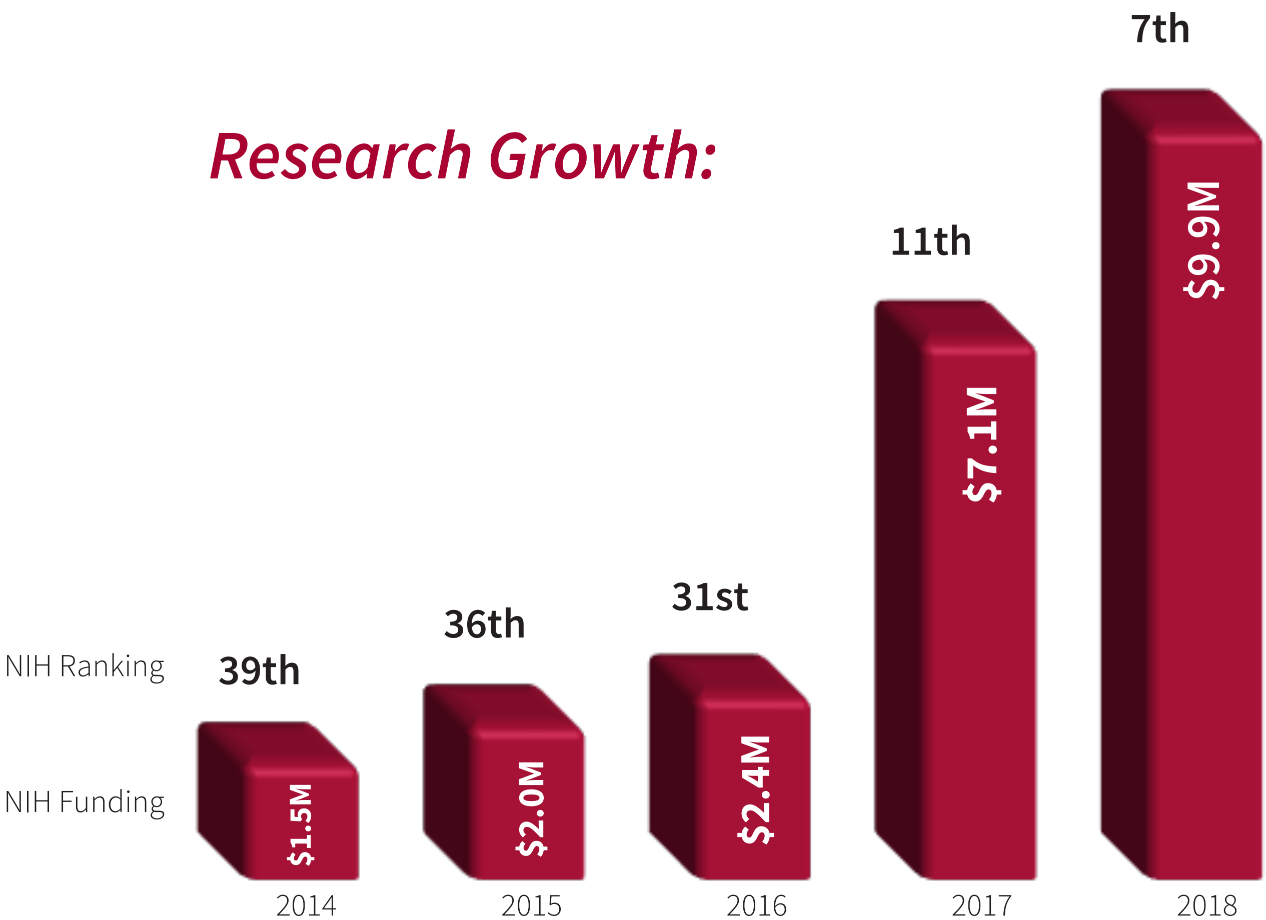
As our department continues to grow our commitment to patient care, research, and education, I want to express my immense gratitude to our faculty and staff, donors, colleagues, alumni, patients, and community for all you bring to building a preeminent department of ophthalmology.

Jeffrey L. Goldberg, MD, PhD
Professor and Chair, Department of Ophthalmology
Byers Eye Institute at Stanford University

Byers Eye Institute

by the numbers

Research Growth:



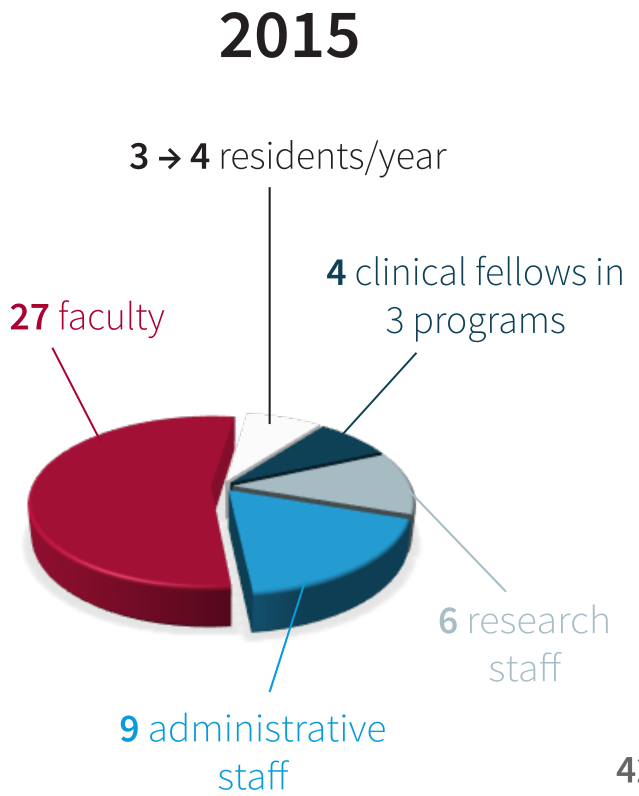
Source: Blue Ridge Institute for Medical Research

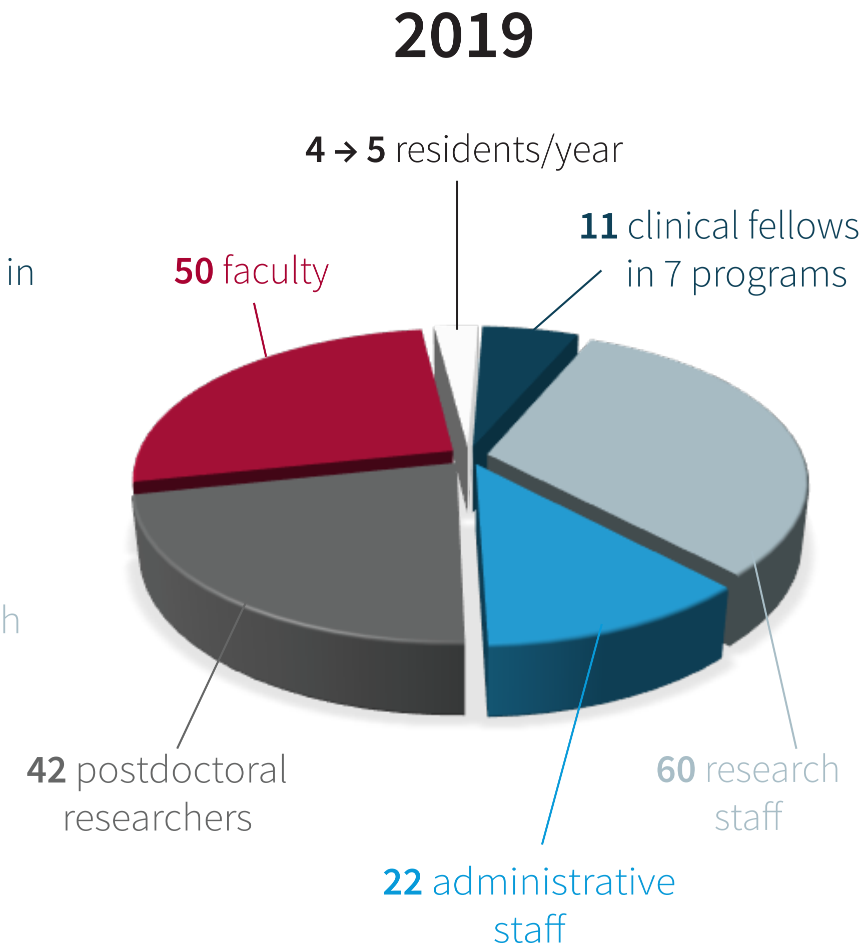
ACTIVE AWARDS
107

TOTAL NIH AWARDS
23

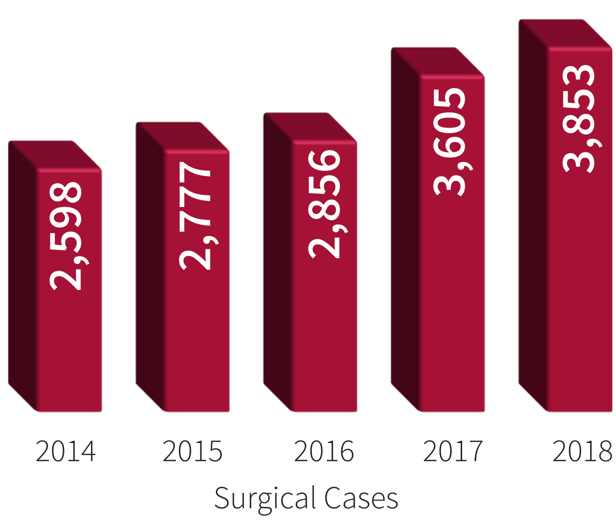
ACTIVE CLINICAL TRIALS
42

Our Team:

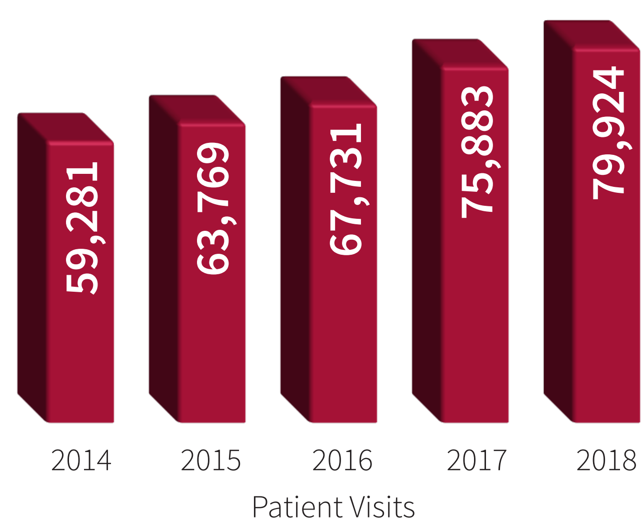




In the OR:



In the Clinic:



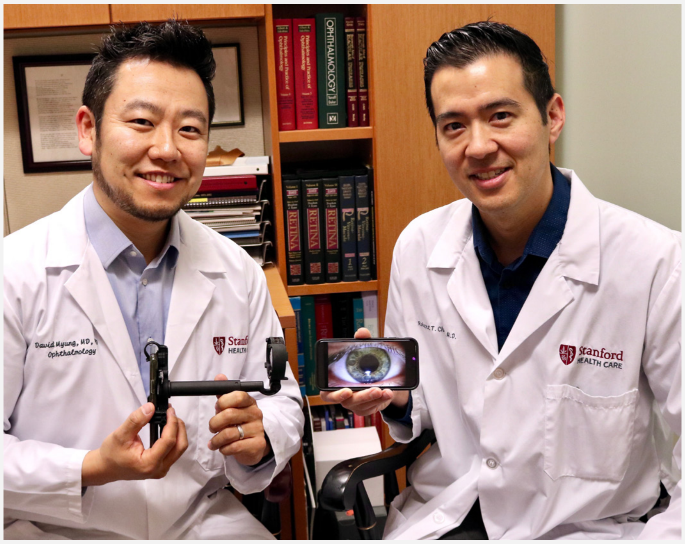
Invented at Stanford

The Stanford Department of Ophthalmology has a **rich history of innovation** and academic accomplishment dating back more than 100 years. In both engineering and biological sciences, Stanford has often led the translation of lab-based advances into clinical diagnostics and therapeutics.

"Stanford is well known for spinning out technologies and inventions and for collaborating with partners in Silicon Valley," said **Mark Blumenkranz, MD,** H.J. Smead professor emeritus of ophthalmology.

