



Stanford | Byers Eye Institute
MEDICINE | *Department of Ophthalmology*

Mary M. and Sash A. Spencer Center for Vision Research



our vision is to protect, enhance, and even restore **your vision**

Close your eyes. Imagine losing your sight. Now open them and imagine the sheer joy of getting it back. At Stanford Medicine, we're privileged to give this joy to many of our patients. But for those with the worst degenerative eye diseases, there are still very few options.

Too many of us live in fear of losing our sight, and with it, our independence. We're facing an epidemic of blindness as America ages.



Stanford's unmatched depth and breadth of expertise in each of these fields is the reason I came here. It's also why my friend and benefactor Mary Spencer established the Mary M. and Sash A. Spencer Center for Vision Research here at the Byers Eye Institute. No other place can leverage all these breakthroughs to find new cures. But finding cures isn't enough. We must get

And if we don't act, the number of us afflicted with diseases like age-related macular degeneration and glaucoma will double by 2050.

Our vision is to prevent this from happening with a comprehensive multidisciplinary research endeavor. Recent breakthroughs in neuroscience, genetics, imaging, stem cell medicine, and technology have given us a real shot at curing these as-yet incurable diseases and reversing the vision loss they cause.

them to patients faster. So we're developing new ways to monitor and even manufacture new therapies to accelerate clinical trials.

From discovery to delivery, we'll bring together the best minds and the best technologies to end blindness no matter what the cause. Please help Mary and me give everyone the joy of sight.


Jeffrey L. Goldberg, MD, PhD

Chair, Department of Ophthalmology



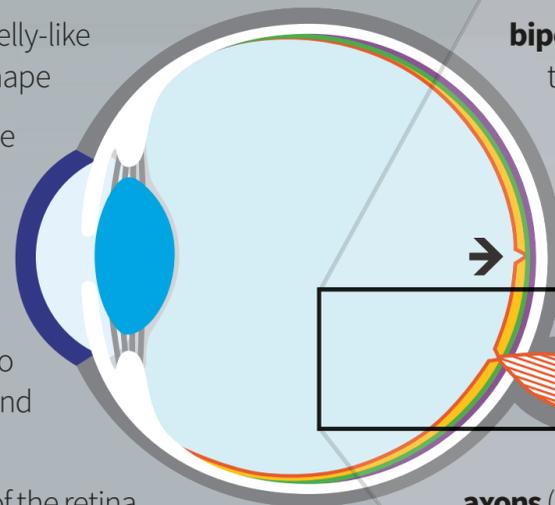
your vision is your primary link to the world

We are visual creatures. Half of our brains are devoted to vision and it's by far our most dominant sense. Most people fear losing their sight more than any other ability. Yet as our population ages, blindness is on the rise. Today, there are no cures for the most common causes of vision

loss, such as glaucoma and macular degeneration. In some cases we can slow them down—but there's no way to reverse the terrible damage they inflict on eyes and lives. Our vision is to change that. And give millions around the world the joy of getting their sight back.



your vision : the eye



cornea (dark blue) clear, dome-shaped “window” light passes through as it enters the eye

lens (medium blue) clear, elastic tissue that changes shape to focus light onto the retina

vitreous humour (light blue) clear, jelly-like fluid that maintains the eyeball’s shape

retina (orange, yellow, green) three layers of transparent cells at the

back of the eye that work together to convert light into electrical signals and send them to the brain

macula (black arrow) small patch of the retina where the concentration of cones is highest and vision is keenest

retinal pigment epithelium (purple) layer of dark-colored cells behind the retina that absorbs stray light and sustains the photoreceptors

rods (light green) cells that can detect dim light and are responsible for peripheral and night vision

cones (dark green) cells that detect color and detail and work best in bright light

bipolar layer (yellow) specialized neurons that process the signals from rods and cones and pass them to the retinal ganglion cells

retinal ganglion cells (orange) specialized neurons that process and transmit the signals from the eye to the brain

axons (orange lines) long nerve fibers that carry the visual signals transmitted by retinal ganglion cells to the brain

optic nerve (orange lines) a bundle of more than a million retinal ganglion cell axons that relays visual information to target neurons deep in the brain

and how it works

Light enters through your cornea (dark blue). Your iris opens or closes your pupil to adjust brightness and your lens focuses light onto the retina.

The light excites rods and cones, (green) cells at the back of the retina that respond to light and color and convert them into electrical signals.