Blumenkranz, chair of ophthalmology from 1997 to 2015 and the inaugural director of the Byers Eye Institute from 2010 to 2015, has been a driving force behind a number of successful innovations, adding to a list of Stanford contributions to ophthalmology that started in the 1960s. In the late 1960s and early 1970s, two volunteer faculty members, **Hunter L. Little, MD,** and **H. Christian Zweng, MD,** helped invent the first slit lamp-based ophthalmic laser delivery systems. In the mid-to-late 1990s, novel research in retina and cornea moved from Stanford labs to patient care. Starting in 1998, multiple cutting-edge diagnostic, therapeutic and surgical tools were developed in the laboratory of **Daniel Palanker, PhD,** professor of ophthalmology and director of the Hansen Experimental Physics Laboratory, and then commercialized in conjunction with pharmaceutical and device companies in Silicon Valley, helping millions of patients worldwide. (See timeline on pages 8-9.)

"**Innovation** is critical to **advancing progress**, because the world is moving at a rapid pace in terms of *information technology, molecular biology, imaging, and globalization*. Leveraging those advances allows us to **deliver care** that results in **better access and outcomes for patients**."



David Myung, MD, PhD, (left) and Robert Chang, MD, display the Paxos Scope, an ophthalmic camera system for smartphones they helped invent.

Many of these "invented at Stanford" successes have leveraged the breadth and depth of the Stanford community, such as the invention and subsequent commercialization of **TrueTear**, a neurostimulation device that activates tearing from the lacrimal gland and is now clinically available for patients with dry eye disease. **Michael Ackermann, PhD,** a Biodesign fellow (see below) and then vision research postdoctoral fellow with Palanker, led a development team in conjunction with others including **Andrea Kossler, MD,** assistant professor of ophthalmology, and **Christopher Ta, MD,** professor of ophthalmology. In addition to prototyping and validating the technology's efficacy clinically, they formed a company **Oculeve** that was later acquired by **Allergan**.

"Being a biodesign fellow and then vision research fellow and postdoctoral fellow at Stanford was an incredible and pivotal two years for me," Ackermann said. "That time helped me make the transition from scientist to entrepreneur, all while gaining ophthalmology experience under the training of phenomenal faculty."

Blumenkranz, who helped commercialize Oculeve, agrees.

"Innovation is critical to advancing progress, because the world is moving at a rapid pace in terms of information technology, molecular biology, imaging, and globalization," Blumenkranz said. "Leveraging those advances allows us to deliver care that results in better access and outcomes for patients."

Establishing the Ophthalmic Innovation Program

Recognizing a successful formula linking identification of unmet needs to discovery, invention, and commercialization, Blumenkranz established the Ophthalmic Innovation Program in 2015. This educational program provides a **unique, one-year post-graduate fellowship for clinicians and scientists**. Fellows are taught the necessary steps to take an idea from conception to clinical use. **David Myung, MD, PhD,** assistant professor of ophthalmology and, by courtesy, of chemical engineering, has co-directed the program since its inception.

"Each year the fellow participates in hands-on projects, formal coursework, close mentorship, and networking and internship opportunities with members of the department, other Stanford departments, Silicon Valley innovators, and colleagues at the Center for Devices and Radiological Health at the Food and Drug Administration (FDA)," Myung said.

This year's fellow is **Frank Brodie, MD, MBA,** whose research includes development of a novel intraocular implant to assist in cataract surgery and custom-printed 3D glasses to help the vision of children with craniofacial abnormalities develop correctly. Through a non-profit organization he started, **The Loving Eyes Foundation**, these glasses are then given to the children at no cost.

"This fellowship is unlike any other," Brodie said. "It is an incredible, unprecedented opportunity to do translational research, learn the process of innovation hand-in-hand with regulatory science, and develop transformative ophthalmic products."

Synergies with Biodesign

Several ophthalmology faculty members are alumni of the **Biodesign Faculty Fellowship (BFF) program** within the **Stanford Byers Center for Biodesign**. **Robert Chang, MD,** assistant professor of ophthalmology, was part of the second BFF class from 2015–2016 and continues to teach medical innovation focused around digital health. One of his original contributions is the creation of the health design sprint, a week-long project-based learning experience leading students through the challenges in starting a health care company.

"We are not just training excellent doctors and researchers but also passing on the innovation method and the entrepreneurial spirit to the next generation of leaders in ophthalmology and vision research," Chang said.

Frank Brodie, MD, MBA, and David Buickians work together on understand-ing the behavior of a novel intraocular implant using a computer-aided design simulation.

Scan the QR code to view more information on inventions from Stanford

https://stan.md/2MCXYaE

Department history and innovation

photo courtesy of Stanford Medical History Center

1855 The Stanford Department of Ophthalmology traces its roots back to the Cooper's Eye, Ear and Orthopedic Infirmary and later, Cooper Medical College

1908 Stanford University absorbs Cooper Medical College as Stanford School of Medicine

1959 Stanford Medicine moves south to Palo Alto under the direction of Acting Chief of Ophthalmology **Jerome Bettman, MD** (1958-1959)

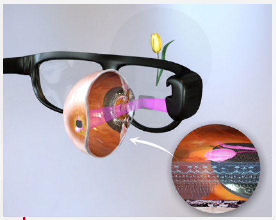
1984 Stanford's Division of Ophthalmology splits from the Department of Surgery with **Michael Marmor, MD,** as the founding chair

1992-1997 **Peter Egbert, MD,** serves as department chair

1997-2015 **Mark S. Blumenkranz, MD,** serves as department chair. Under his leadership, the **department doubles its full-time faculty to 27**

1998-2011 The **Pulsed Electron Avalanche Knife (PEAK)** was invented by **Daniel Palanker, PhD,** and acquried by Medtronic in 2011

2004-2017 Blumenkranz and Palanker invent two laser systems—the **PAttern SCAnning Laser (PASCAL)** and the **Femtosecond Laser System** and both are acquired by different companies



2005-2018 Palanker and his lab invent a photovoltaic retinal prosthesis, licensed to Pixium Vision as the **PRIMA implant**

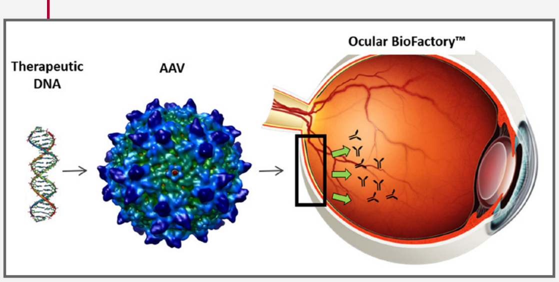
2010 Blumenkranz and Palanker develop a smartphone-based app, **SightBook**, for evaluation of visual function at home, and web-based connection of patients with physicians; it is later commercialized

2010-2017 The concept of neuromodulation to stimulate abnormally low production of tears in dry eye patients is patented and commercialized by Biodesign students and spearheaded by **Michael Ackermann, PhD,** working in conjunction with members of the department. After being acquired by Oculeve, the device is named **TrueTear**

2017 The Mary M. and Sash A. Spencer Center for Vision Research at the Byers Eye Institute is established and two new basic and clinical research buildings open

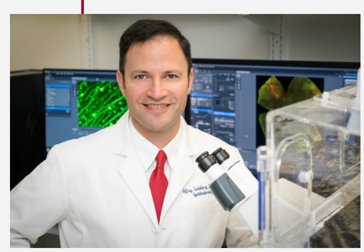
2015 Blumenkranz establishes the **Ophthalmic Innovation Program**

2005-2016 Research on a retinal biofactory using new gene therapy techniques for in vivo production of synthetic proteins is the genesis of a new startup company **Avalanche Biotechnologies**



2010 The department moves from the main campus to the newly established **Byers Eye Institute**, co-locating all vision services.

2012-2015 Myung, Chang, and Blumenkranz, with **Alexandre Jais, MS,** patent and publish on the **Paxos Scope**, a ophthalmic anterior segment and retinal camera system for smartphones



2015 Jeffrey Goldberg, MD, PhD, joins the department as professor and chair

The gift of sight

Former thyroid eye disease patient volunteers at Byers Eye Institute

Almost four years ago, **Peggy Kixmoeller** was diagnosed with **thyroid eye disease (TED)**. This is an autoimmune disorder where the body mistakenly attacks healthy cells, specifically the thyroid gland and the tissues around the eye.

"TED is a complex and potentially disfiguring condition that can have significant effects on the appearance and function of the eye," **Andrea Kossler, MD,** assistant professor of ophthalmology, said. "These patients are at risk of vision loss and when severe, patients may require steroids, radiation, or new targeted therapies, plus multiple surgical procedures to rehabilitate the eyes."

Symptoms of TED include eye redness, pain, double vision, blurry vision, and swelling that can result in eye bulging, inability to close the eyes, and loss of vision. TED also affects patients emotionally, because it can change a patient's appearance and impact quality of life.

Before coming to Stanford, Kixmoeller endured months of doctor's appointments, eye drops, medications, and intravenous infusions while she continued to lose vision.

"I started to notice indoors I was losing my color vision, now swapped for shades of gray, and even outdoors I could only see the brightest colors," Kixmoeller said.

With no improvement, her son Matt, daughter Sara, and daughter-in-law Wakana, recommended she get a second opinion at Stanford.

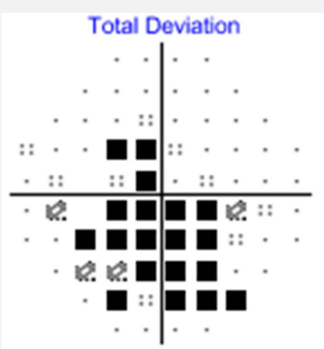
Comprehensive diagnosis and therapy at Stanford

When Kixmoeller first came to the Byers Eye Institute at Stanford, she knew being Kossler's patient would be different.

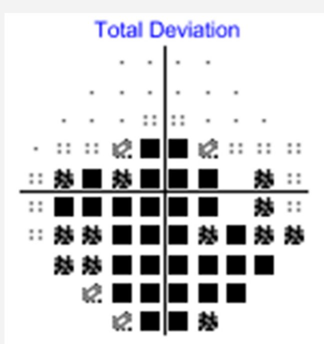
"During that first meeting, Matt and I spent two hours in Dr. Kossler's office where I quickly came to see how kind and understanding she is," Kixmoeller said. "She demonstrated a love for what she did and confidence about the plan going forward."

Kossler is the director of the **Ophthalmic Plastic, Reconstructive Surgery and Orbital Oncology Service** at Stanford. She has over eight years of experience in treating patients with severe TED and is researching new, targeted therapies to treat and reverse the effects of TED. Kossler also co-directs the Thyroid Eye Disease Multi-Disciplinary Center at Stanford Hospital, where she works with a team that includes an endocrinologist, **Chrysoula Dosiou, MD, MS,** and a

A look at Kixmoeller's visual field tests before and after surgery

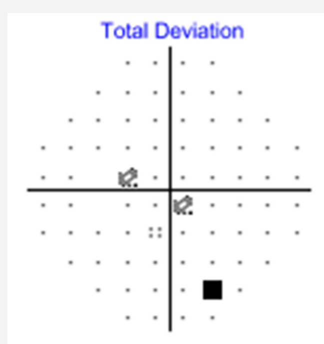


Visual field left eye

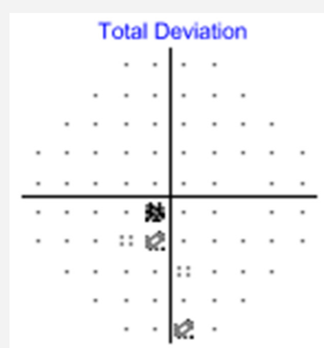


Visual field right eye

Before decompression



Visual field left eye



Visual field right eye

After decompression

Before (2016)

Kixmoeller's eye were swollen, red, and painful when she first arrived at Stanford.

After (Now)

Almost four years later, Kossler and Kixmoeller remain friends after Kixmoeller's recovery.

radiation oncologist, **Susan Hiniker, MD.** This trio and other members of the care team oversaw Kixmoeller's journey at Stanford.

Kossler diagnosed Kixmoeller with severe active TED with compressive optic neuropathy. Her orbital swelling put pressure on her optic nerve resulting in vision loss. Kossler recommended urgent orbital decompression. Decompression surgery would remove the bone between her sinuses and eye cavity to create more space and relieve the compression on the nerve that controls her vision. Kixmoeller underwent orbital decompression surgery. She awoke the next morning and could see.

"I fought back tears when I realized that for the first time in ages I could see the eye chart and I could see colors," Kixmoeller said. "I had been told by other ophthalmologists I would likely lose my vision, but **at Stanford I regained my vision**."

After restoring vision with bilateral decompression surgery, she required eye muscle surgery to correct double vision and eyelid surgery to improve eye closure, comfort, and symmetry. Three years after being diagnosed with TED, she feels like herself again.

"I feel those years went by fast and I saw everything come full circle," Kixmoeller said. "I can truly say this journey was worth it, because I now have the gift of vision again that Dr. Kossler gave to me. She was both meticulous and caring in her work and exceeded my expectations on every level."

Out of gratitude for Kossler and her team, Kixmoeller decided to give back to Stanford. In 2018, she began volunteering at the Byers Eye Institute, where she can help those who don't have their vision navigate the building.

"Patients like Peggy and her family, are the reasons I love my job," Kossler said. "Seeing her enjoying life and volunteering at the Byers Eye Institute each week always brings a smile to my face. She is an inspiration to doctors and patients alike."

"I have a whole new perspective on life" Kixmoeller said. "Now that I have my vision back, I get to enjoy the things I did before like sewing, running, or most importantly spending time with family. **I am forever grateful to Dr. Kossler and her team for changing my life**."

"I now have the **gift of vision** again that **Dr. Kossler** gave to me. She was both **meticulous** and **caring** in her work and **exceeded my expectations** on every level."

Stopping cancer in its tracks

Stanford Ocular Oncology team saves the life of child with retinoblastoma

To a passerby, **Cru Silva** looks like your average three-year-old. His energy is contagious as he runs around the room laughing and playing with his new toy garbage truck.

It seems that he hasn't a care in the world, but Cru has spent the past two years battling **bilateral retinoblastoma**, a serious eye cancer that occurs in children. Only 300 patients are diagnosed with retinoblastoma in the United States annually.

Cru's mother, **Janelle Silva,** who previously worked at an eye clinic located on their home island of Maui, Hawaii, noticed a glare in his eye when he was just 18 months old in a photograph taken at a party. She then began to notice his left eye was swollen and turning inward.

This white reflection or glare is an important clinical sign called **leukocoria**, seen in some cases of retinoblastoma, instead of the typical red reflex. Janelle thought it best to have Cru seen by an ophthalmologist, who after finding tumors in both of Cru's eyes, immediately contacted Stanford and was connected to **Prithvi Mruthyunjaya, MD, MHS,** an ophthalmologist and ocular oncologist and director of the **Stanford Ocular Oncology Service**.

Arriving at Stanford

Within a week, Cru was brought to Byers Eye Institute with his mother and **Shane,** his father.

"When we first came to Stanford, we didn't know whether Cru's left eye would have to be removed," Janelle said. "His left eye's tumor was larger than the right eye's tumor, and particles had begun to break off, so there was a possibility the cancer had spread."

At Byers, Cru was seen by a multidisciplinary team in the **Pediatric Ocular Oncology** service including Mruthyunjaya; **Arun Rangaswami, MD,** a pediatric hematologist/oncologist; and **Huy Do, MD,** an interventional neuroradiologist.

"Stanford's Ocular Oncology is a new service where we care for both adults and children with life- and vision-threatening cancers by seeking to improve and save lives," Mruthyunjaya said.

Mruthyunjaya said that ocular oncology differs from other fields in ophthalmology that seek primarily to restore or protect vision. Even greater than these goals, the main priority in ocular oncology is saving lives.

"We are so thankful to Dr. Mruthyunjaya and his team. If it weren't for him, Cru wouldn't be where he is now."

"Our ultimate mission on the ocular oncology service is to have healthy children who can lead not just functional, but exceptional lives," Mruthyunjaya said.

Mruthyunjaya, who came to Stanford in 2016, was

After the first round of intra-arterial chemotherapy treatment, Cru had a reaction in which his left eyelid swelled shut for about a month. Since then, he has slowly regained control over that eyelid. Photo courtesy of Janelle Silva.

previously a faculty member at Duke University for 15 years, where he helped build the Retina-Ocular Oncology Program as the director of the Ocular Oncology Service. He saw patients with similar conditions and built a team comprised of colleagues from many specialties.

“In my experience, I have seen the importance of collaborating and partnering with individuals of different expertise,” Mruthyunjaya said. “It’s a well understood model of pediatric cancer that has continued to advance here at Stanford.”

Resilient through rounds of chemotherapy

In Mruthyunjaya’s evaluation of Cru’s condition, he identified the extent of the disease, assessed tolerance for various treatments, and discussed with the team the options that would be safest and most effective.

Cru began treatment with **systemic chemotherapy** over a period of six months. When Mruthyunjaya detected continued tumor activity, chemotherapy was then carefully injected into Cru’s eyes and then a new treatment, **intra-arterial chemotherapy (IAC)**, was used.

“Intra-arterial chemotherapy is a delicate treatment where a small catheter is threaded into the tiny ophthalmic artery that brings blood to the eye, and in turn the tumor,” Mruthyunjaya said. “This targeted chemotherapy allows precise delivery of medication only into the eye without having to treat the rest of the patient’s body. It helps to significantly reduce side effects from the chemotherapy.”

Pictured are Mruthyunjaya, Cru, and Masha Levina (L to R). Levina, Assistant Clinic Manager, was responsible for coordinating Cru’s care and travel during his treatment.

The Silva family after Cru’s recovery: Janelle, Shane (top row L to R) and Blaze and Cru (bottom row L to R). Photo courtesy of @JaseKellyMaui Photography.

“It was crucial that we adapt to any new changes that developed in the tumor, and because of the severity, we decided to bring in Dr. Do’s IAC treatment,” Mruthyunjaya said.

“The first several months during systemic chemotherapy were difficult,” Janelle said. “As a parent you want to set a good example for your children, but it was really Cru who gave us inspiration through his resilience and happy attitude.”

Now after nearly two years, the tumors in both his eyes appear inactive and well treated, but they must be monitored closely over the next few years. Cru returned home to Maui in 2018 and travels to Stanford for his monthly check-ups with Mruthyunjaya.

“Throughout Cru’s treatment, the Silva parents were dedicated to keeping things normal, and even through the many rounds of chemotherapy he could always be brought to a smile,” Mruthyunjaya said.

“We are so thankful to Dr. Mruthyunjaya and his team,” Janelle said. “He made this process comfortable and seamless, and if it weren’t for him, Cru wouldn’t be where he is now.”

Training for breakthroughs

Funds support the next generation of physician-scientists in developing innovative therapies

Lopa Y. Gupta, MD, a leading eyelid and cosmetic surgeon in New York City and a past Stanford ophthalmology resident, has generously established two funds to support current and future residents' research: The **Marmor-Blumenkranz Ophthalmology Residents Research Fund** and the **Lopa Yogesh Gupta Ophthalmology Residents Research Fund**.

Dr. Gupta has built a career marked by accolades and philanthropic endeavors and credits part of her success to the residency training she received at Stanford. She was motivated to establish these funds so that Stanford residents today and, in the future, can benefit from the same enriching research experience that she found so impactful during her residency. Dr. Gupta seeks to encourage residents to become physician-scientists who will strive to push the boundaries of science to improve eye care for patients worldwide.

Dr. Gupta and her son, Dilan celebrating at his high school graduation. Photo courtesy of Dr. Lopa Y. Gupta.

During her time at Stanford, Dr. Gupta conducted clinical and basic science research on retinal diseases, and her findings were published in peer-reviewed journals. As a resident, Dr. Gupta trained under the supervision of **Michael Marmor, MD,** professor of ophthalmology, and **Mark S. Blumenkranz, MD,** H.J. Smead professor emeritus of ophthalmology. Part of the Marmor-Blumenkranz Ophthalmology Residents Research Fund was used to establish a prize awarding successful residents the opportunity to attend and present at a national or international conference.

"My beloved son, **Dilan,** who passed on from the consequences of an inoperable brain lesion on June 21, 2018, was instrumental in establishing these funds at Stanford," Dr. Gupta said.

Dilan lived a life of compassion. He was heavily involved in philanthropic work in underprivileged parts of India with his mother and the rest of their family. Dilan, who was an undergraduate student at Columbia University, spent his Saturdays mentoring teenage boys in Harlem and began a start-up company focused on sports and altruism.

"Through these endowed funds, his altruism and philanthropic endeavors will live on forever," Dr. Gupta said. "Training the next generation of brilliant ophthalmic physician-scientists will be part of Dilan's legacy and will support Stanford's effort to develop improved treatments for patients with debilitating eye disease and vision loss."

Transforming vision care

Generous gift accelerates discovery and its translation into patient treatments

In May 2017, Stanford University announced the establishment of the **Mary M. and Sash A. Spencer Center for Vision Research at the Byers Eye Institute**, made possible by a transformative gift from Mary Spencer in honor of her late husband, Sash.

The center's mission is to conduct innovative and cutting-edge research so we can develop new treatments and cures for eye disease and deliver them to patients as quickly as possible.

Thanks to this gift and the commitment and support of Stanford Medicine's leadership, the center has recruited more than 20 new world-class researchers and physician-scientists. These outstanding new faculty have formed collaborations across campus, leveraging Stanford's deep strengths in fields that include genetics, neuroscience, stem cell biology, imaging, and biotechnology. The center acquired two new state-of-the-art lab facilities and recently was allocated additional space to accommodate new faculty hires and to expand research capacity.

Others have been inspired to support the work of the center, which is now conducting some of the most exciting vision research happening anywhere. Their generosity is fueling the work of outstanding researchers such as **Daniel Palanker, PhD,** who has developed a retinal prosthesis to restore vision in patients with advanced dry age-related macular degeneration (AMD). So far, five patients have been implanted with the retinal prosthesis, and for the first time in years, these patients are able to identify numbers, letters, and symbols with the highest visual acuity to date. A lot more work is needed before the retinal prosthesis becomes broadly available to patients. And Palanker is now working on the next phase of this research—developing a 3D microchip that can increase visual acuity even further, allowing patients to read, drive, perform close tasks, and recognize faces.

Philanthropy plays a critical role in advancing science, such as the retinal prosthesis described above: it supports early-stage, high-risk, high-reward research where federal funding is generally not available, and it supplements subsequent federal and other grant funding to allow us to more rapidly move discoveries into patient care.

The Mary M. and Sash A. Spencer Center for Vision Research at the Byers Eye Institute was made possible by a generous gift from Mary Spencer in honor of her late husband, Sash.

"We are very grateful to our donors for their support," said **Lloyd Minor, MD,** dean of the School of Medicine. "In the short period since the launch of the Mary M. and Sash A. Spencer Center for Vision Research, we have seen immense progress on research into vision protection, enhancement, and restoration. Thanks to the foresight and generosity of Mary Spencer and others like her, we've intensified our efforts and are more optimistic than ever that the center's breakthroughs will restore the joy of sight to millions."

Scan the QR code to view more information on giving

https://stan.md/2IFcRnw

Going global

Stanford Ophthalmology fights blindness internationally

About 1.3 billion people worldwide live with some form of visual impairment, 80 percent of which could have been prevented or is treatable, according to the World Health Organization. However, in many parts of the world, access to appropriate vision care and supplies is not readily available. In response to this need, Stanford Ophthalmology has taken innovation in patient care beyond the local community and indeed outside the U.S. Two of the department's most recent global outreach efforts include collaborations with the **Stanford Belize Vision Clinic (SBVC)** and the **Himalayan Cataract Project (HCP, www.cureblindness.org)**.

Establishing the Himalayan Cataract Project

Two years ago, the Department of Ophthalmology recruited **Geoff Tabin, MD,** professor of ophthalmology, to be the inaugural Fairweather Foundation Professor of Ophthalmology and Global Medicine. Co-founder of one of the most successful global ophthalmology programs dedicated to wiping out reversible blindness, Tabin recalls discovering his career calling.

"After summitting the peak of Mount Everest in the 80's, I was in Nepal and met a Dutch medical team performing cataract surgery on a woman who had lost her vision for years," Tabin said. "When I saw the miracle of sight restored, I began pursuing a career in global ophthalmology."

When Tabin completed his ophthalmology residency and fellowship training, he returned to Nepal in 1994. A year later, with his Nepali partner, **Sanduk Ruit, MD,** Tabin founded the HCP. Their mission was to cure needless blindness with the highest quality care at the lowest cost.

Cataracts lead to loss of vision as the lens of the eye becomes opaque. While this disease is easily treatable, eye surgeons are not easily accessible in most parts of the world. The HCP harnesses Ruit's method of small incision cataract surgery, a procedure that now takes less than 10 minutes and costs $25 in materials, to start reversing cataract blindness in that part of the world.

Since its inception, HCP and its partners have provided screening and basic eye care for more than six million patients, including 860,000+ sight-restoring surgeries to transform lives, families, and communities in under-resourced areas of the world.

Tabin and Ruit realized early on that high-quality surgery was the cornerstone of eliminating cataract blindness and that the majority of surgeries must be performed by trained local eye care personnel. Thus, in addition to delivering cataract surgery, they train eye care providers and surgeons to develop self-sustaining sys-

Geoff Tabin, MD, stands among patients who have received sight-restoring cataract surgery in Ethiopia. Photo courtesy of Ace Kvale and all photos on pages 14-15 courtesy of the Himalayan Cataract Project.