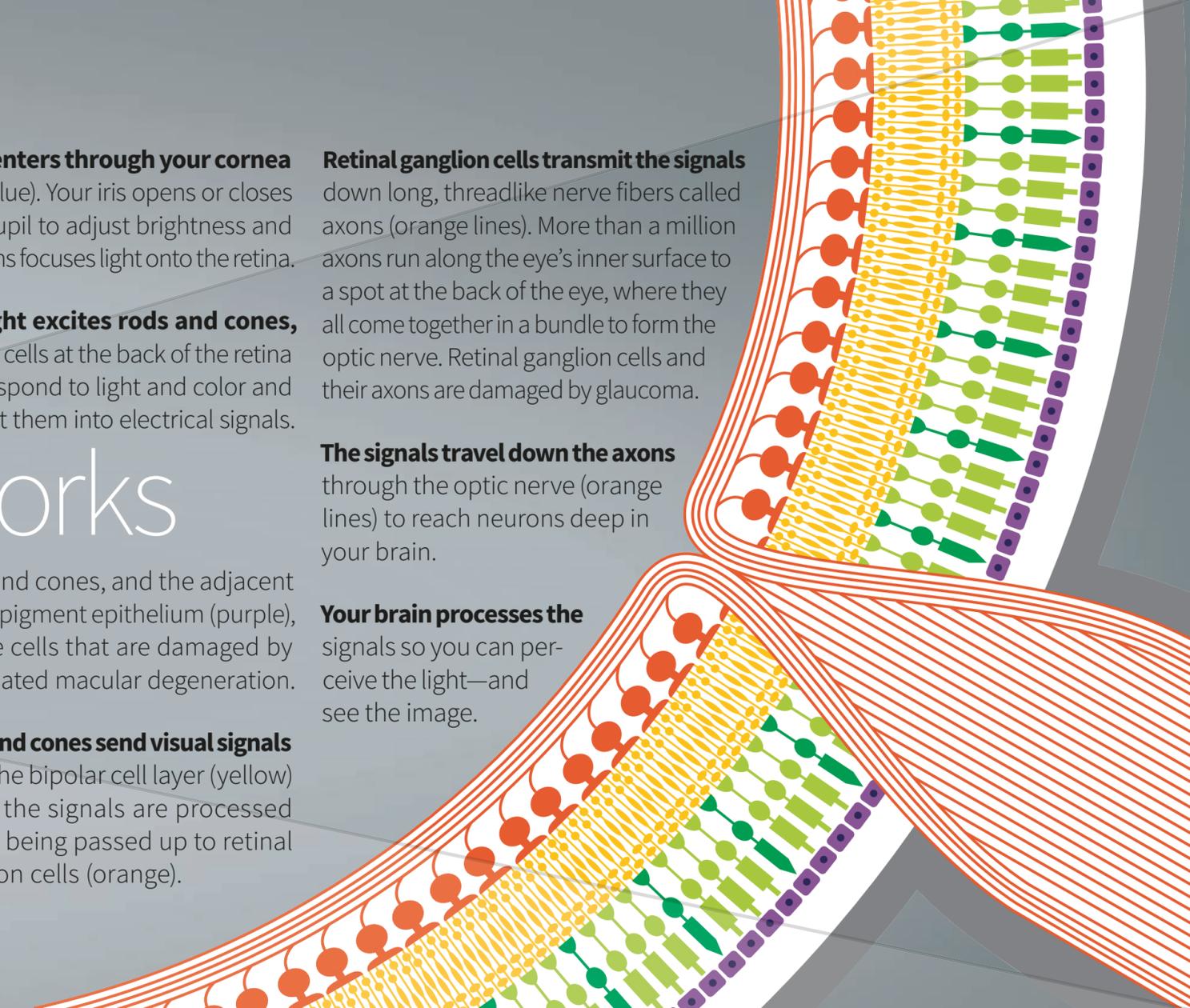
Rods and cones, and the adjacent retinal pigment epithelium (purple), are the cells that are damaged by age-related macular degeneration.

Rods and cones send visual signals up to the bipolar cell layer (yellow) where the signals are processed before being passed up to retinal ganglion cells (orange).

Retinal ganglion cells transmit the signals down long, threadlike nerve fibers called axons (orange lines). More than a million axons run along the eye’s inner surface to a spot at the back of the eye, where they all come together in a bundle to form the optic nerve. Retinal ganglion cells and their axons are damaged by glaucoma.

The signals travel down the axons through the optic nerve (orange lines) to reach neurons deep in your brain.

Your brain processes the signals so you can perceive the light—and see the image.





our vision builds on the foundations of Stanford **neuroscience**

“In a scientific first, blind mice regain eyesight.” That was the headline of a recent *Time* magazine story about how researchers at Stanford Medicine regrew damaged optic nerves in mice and restored their vision. A truly profound breakthrough, this work is a perfect example

of how we’re building on Stanford’s unmatched expertise in neuroscience. Working shoulder-to-shoulder with the best neurobiologists, molecular biologists, biochemists, bioengineers, and others from across our campus, we’re discovering exciting new approaches to ending blindness.