Himalayan Cataract Project Co-Founders, Geoff Tabin, MD, and Sanduk Ruit, MD, at a cataract outreach event together in Nepal. Photo courtesy of Ace Kvale.

The joy of sight-restoration in Harar, Ethiopia. Photo courtesy of Amanda Conde.

tems of eye care.

"We seek not just to help current and future ophthalmologists in other countries, but to transfer skills through training, so that we can all work together to eliminate global blindness one surgery at a time," Tabin said.

HCP's academic home is Stanford, and its home base abroad is the Tilganga Institute of Ophthalmology, a world-class treatment and education center in Kathmandu, Nepal. With support from HCP, Tilganga has expanded from an eye center to a central training facility for partners worldwide. The Stanford residency program is linked with Tilganga's, where all senior residents at Stanford are invited to gain exposure to the global burden of eye disease and share their education in a month-long elective. Asian and African doctors are also receiving subspecialty training with Stanford faculty helping develop the skills of the teachers for the next generation of ophthalmologists in the developing world.

"We seek not just to help current and future ophthalmologists in other countries, but to transfer skills through training, so that we can all work together to eliminate global blindness one surgery at a time."

During the past 20 years, HCP has been working to replicate that same successful eye care service delivery model across South Asia and sub-Saharan Africa with active programs in Nepal, India, Bhutan, Myanmar, Ethiopia, and Ghana. The Stanford faculty, fellows, and now residents are involved in all of these countries.

Stanford Belize Vision Clinic delivers adult and pediatric eye care

In August 2016, Hurricane Earl devastated the town of San Pedro, located on the tropical island of Ambergris Caye, in northern Belize. Shortly after the hurricane, a donor contacted **Caroline Fisher, MD,** clinical assistant professor of ophthalmology at Stanford, asking if she could establish an eye clinic in that area to reach the significantly underserved population there.

"I realized the great need for an eye clinic in San Pedro," Fisher said. "There is very limited access to medical care, limited medical supplies, and limited medical training, with most people getting their care in Guatemala or Mexico if they can manage the travel."

After doing a site assessment, Fisher presented the idea of starting an eye clinic in Belize to **Michele Barry, MD,** director of **Stanford's Center for Innovation in**

Global Health (CIGH) and to the department leadership. With strong support from the department and the School of Medicine, Fisher started Stanford Belize Vision Clinic (SBVC), a program that promotes eye health and care for adults and children in Ambergris Caye and surrounding areas.

"SBVC began thanks to the interest and vision of Don Listwin, founder of BelizeKIDS.org, which is a non-profit aimed at helping children in Belize," Fisher said. Listwin is also the founder and chairman of Canary Foundation, a non-profit organization focused on early cancer detection.

Fisher also established collaborative relationships with the Belize Council for the Visually Impaired (BCVI), a local non-profit that provides glasses and follow-up eye care for patients shared with SBVC.

Since starting SBVC, diseases often diagnosed include cataracts, glaucoma, diabetic retinopathy, dry eyes, and pterygium; the clinic has also dispensed nearly 600 pairs

Caroline Fisher, MD, who founded the Stanford Belize Vision Clinic.

Robert Chang contributes to mobile eye-hospital train in China

Robert Chang, MD, assistant professor of ophthalmology, journeys to China annually in conjunction with **Lifeline Express**, a mobile eye-hospital train that travels to remote parts of the country to provide free cataract surgeries. He went for the first time in 2010 and since then has visited many different provinces to teach local doctors phacoemulsification and glaucoma surgery techniques.

Chang has worked closely with Hong Kong-based **Nellie Fong,** the founder of Lifeline Express, who is the visionary behind creating a network of eye centers in China and beyond.

The mobile eye-hospital train travels throughout remote parts of China. Photo courtesy of Lifeline Express.

Over the past nine years, Chang has trained doctors through didactic lectures, videos, and supervision of local doctors in the clinic and operating theater. Most of the centers have modern equipment such as a phacoemulsification machine but lack some basics and often do not have exposure to a standardized teaching curriculum.

"My first trip with Lifeline Express began as an international consulting program," Chang said. "I've really enjoyed making friendships and not just teaching but also learning new things myself."

Many other professors have joined Chang on these trips, including **Yang Sun, MD, PhD,** associate professor of ophthalmology.

"We are really able to make a sustained impact on the lives of many indigent patients," Sun said.

"Volunteering regularly has shown me the importance of global health," Chang said. "I have been very fortunate for the opportunity to train others and have world-wide impact."

of glasses.

"Stanford provides full-spectrum clinical care for adult and pediatric SBVC patients, and in the future, we hope to expand to offer needed surgical treatment as well," Fisher said.

Training new global leaders at Stanford

Through SBVC and Tabin's connections to clinics around the world, Stanford faculty, fellows, and residents are getting crucial exposure to the current state of global eye care, while bringing their strong educational backgrounds to communities abroad. For example, at SBVC, residents and accompanying faculty spend every day in the country running a comprehensive clinic and seeing 20 to 30 patients a day.

"My trips to Belize continue to be exceptional experiences both personally and professionally," said **Jill Beyer, OD,** clinical assistant professor of ophthalmology. "It's a very fulfilling experience."

Carmel Mercado, MD, traveled to Belize before graduating from the Stanford residency program and was deeply moved by how much impact she could bring in even a short time.

"Seeing that there is this need for eye services outside of the United States has inspired me to continue to be involved in global health in the future," Mercado said. "And my experience in Belize helped me be better prepared for my subsequent fellowship in pediatric ophthalmology and strabismus."

With Tabin's arrival at Stanford in June 2017, the Byers

Carmel Mercado, MD, teaches a child how an eye doctor checks the patient's vision.

A sign hangs outside the SBVC clinic advertising free vision check-ups.

Eye Institute established a new Global Ophthalmology Fellowship. This one-year post-graduate clinical training program is certified through the Association of University Professors of Ophthalmology. Current fellow **Allison Jarstad, DO,** has literally traveled the world providing care and teaching while learning how to deliver the highest level of care to the least-resourced patients. She spoke about her upcoming trip to a refugee camp in South Sudan.

"Going to South Sudan will be a wonderful, full-circle experience for me, because I went there as a medical student after I matched into ophthalmology for residency," Jarstad said. "At the time I wasn't able to perform surgery and I knew I wanted to return. I now get to see that dream come true and help this community that I met years ago."

Tabin speaks warmly about the experience of taking students and fellows abroad and exposing them to global health opportunities, and Jarstad's experience has fulfilled this promise.

"Working side by side with ophthalmologists in various countries has allowed me to develop professional relationships that I hope to foster throughout my career and that will give me the ability to continue international ophthalmology in the future," Jarstad said. "I am impressed and pleased that Stanford cares about global medicine, not just ophthalmology, and makes outreach a priority at this institution. Leveraging Stanford University's support has made our impact truly incredible."

"We want to build a global network of ophthalmologists as we train future leaders," Fisher said. "What I love about the Stanford environment is that a simple idea has the capability to blossom into something so much bigger."

SOAR Residency Program lays foundation for independent research careers

The Department of Ophthalmology at Stanford prides itself on training undergraduates, medical students, residents, and clinical fellows in both clinical care and innovative research. While all residents participate in basic science or clinical research during residency, the newly established **Stanford Ophthalmology Advanced Research (SOAR) Residency Program** allows residents who want to accelerate their academic research program to dedicate an extra year to full-time basic science or translational research. Typically, this year takes place after the internship year and prior to beginning the rest of the three-year ophthalmology residency, and the research continues using elective time during the next three years. Through SOAR, the department sponsors the resident's career growth with funding, mentorship, and other resources according to each trainee's research needs, both during the research year and the following three clinical training years.

"Mentorship is critical, and SOAR residents develop their own research program under the guidance of one or more faculty mentors," **Jeffrey Goldberg, MD, PhD,** professor and chair of ophthalmology said. "The purpose of the SOAR Residency Program is to help residents transition to independence as clinician-scientists, to carry their research into the future as faculty members, and to position themselves as strong applicants for NIH and other independent funding."

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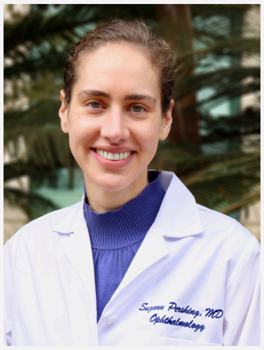
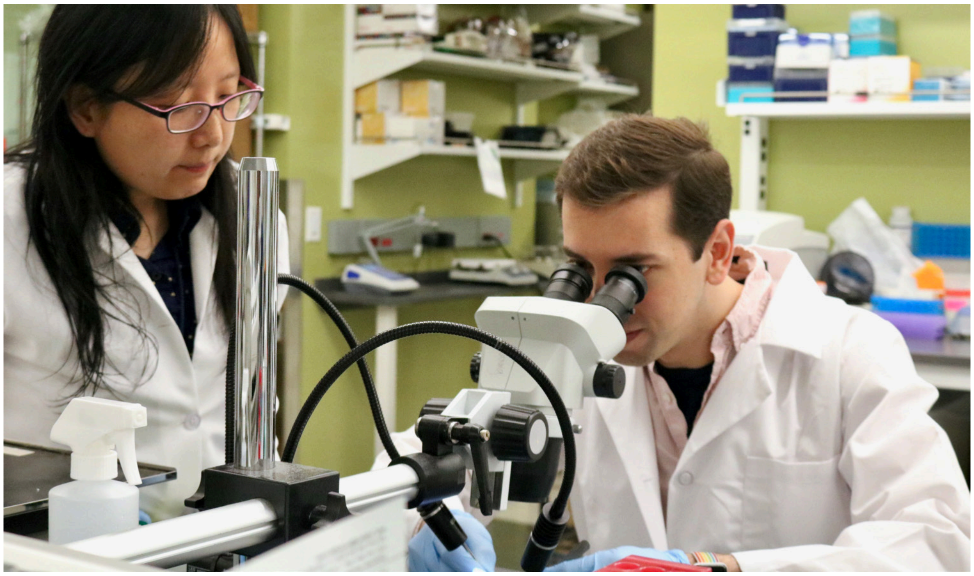
Through the eyes of a SOAR resident

Luciano Custo Greig, MD, PhD, is a current trainee in the SOAR Residency Program. He graduated from Harvard Medical School with a PhD in genetics in 2015 and earned his MD, magna cum laude, in 2017. After completing his internship year, Greig has begun collaborating with **Sui Wang, PhD,** assistant professor of ophthalmology, and Goldberg to develop new strategies for replacement of retinal ganglion cells that will help patients with glaucoma and other degenerative eye diseases.

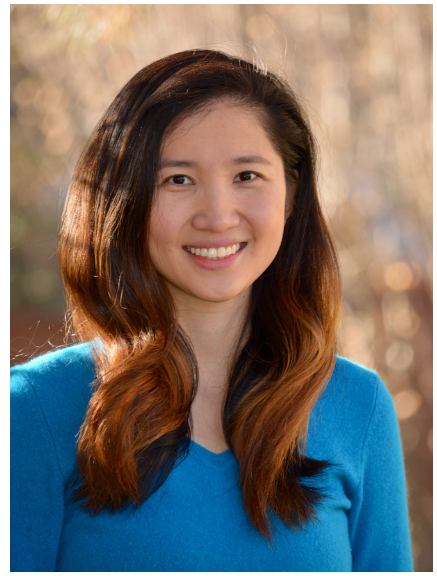


Suzann Pershing, MD, serves as the director of Stanford's ophthalmology residency program, and is implementing the new SOAR curriculum.

Retinal ganglion cells are the neurons that send visual information to the brain through the optic nerve, and degenerate in glaucoma. These same neurons are also compromised in developmental disorders such as optic nerve hypoplasia and are injured in traumatic or ischemic optic neuropathy. Greig aims to use precursor cells present in the adult eye to gene-



Luciano Custo Greig, MD, PhD, (left) collaborates with Sui Wang, PhD, on research to discover new sources of stem cells hiding in the human retina.



Lucie Guo, MD, PhD, finished her thesis research on epigenetics before matching to the SOAR Program.

rate new retinal ganglion cells and replace those that have died from disease. His studies draw on expertise developed during his PhD, which focused on how different types of neurons in the cerebral cortex are generated during development.

Greig has also had the opportunity to interact with and be mentored by other ophthalmology faculty members such as **Vinit Mahajan, MD, PhD,** associate professor of ophthalmology.

"Dr. Greig is a superstar already, and the opportunity to mentor rising stars like him is one of the reasons I joined the faculty at Stanford," Mahajan said.

"It is really fantastic to be in a department where there are many physician-scientists, who are not only excellent role models, but are also generous with their time and excited to help trainees navigate this career path," Greig said.

Like Greig, next year's SOAR resident **Lucie Guo, MD, PhD,** also plans to pursue an academic career as a physician-scientist. Guo graduated from the Perelman School of Medicine at the University of Pennsylvania in 2018, earning her MD with Alpha Omega Alpha honors and a PhD in biochemistry and molecular biophysics. She is currently completing her internship year at the nearby Santa Clara Valley Medical Center.

During her PhD, Guo made advances in the epigenetic mechanisms of centromere inheritance, using tools in biophysics, quantitative cell biology, and gene editing. She plans to apply her basic science skillset to ophthalmology.

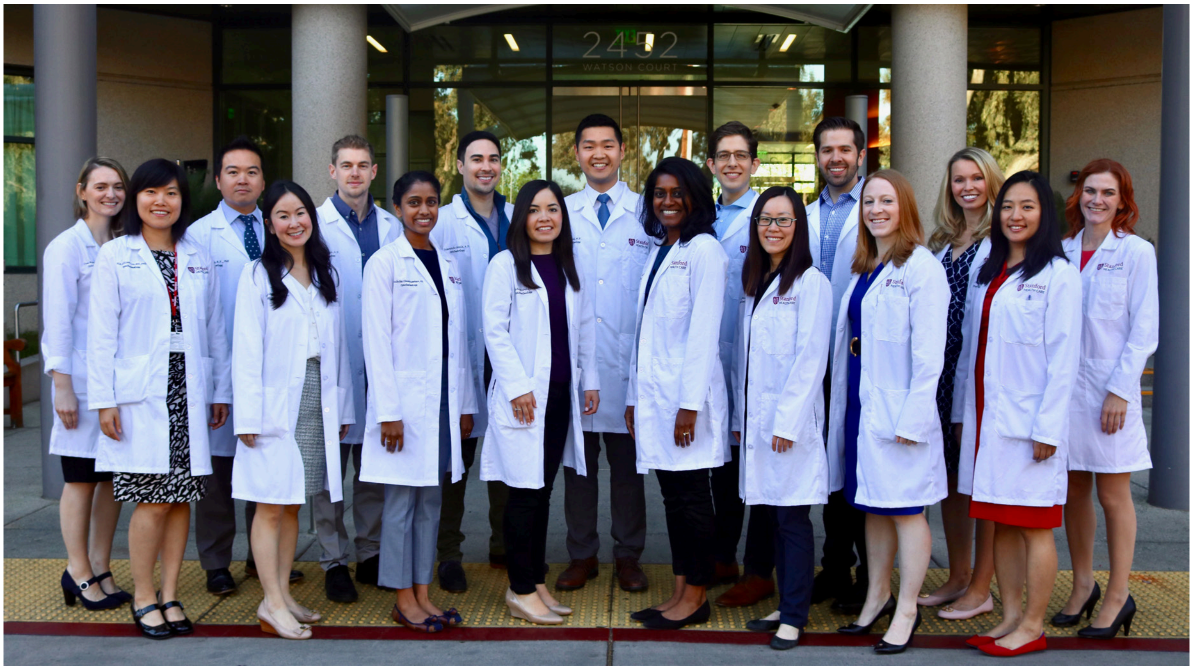
"There are new, powerful tools for probing and altering the human genome and epigenome," Guo said, "and the eye is a uniquely ideal space for developing innovative therapies."

"I am excited to join the SOAR Residency Program to build a research foundation to maintain during my clinical training," Guo said. "It's great to be part of a department that invests in our scientific productivity and growth during residency, while still delivering unbelievably strong clinical and surgical training."

Greig said that training programs tailored to physician-scientists with dedicated time for research are common in other specialties but are rare in ophthalmology, which is what drove his decision to come to Stanford.

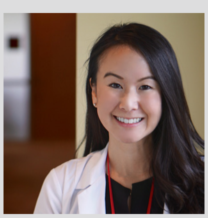
"Most universities don't offer the unique opportunity that Stanford does," Greig said. "When I started the residency application process, I was worried that I would have to give up science for the next four or more years of clinical training, but as a SOAR resident I can do both. The strong integration of research into the residency program here is rare, and ultimately the goal is to lay a strong foundation for independent research projects that I can carry through into my future career as a physician-scientist."

Residents and Fellows

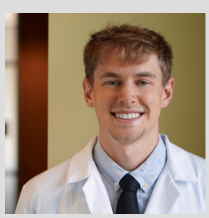


Front row (L to R): Allison (Yin) Liu, MD; Laura Huang, MD; Arthika Chandramohan, MD; Angelica Ortiz, MD; Malini Veerappan, MD; Luo Luo Zheng, MD; Cassie Ludwig, MD, MS; and Dolly Chang, MD, MPH, PhD. **Back row** (L to R): Irma Muminovic, MD; Peter Tang, MD; Ryan Shields, MD; Giancarlo Garcia, MD; Jong Park, MD; Jose Davila, MD; Ryan Smith, MD; Natalia Callaway, MD, MS; and Allison Jarstad, DO. **Not pictured**: Zachary Bodnar, MD; Frank Brodie, MD, MBA; Emily Charlson, MD; Jonathan Chou, MD; Kristin Hirabayashi, MD; Sophia Wang, MD.

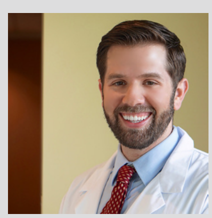
Residents Class of 2019



Laura Huang, MD



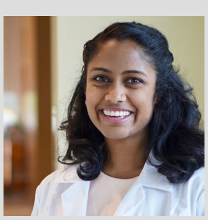
Ryan Shields, MD



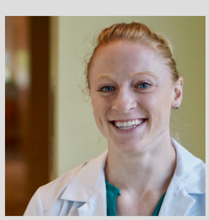
Ryan Smith, MD

"The Stanford Ophthalmology residency program has provided me with an unparalleled experience in both clinical teaching and research mentorship. I could not be more grateful for the skills and training I have received here. I look forward to applying all of this in my future career as a pediatric ophthalmologist."
--Laura Huang, MD, current resident

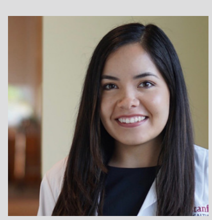
Residents Class of 2020



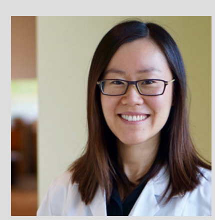
Arthika Chandramohan, MD



Cassie Ludwig, MD, MS



Angelica Ortiz, MD

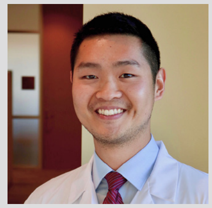


Luo Luo Zheng, MD

Residents Class of 2021

Jose Davila, MD

Giancarlo Garcia, MD



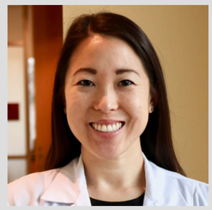
Jong Park, MD

Malini Veerappan, MD

Clinical Fellows Class of 2019

Zachary Bodnar, MD
Retina

Jonathan Chou, MD
Glaucoma

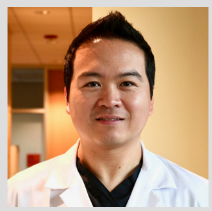


Kristin Hirabayashi, MD
Cornea

Allison Jarstad, DO
Global Health

Allison (Yin) Liu, MD
Neuro-Ophthalmology

Irma Muminovic, MD
Pediatrics



Peter Tang, MD
Retina

Sophia Wang, MD
Glaucoma

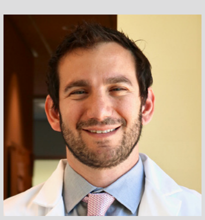
Clinical Fellows Class of 2020

Natalia Callaway, MD, MS
Retina

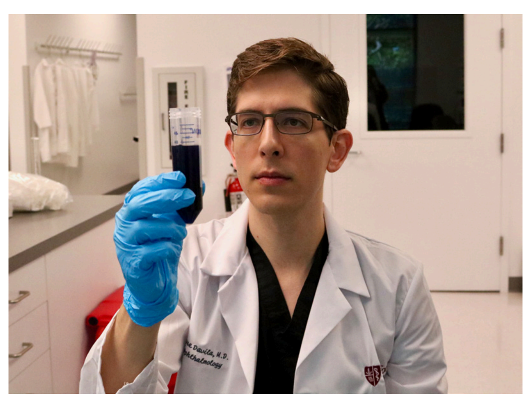
Dolly Chang, MD, MPH, PhD
Glaucoma

Emily Charlson, MD
Oculoplastics

Innovation Fellow Class of 2019



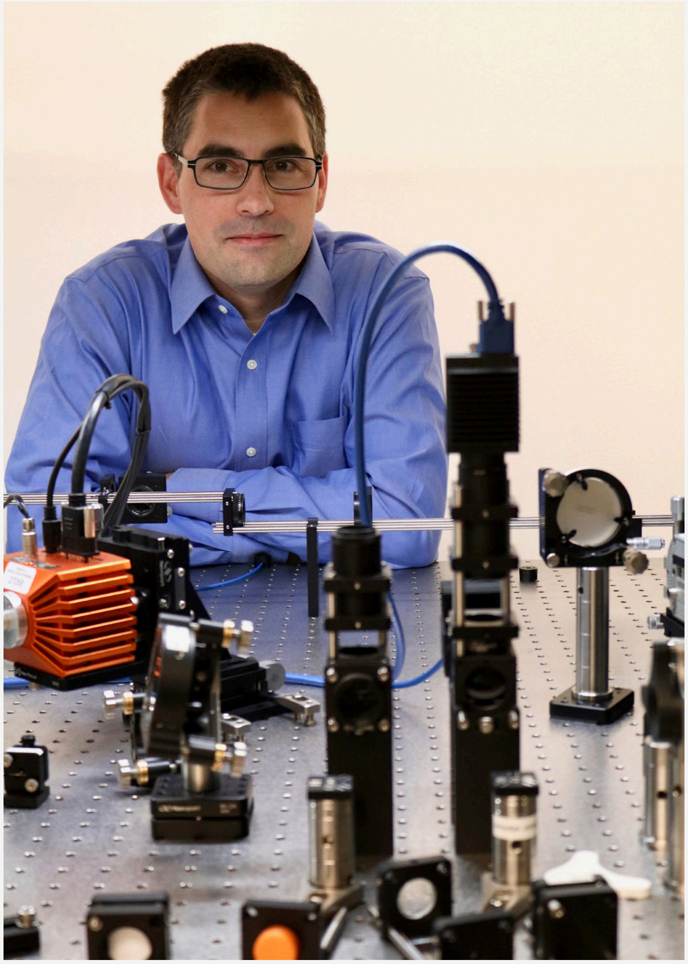
Frank Brodie, MD, MBA



"As a resident, it's been very gratifying to pair intense clinical training with a research project testing patient samples for new signs of disease." --Jose Davila, MD, current resident

One cell at a time

Focusing on the future of precision health through adaptive optics



Alfredo Dubra, PhD, and his laboratory develop the highest resolution ophthalmoscopes for research and clinical purposes.

Retinal cell death due to glaucoma, diabetic retinopathy, macular degeneration, and a myriad of other conditions leads to irreversible vision loss. **Alfredo Dubra, PhD,** associate professor of ophthalmology, believes that the best way to mitigate, and ultimately prevent, this vision loss is to monitor retinal health at the cellular level. This is the very definition of precision health, and the Dubra laboratory is devoted to the development of **non-invasive imaging technologies** to make this a reality.

The key to viewing the retina with microscopic detail is **adaptive optics**, a technology originally proposed for and demonstrated in astronomical telescopes to capture the sharpest images of planets, stars, and galaxies by correcting optical imperfections caused by the atmosphere. In the same way, Dubra uses adaptive optics to sharpen the view of the living retina by correcting optical imperfections unique to each eye, which allows him to study and monitor individual retinal cells.

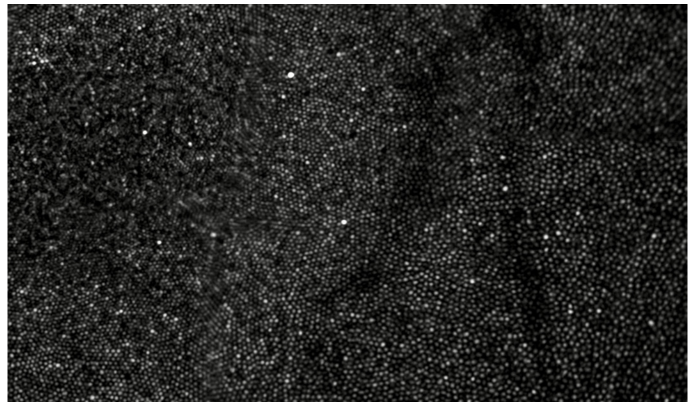
"Adaptive optics can be especially beneficial for patients with retinal diseases, because we can use it to **detect the most minute changes due to disease progression or even detect disease at its earliest stage before patients experience vision loss**," Dubra said. "This is very exciting, because in collaboration with the specialized clinical team at Byers, this advanced imaging can guide treatment and reduce, or even prevent, vision loss. Also, by being able to image individual cells, we help the basic scientists at the Mary M. and Sash A. Spencer Center for Vision Research at the Byers Eye Institute understand how diseases work, so that they can develop more effective treatments."