From figuring out how individual synapses fire to mapping every neural connection in the brain, scientists at Stanford’s interdisciplinary initiatives—the Stanford Neurosciences Institute, Bio-X, and ChEM-H—are untangling how the brain works. And because the retina and optic nerve are parts of the brain, we’re working with these researchers to retrain and even regenerate the neurons we use to see.

Axons in the brain don’t naturally regenerate in humans or other adult mammals. So when the axons

that form the optic nerve are damaged, it results in permanent vision loss. One reason for this is that the mTOR cell signaling pathway, a cascade of chemical interactions that promotes axon growth when we’re young, winds down—and our axons stop growing.

We restarted this pathway in adult mice whose optic nerves were disconnected in one eye. We then showed each mouse high-contrast moving images while its good eye was covered. The combination of

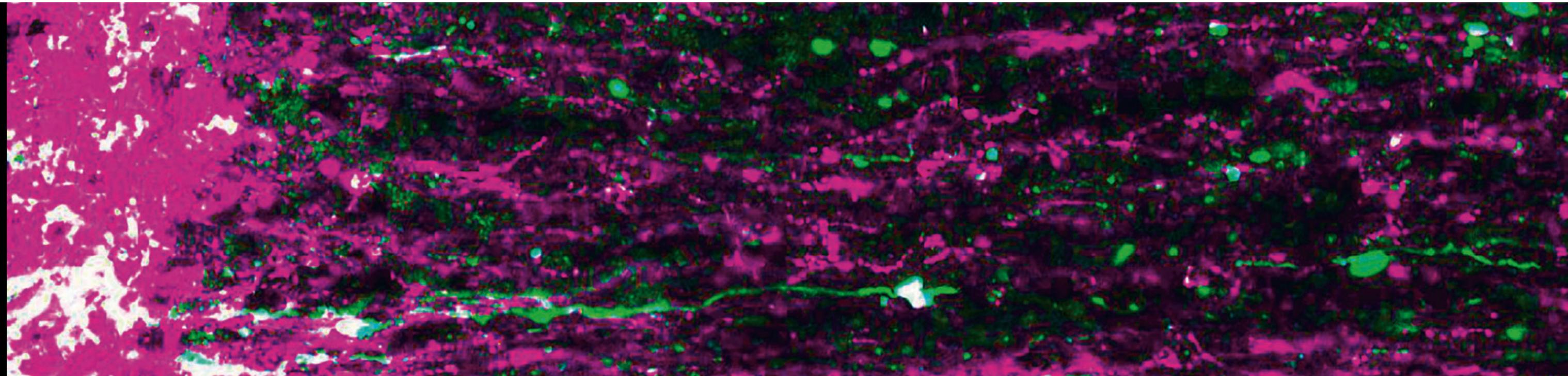
kicking mTOR signaling back into gear and forcing the mouse to use its bad eye worked. Axons in the damaged optic nerve regrew and connected to target neurons deep in the brain, restoring sight to the blind eye.

Tricking neurons into making new connections is another avenue we’re exploring. There’s a brief window of time when a newborn’s eyes first connect to the brain. But a protein called PirB attracts other proteins that close this window soon after birth. By luring those proteins away from the real PirB with a decoy

version of it, we can reopen that window so new neural connections can be made. This approach has the potential to restore sight to people whose eyes never had a chance to make those connections, like babies born with cataracts or patients with amblyopia or “lazy eye.”

These are just two neuroscience breakthroughs we’re using to fight blindness. With Stanford’s deep expertise on the brain and how its neurons connect, we’ll find more ways to protect, enhance, and even restore sight—our primary link to the world.

Using an innovative combination of gene therapy and visual stimulation, Stanford neuroscientists restored sight in mice whose optic nerves were completely disconnected from their brains. Here you can see axons from retinal ganglion cells (pink and green) regenerating and extending down the optic nerve from the injury site (far left of image). Amazingly, the regrown axons find their way to the correct regions of the brain and reconnect.



A close-up, high-angle portrait of a woman with vibrant, wavy red hair. Her eyes are a striking golden-brown color, and her skin shows signs of aging with visible wrinkles around her eyes. The background is a soft, out-of-focus grey. The text is overlaid on the right side of the image.

our vision harnesses the regenerative power of **stem cells**

Stanford launched a new medical era when we were the first to isolate human blood-forming stem cells in 1988. Since then, we've led the way in stem cell research. We discovered the stem cells that develop into brain cells and those that drive many types of cancer. Researchers every-

where use technologies we invented. And we were among the first to translate our discoveries into treatments. Today we're using stem cells to fight cancers, fix genetic disorders, and possibly even wake up arms and legs after strokes. Tomorrow? We'll use them to give people their sight back.

The power of stem cells to regenerate any tissue holds enormous promise for treating even the most devastating eye conditions. From regrowing retinal ganglion cells and axons killed in advanced glaucoma, to replacing cells destroyed by the leaky blood vessels of macular degeneration, we're on the verge of using stem cells to restore sight in patients suffering from these as-yet incurable diseases.

Our scientists are already making real progress. As you can see in the microscopy images below,

we've successfully transplanted retinal ganglion cells in rats. These cells settle into the retina, respond to light, and actually grow new axons down the optic nerve toward the brain. But that's just one of the roles stem cells play in our research.

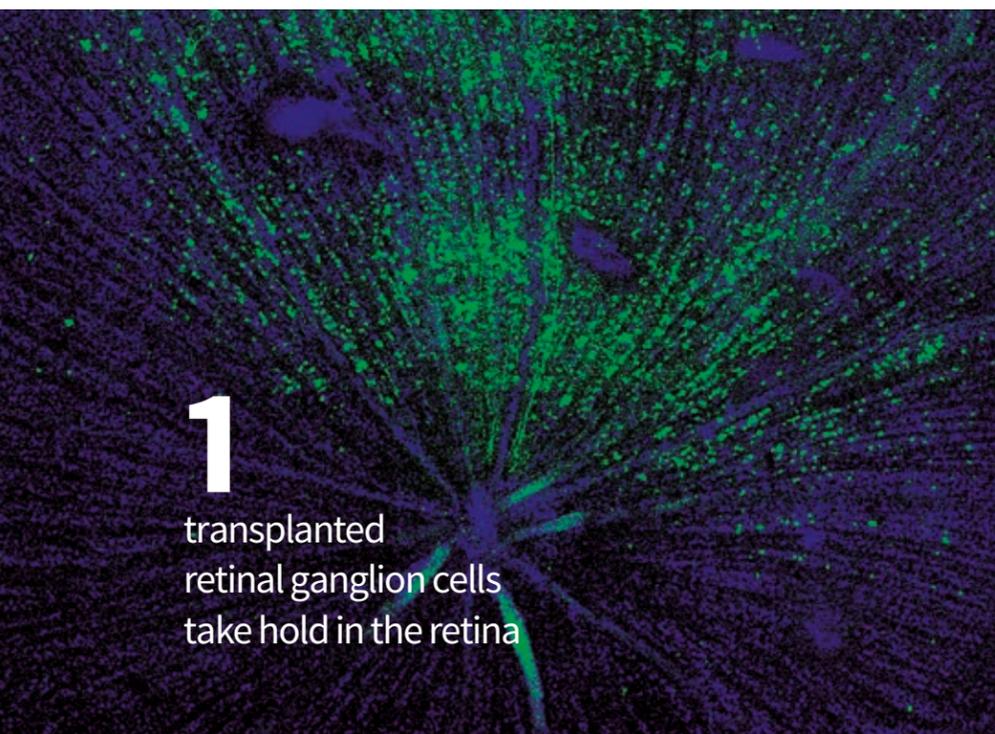
Stanford performed California's first transplant of adult neural stem cells behind the retinas of patients with macular degeneration. We're perfecting ways to grow fully developed rods and cones from stem cells and transplant them in sheets so they

have a better chance of thriving and connecting. And soon we'll be performing the next generation of stem cell transplants to replenish the cornea as it loses cells to wear and tear.