Of equal importance, viewing progress of disease at the microscopic level can dramatically reduce the time spent testing new therapies. This would make new treatment available to patients faster. In addition, shorter testing would reduce costs and make it possible to test more new drugs, which would benefit patients.

Other faculty are using adaptive optics retinal imaging to bridge the gap between animal and human testing. Often, researchers use animals when searching for new therapies, but the modeling of a disease in animals can greatly differ from the human form of the disease. Dubra is working with basic scientists such as **Yang Hu, MD, PhD,** assistant professor of ophthalmology, and others at the Byers Eye Institute to identify and help develop the best animal models of eye disease in order to develop novel treatments.

Childhood goals launch his career

Dubra, a recent recruit to the Stanford faculty, knew the career he wanted to pursue from an early age. Born and raised in Uruguay, he underwent several **strabismus** surgeries and eye patching as an infant. The battle with his own amblyopia and hyperopia led him to devote his life's work to helping others with visual impairments. Dubra began studying physics and optics during his undergraduate and graduate education in Uruguay, where he was first exposed to research in an applied optics group. He then went to London to further his education by obtaining a PhD in physics in 2004 from the Imperial College London, while studying the optics of the eye and the tear film. In 2006, Dubra traveled to the University of Rochester, the birthplace of adaptive optics retinal imaging, to further his training. Five years later, having started his own lab, he advanced the technology to the point that the full cone and **rod photoreceptor** mosaic, as well as the **finest retinal capillaries** and even individual blood cells, could be visualized in patients. The visualization of rod photoreceptors was significant, because they are often the starting point for many blinding conditions. After six years at the Medical College of Wisconsin, where he devoted himself to the advancement and dissemination of his technology to research institutions worldwide, Dubra joined Stanford in the fall of 2016.

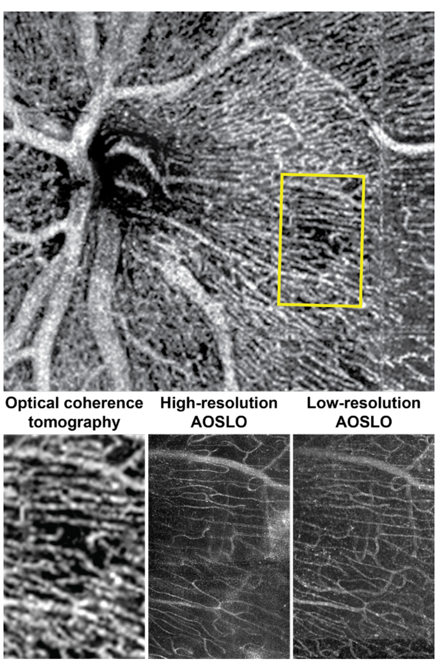


The instrumentation developed in Dubra's lab is used in leading research institutions worldwide to study among other inherited conditions that affect the cone photoreceptor mosaic, such as that shown here.

Discovery leads to new advances

The Dubra lab moved into the newly built Spencer Center for Vision Research in June 2017. At the new location, the lab is part of a unique environment in which clinicians and scientists can work closely, accelerating the pace of research. The team is developing novel instruments to see not only finer details but also microscopic features that are currently not visible by other imaging methods. The team includes computer and vision scientists and electrical and optical engineers, all devoted to the ultimate goal of developing the ability to check the shape and health of each individual retinal cell, so that doctors can avoid vision loss altogether by initiating and personalizing treatment sooner. Central to materializing the benefits of adaptive optics retinal imaging is collaboration with other faculty members at the Byers Eye Institute, including **Jeffrey Goldberg, MD, PhD;** Hu; **Theodore Leng, MD; Heather Moss, MD, PhD; Quan Dong Nguyen, MD, MSc; and Ruwan Silva, MD, MPhil.**

Dubra is also widely regarded as one of the most collaborative vision scientists in the world. Instruments created by the Dubra Lab are currently being used at the New York Eye and Ear Infirmary of Mount Sinai; Moorfields Eye Hospital/the University College London; the Medical College of Wisconsin; the National Eye Institute Intramural Research Program; University of California, San Diego; and the University of Pennsylvania. Many of these instruments are used to select candidates for clinical trials, and then to monitor the efficacy of these treatments. Widespread dissemination of Dubra's technologies are also allowing teams of researchers to study a large number of rare inherited retinal conditions that may soon become curable with gene and/or stem cell therapies.



Dubra and his laboratory develop ophthalmoscopes for research and clinical purposes such as adaptive optics scanning light ophthalmoscopes (AOSLOs) with higher resolutions than the commercial state-of-the-art, such as optical coherence tomography. The images here show the retina's finest capillaries.

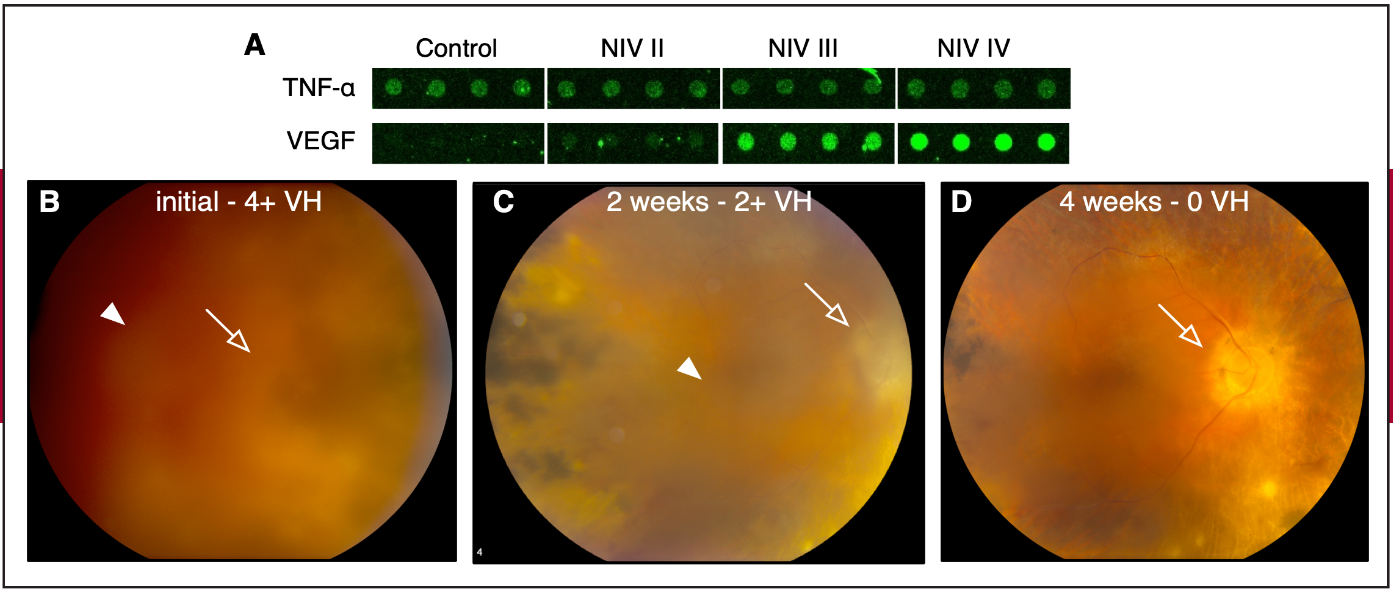
Creating a field of molecular surgery to guide new therapies

A significant challenge for ophthalmologists is diagnosing diseases that appear clinically similar. Inside the eye, a "snowstorm" of white cells can be due to an autoimmune disease, cancer, or an infection, each requiring very different therapies. Current hospital laboratory testing is slow, and results can be inconclusive. **Vinit Mahajan, MD, PhD,** associate professor of ophthalmology, believes new molecular technologies in precision health will overcome these challenges.

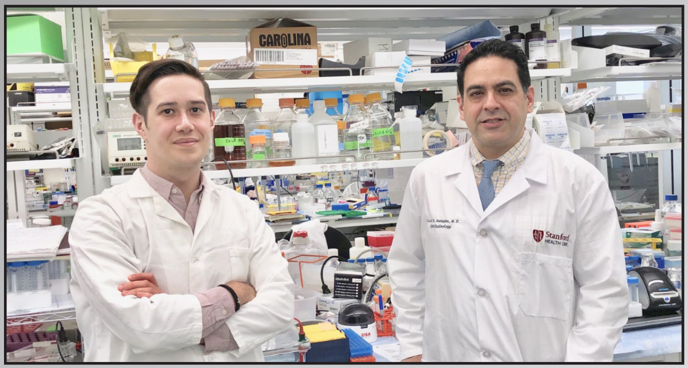
After conventional therapies failed a family of patients going blind from severe inflammation, Mahajan and his research team surveyed their eye fluid and found unexpected protein signatures responsible for the inflammation, bleeding, and scar tissue formation. The team was able to select the right drugs—typically not used for eye diseases—to target the abnormal proteins and restore sight. At the same time, they were able to avoid some drugs most doctors were prescribing, because they knew their target proteins were absent in the diseased eyes.

"Analyzing fluid samples from the eye can completely change how we treat patients," Mahajan said.

Mahajan and his research team are experts in characterizing proteins from liquid eye biopsies using **proteomics technology**. In only a few drops of fluid, they can measure thousands of molecules to identify overabundant proteins that trigger vision loss. Those proteins can then be matched with on-the-market drugs.



Proteomic analysis of NIV vitreous showed that TNF-alpha levels were normal, explaining why prior trials of anti-TNF-alpha therapies failed in these patients. Anti-vascular endothelial growth factor (VEGF) injections resolved vitreous hemorrhages in those with NIV, and prevented patients from having to undergo vitrectomy surgery. Photo courtesy of Gabe Velez, Alexander Bassuk, Diana Colgan, Stephen Tsang, and Vinit Mahajan.



Gabe Velez (left) is an MD/PhD candidate working in the lab of Vinit Mahajan, MD, PhD.

The success of this molecular approach demonstrates the potential of treating rare and complex eye conditions by matching drugs with individual disease proteins. With this in mind, Mahajan established the **Molecular Surgery Program at Stanford's Byers Eye Institute**. This program now supports the collection and analysis of eye fluid from patients with macular degeneration, glaucoma, corneal transplants, infections, and cancer.

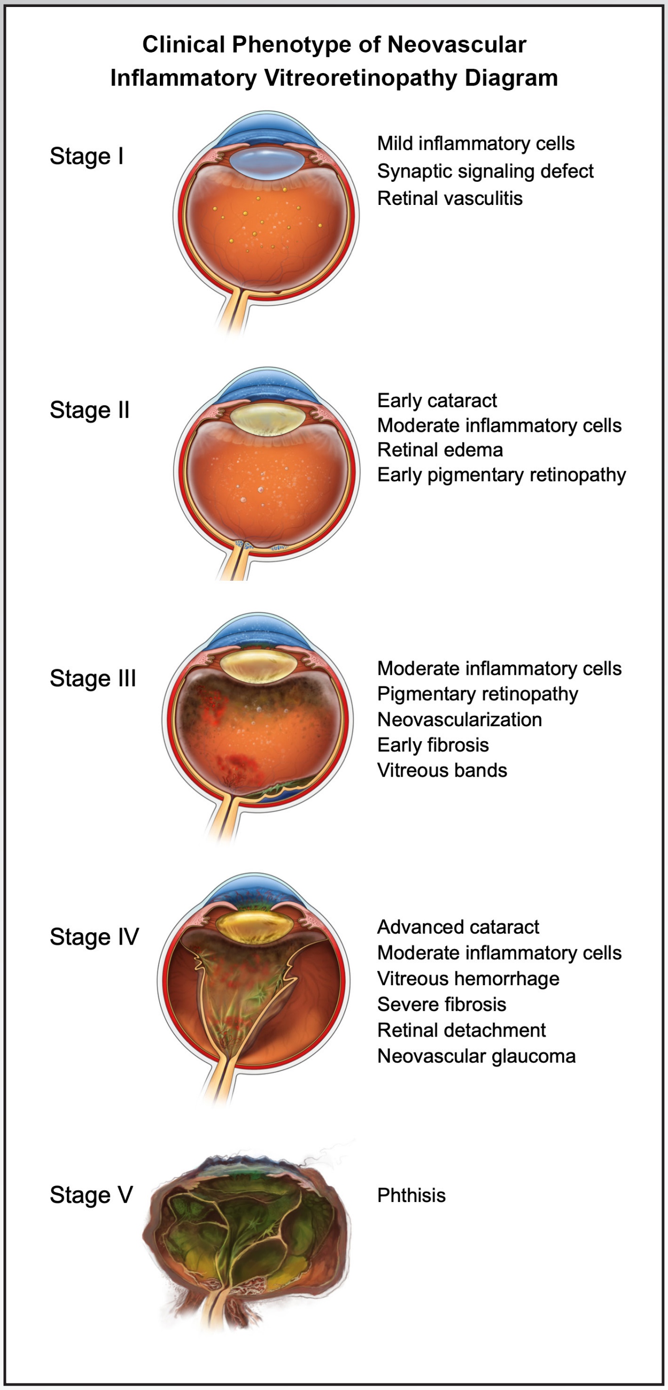
"**If we can identify the molecules linked to eye disease, we can make precise diagnoses, choose the right medicines, and improve our surgical outcomes**," Mahajan said.

Using new proteomics technologies, Mahajan's team can quickly find specific protein expression signatures that distinguish each of these conditions. Getting the correct diagnosis as soon as possible is essential to choosing the right therapy approach, and these protein biomarkers can provide the needed clarity.

Fluid analysis has also pointed to novel retinal disease proteins that do not yet have a drug therapy. Mahajan's team is exploring these new disease proteins at the atomic level and working with colleagues in Stanford's Chemistry and Structural Biology programs to design innovative small-molecule drugs.

"We can now think beyond using surgery as a means of manipulating tissues," Mahajan said. "Manipulating molecules through surgery is the next step in highly personalized, precision medicine."

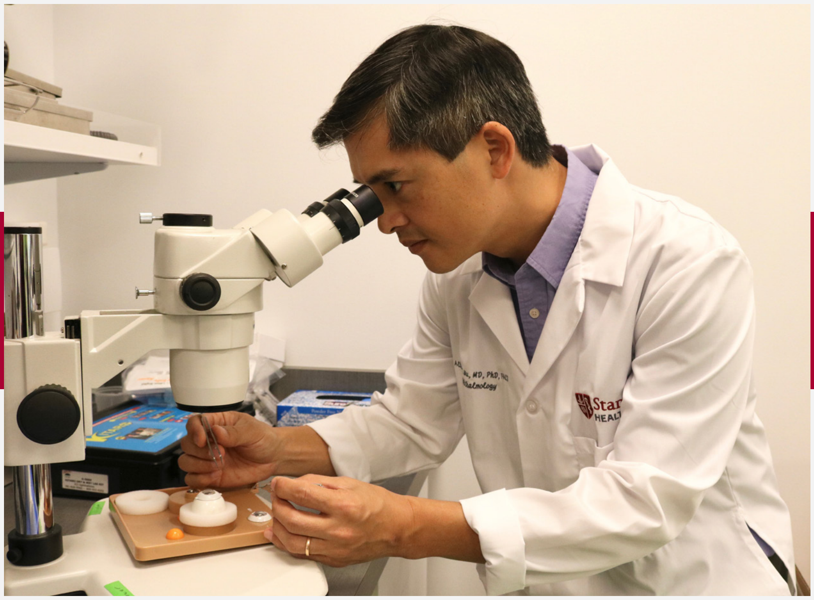
Once surgeons and scientists have a molecular target in their sights, numerous molecular drugs are available to them. These may involve enzymes, genes, antibodies, or chemicals. Eye surgeons can precisely and safely deliver any of these molecules near specific cells in the eye, avoiding the toxicity and issues associated with drugs taken by mouth or injected into the blood stream. Once delivered, patients can be observed noninvasively in the clinic using ultra-high-resolution cameras.



Pictured are the five stages of the blinding uveitis disease, neovascular inflammatory vitreoretinopathy (NIV), for which Vinit Mahajan, MD, PhD, co-discovered the underlying molecular basis. Illustration courtesy of Alton Szeto.

"**Recasting eye surgery in molecular terms will allow Stanford ophthalmologists to take innovative approaches to curing blindness**," Mahajan said.

Developing cures with stem cells and regenerative medicine



Albert Wu, MD, PhD, FACS, uses patients' own cells in an effort to create personalized treatment options.

Too many major eye diseases lead to loss of vision that, even with current medicine or surgery, is irreversible. In macular degeneration, glaucoma, and the major corneal diseases, the cells responsible for normal visual function die and are not replaced through natural healing mechanisms. **Researchers in the Department of Ophthalmology at Stanford are seeking to reverse this limitation through development and testing of groundbreaking stem cell and regenerative medicine therapies**.

"Our goal is to stabilize, better diagnose, and find cures for common eye diseases, so that we can help not just our patients, but patients globally as well," said **Jeffrey Goldberg, MD, PhD,** professor and chair of ophthalmology at Stanford, noting that some 1.3 billion people worldwide suffer from vision impairment. "Restoring vision in these diseases has become a major focus for our research at Stanford."

Department faculty are now paving the way in battling vision loss through stem cell research focused on diseases that range from the cornea on the front of the eye to the retina and optic nerve in the back.

Repairing the cornea

The cornea's outer surface is covered with a layer of epithelial cells that are constantly sustained and replenished by stem cells that normally live in a specialized niche at the edge of the cornea called the limbus. However, in chemical burns, severe infections, and certain immune system diseases such as Stevens-Johnson Syndrome, these limbal stem cells are depleted and the corneal epithelium degenerates, leading to significant visual impairment. **Replacing limbal stem cells with advanced tissue transplant surgery has long been a strength at the Byers Eye Institute, critical to patient care in these devastating diseases, but simplifying such tissue transplants with a limbal stem cell replacement therapy could provide a safer,**

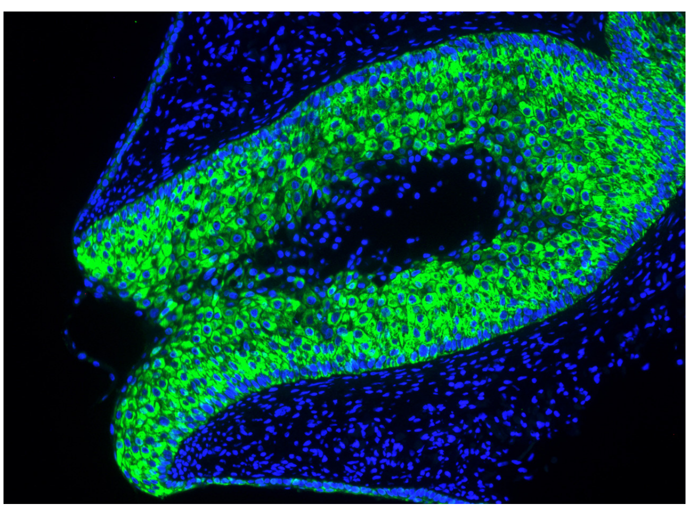
more durable approach while broadening patient access.

Albert Wu, MD, PhD, FACS, assistant professor of ophthalmology, is pushing this approach further by developing ways to regenerate a patient's damaged corneal tissue with stem cells created directly from that patient's blood or skin. Using the patient's own cells, rather than donor cells, vastly decreases the chance of immune rejection. Wu, who joined the department at the end of 2017, now serves as the director of oculoplastics research at Stanford, where he heads the **Ophthalmic Stem Cell and Regenerative Medicine Laboratory**.

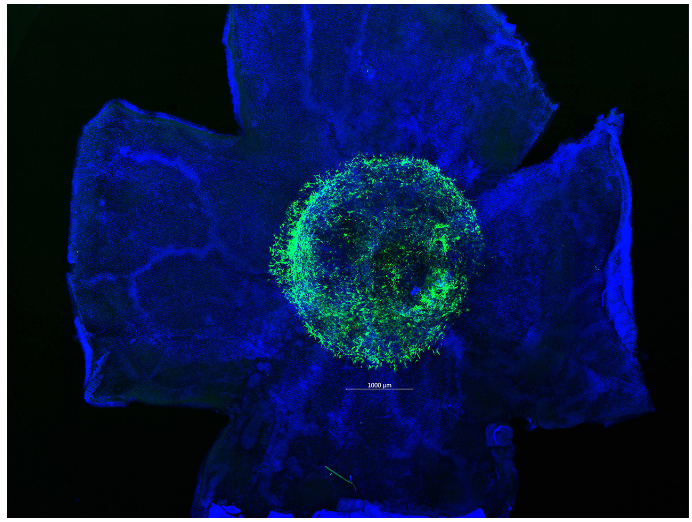
Wu's research on recreating ocular stem cells from a patient's cells began with a five-year National Eye Institute grant, and at Stanford he has received philanthropic support to accelerate this research. He is also advancing Stanford's deep strengths in stem cell biology by collaborating with **Irving Weissman, MD,** director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, and **Marius Wernig, MD,** associate professor of pathology and a member of this institute. They are currently studying how stem cells are converted into ocular tissue and how they interact with their local environment, and moving this research into models for preclinical testing.

"My goal is to perform translational research, bringing breakthroughs in stem cell biology and tissue engineering to clinical ophthalmology and reconstructive surgery," Wu said.

The innermost layer of the cornea presents a similar challenge. There, a fragile layer of corneal endothelial



Wu's research aimed at recreating ocular stem cells shows a paraffin-embedded section of developing human eyelid tissue stained with cytokeratin-14 immunofluorescence.



Green fluorescent protein-expressing retinal ganglion-like cells integrate after transplantation into a rodent eye.

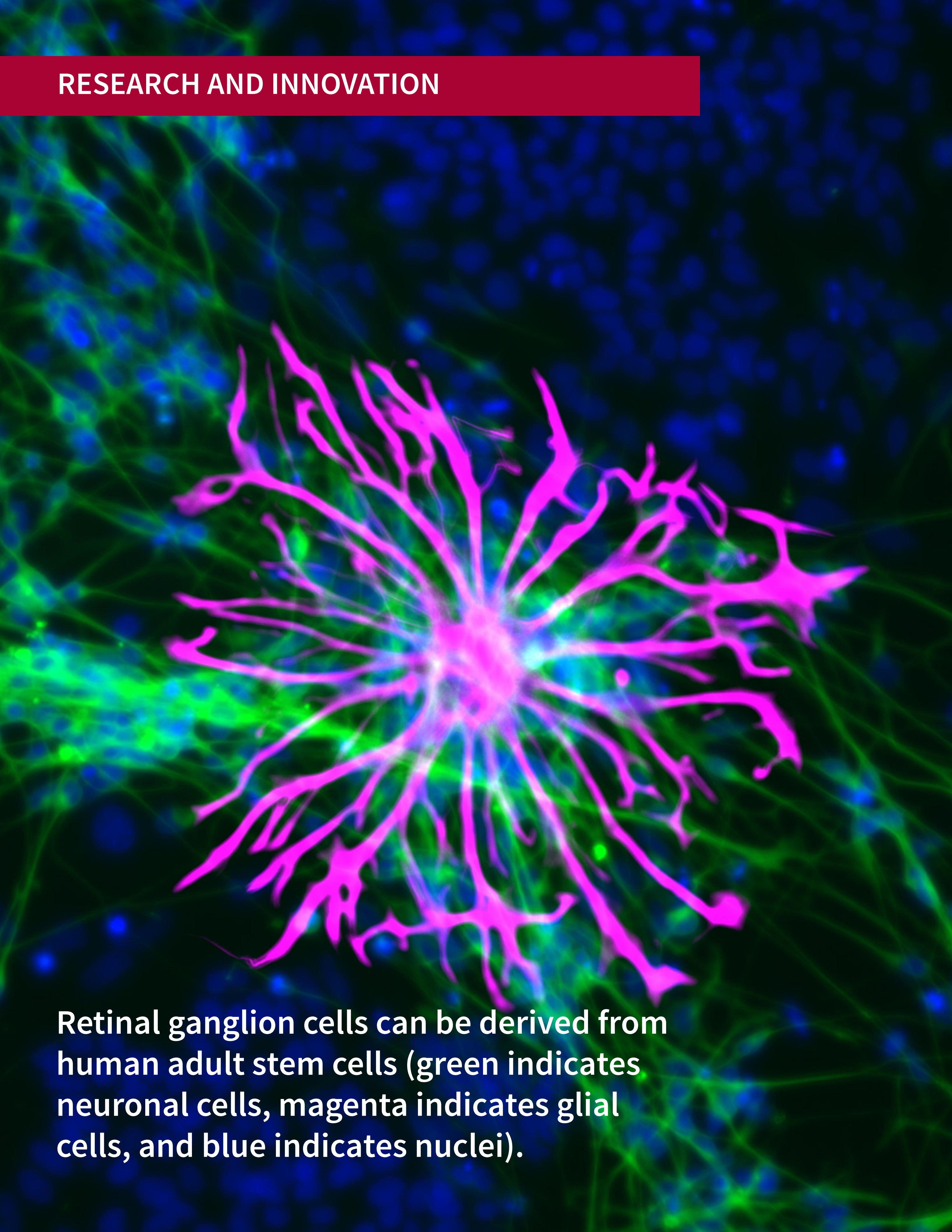
cells can degenerate with age, after cataract or other eye surgery, or in genetic diseases such as Fuch's dystrophy, and in humans they are not repaired or replaced endogenously. These cells are responsible for pumping fluid out of the cornea and, in so doing, keep the cornea clear. Their loss leads to visual decline and, in some cases, severe pain that can only be treated with surgery.

"Partial thickness corneal transplants such as Descemet stripping automated endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty (DMEK) can fix the problem, but it would be even better to have cell-based therapies that could help more patients," said **Charles Lin, MD,** clinical assistant professor of ophthalmology and a leader in complex cornea transplant surgery.

Delivering corneal endothelial cell therapies could help avoid surgery altogether. With a grant from the California Institute for Regenerative Medicine, Goldberg worked on converting human stem cells derived from adult patients into corneal endothelial cells. He previously showed that using magnetic nanoparticles and external magnets could help deliver corneal endothelial cells to the right spot inside the eye. After growing new corneal cells, the cells are then placed toward the inside of the cornea and held in place by the magnet.

Lin is excited to move this type of research into clinical trials.

"Generating cells for thousands of patients is particularly important when considering the worldwide shortage of access to corneal transplant surgery," Lin said.



Retinal ganglion cells can be derived from human adult stem cells (green indicates neuronal cells, magenta indicates glial cells, and blue indicates nuclei).

Developing therapies for age-related macular degeneration

Within the department, there is also ongoing research aimed at treating **age-related macular degeneration (AMD)**, a leading cause of vision loss for Americans 50 years and older, according to the National Eye Institute. AMD causes damage to the retina in two ways. In **dry AMD**, the more common form, the retinal pigment epithelial cells and the photoreceptors in the center of the retina atrophy and die. **Wet AMD** is less common, but more acutely vision threatening, and is associated with blood vessels that grow under the retina and leak or bleed. While there are successful treatment options for wet macular degeneration, an effective treatment for the cellular loss in dry macular degeneration has not been found, and both of these forms dramatically disrupt patients' central vision. **Theodore Leng, MD,** assistant professor of ophthalmology, has focused his research on developing treatments for those with dry AMD.

"While this disease is a slow, progressive form of vision loss, patients can still eventually become blind from it," Leng said.

Leng notes that a number of other retinal degenerative diseases, such as those associated with high levels of myopia, or nearsightedness, and other less common genetic diseases, are closely related and likely stand to benefit from cell therapies.

Leng has been the principal investigator in a number of clinical trials for dry AMD using cell therapies and other therapeutic candidates, and he remains optimistic in pursuing a cure. Recently, he was awarded a $4.2 million grant from the California Institute for Regenerative Medicine to develop a stem cell therapy for dry AMD. Leng and his collaborators are studying adult neural stem cells derived from brain tissue that can only become other cells within the central nervous system, and optimizing them for human clinical trials.

"These cells secrete growth factors and other supportive nutrients for the remaining nerve cells of the eye, so when we surgically implant them under the retina, they will live there and create a favorable environment for the other cells in the retina," Leng said.

Other cell replacement programs Leng is collaborating on are specifically designed to replace the retinal pigment epithelial cells, and the rod and cone photoreceptors.

"The hope is that we will move into human clinical trials in the next two to three years," Leng said.

Stem cells for glaucoma and optic nerve disease

In the retina, just a millimeter away from the retinal photoreceptors that degenerate in AMD, are the retinal ganglion cells, whose axon fibers carry visual information from the eye down the optic nerve to the brain. These neurons degenerate in **glaucoma, as well as in other optic nerve degenerations such as with ischemia, or compression from tumors**. Like other neurons in the retina and the brain, once they degenerate, there is no natural replacement, making retinal ganglion cells a strong candidate for cell replacement therapy. Great progress has been made in recent years in understanding how to differentiate stem cells into retinal ganglion cells in the laboratory, and in transplanting retinal ganglion cells into the retina.

"The challenge for cell therapy for glaucoma is even greater, because not only do the donor cells have to integrate into the retina, they have to regrow their axons to the brain," Goldberg said.

A team of faculty at Stanford faculty is focused on exactly this challenge of optic nerve regeneration, including **Yang Hu, MD, PhD**, assistant professor of ophthalmology; **Y. Joyce Liao, MD, PhD**, associate professor of ophthalmology and neurology; **Michael Kapiloff, MD, PhD**, associate professor of ophthalmology and of medicine; **Andrew Huberman, PhD**, associate professor of ophthalmology and neurobiology; and Goldberg, who anticipates the application of approaches to promote optic nerve regeneration to his stem cell research for retinal ganglion cell replacement.

Looking to the future

Together, these programs have used the research and clinical environment at Stanford to accelerate progress toward cell therapies for otherwise untreatable conditions.

"Stanford has been great for facilitating the movement of science between the lab and clinic," Wu said, noting the increase in clinical trials for regenerative therapies in the last few years.

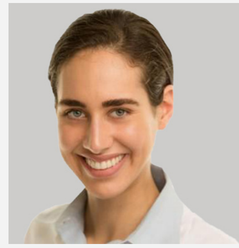
"This stem cell research coming from the Wu, Leng, and Goldberg laboratories really showcases the deep commitment of this ophthalmology department to include stem cell biology approaches to find cures for currently incurable diseases of the eye," Weissman said. "I am excited to see how these continued studies and advanced clinical trials can help return vision to patients."

FACULTY BY SPECIALTY

Comprehensive Ophthalmology and Cataracts

Henry Kistler, MD, PhD
clinical assistant professor

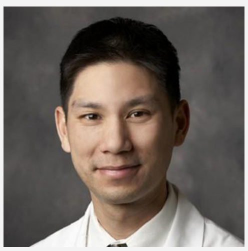
Artis Montague, MD, PhD
clinical associate professor



Suzann Pershing, MD
assistant professor

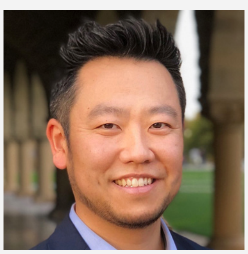
Susan Ryu, MD
clinical assistant professor

Corneal and External Eye Diseases



Charles Lin, MD
clinical assistant professor

Edward Manche, MD
professor



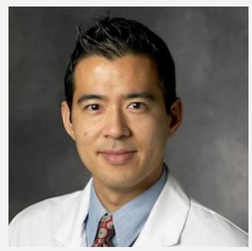
David Myung, MD, PhD
assistant professor

Christopher Ta, MD
professor

Geoff Tabin, MD
professor

Charles Yu, MD
assistant professor

Glaucoma

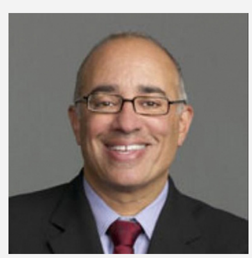


Robert Chang, MD
assistant professor

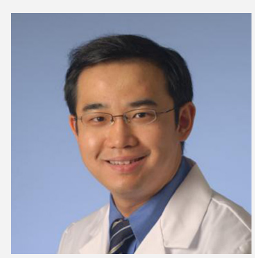
Caroline Fisher, MD
clinical assistant professor

Jeffrey Goldberg, MD, PhD
professor and chair of ophthalmology

Wen-Shin Lee, MD
clinical assistant professor



Kuldev Singh, MD
professor



Yang Sun, MD, PhD
associate professor

Neuro-Ophthalmology

Shannon Beres, MD
clinical assistant professor

Joyce Liao, MD, PhD
associate professor

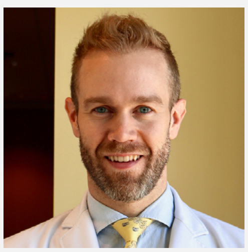
Heather Moss, MD, PhD
assistant professor

Ophthalmic Pathology

Ryan Basham, MD
clinical instructor

Peter Egbert, MD
professor emeritus

Ophthalmic Plastic and Reconstructive Surgery | Orbital Oncology



Benjamin Erickson, MD
clinical assistant professor

Andrea Kossler, MD
assistant professor

Albert Wu, MD, PhD
assistant professor

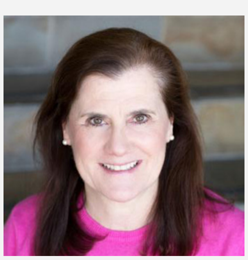
Optometry

Jill Beyer, OD
clinical assistant professor

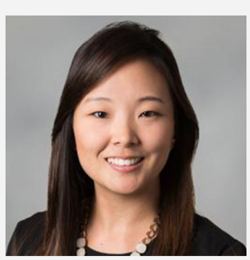
Steven Binder, OD
clinical assistant professor

Katherine Warner, OD
clinical assistant professor

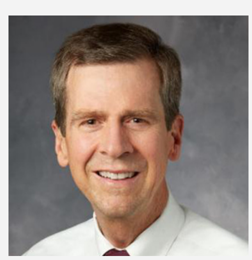
Pediatric Ophthalmology and Adult Strabismus



Deborah Alcorn, MD
associate professor



Euna Koo, MD
clinical assistant professor



Scott Lambert, MD
professor

FACULTY BY SPECIALTY

Retinal and Macular Diseases and Surgery

Mark Blumenkranz, MD
H.J. Smead professor emeritus

Diana Do, MD
professor

Theodore Leng, MD
assistant professor

Loh-Shan Leung, MD
clinical assistant professor

Vinit Mahajan, MD, PhD
associate professor

Michael Marmor, MD
professor emeritus

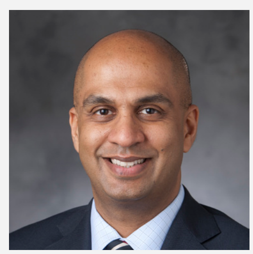
Carolyn Pan, MD
clinical assistant professor

Steve Sanislo, MD
clinical professor

Ira Schachar, MD
assistant professor

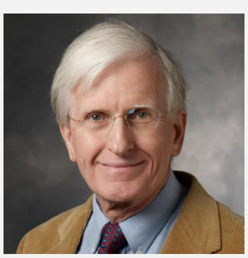
Ruwan Silva, MD
clinical assistant professor

Retina and Ocular Oncology



Prithvi Mruthyunjaya, MD
associate professor

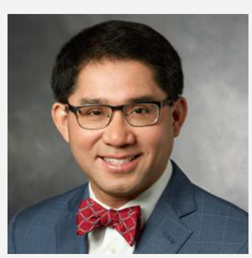
Pediatric Retina



Michael Gaynon, MD
clinical professor

Darius Moshfeghi, MD
professor

Uveitis

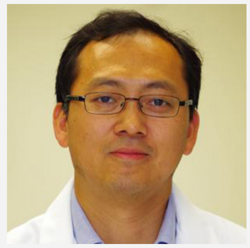


Quan Dong Nguyen, MD
professor

Ira Wong, MD
clinical professor

Research

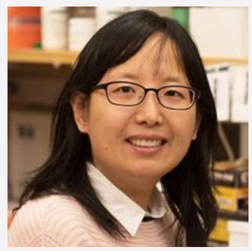
Alfredo Dubra, PhD
associate professor



Yang Hu, MD, PhD
assistant professor

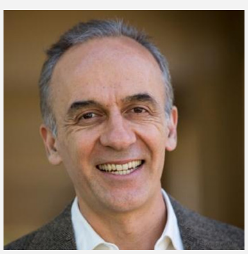
Michael Kapiloff, MD, PhD
associate professor

Daniel Palanker, PhD
professor



Sui Wang, PhD
assistant professor

Other Ophthalmology and Vision Science Faculty at Stanford



E.J. Chichilnisky, PhD
professor

Andrew Huberman, PhD
associate professor

Daniel Rubin, MD
professor

Creed Stary, MD, PhD
assistant professor

Douglas Vollrath, MD, PhD
associate professor

Brian Wandell, PhD
professor

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Adult Operating Rooms
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Palo Alto, CA 94303

Stanford Children's Health Pediatric Ophthalmology, Los Gatos
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Los Gatos, CA 95032

Stanford Children's Health Pediatric Ophthalmology, Palo Alto
Mary L. Johnson Specialty Services Building
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Palo Alto, CA 94304

For adult clinical appointments, call (650) 723-6995.
For pediatric clinical appointments, call (650) 723-1143.

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