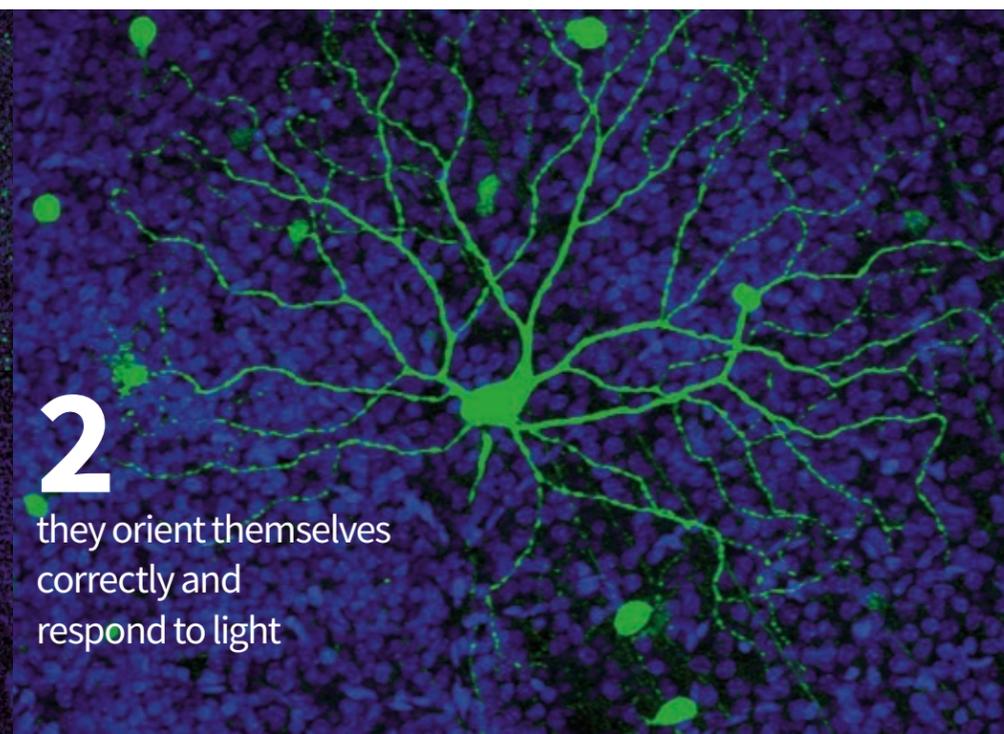
We're also using stem cells as tiny drug factories. Stem cells secrete high levels of potent survival and growth factors such as ciliary neurotrophic factor (CNTF) that promote neuroprotection and regeneration. We're already conducting some of the only clinical trials of growth factors for glaucoma and other diseases,

delivering them with eyedrops, injections, and even tiny capsules of implanted cells that produce and release these growth factors over time.

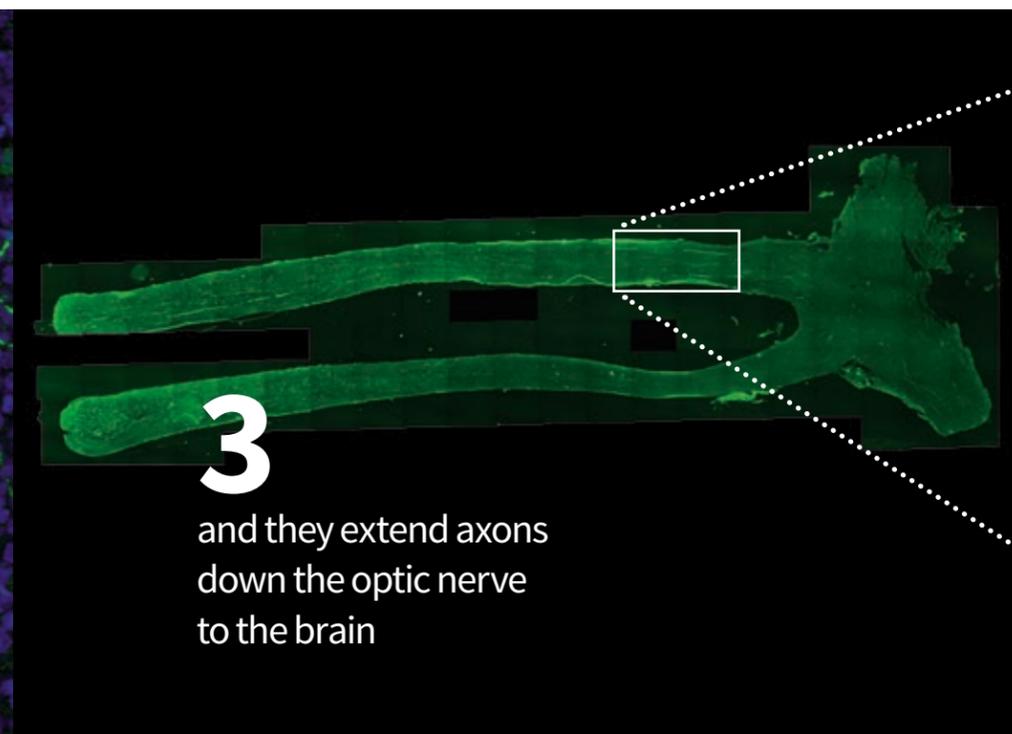
We've demonstrated the awesome potential of stem cells, but there's still much to do before they're ready for widespread use. By tapping Stanford's unparalleled expertise in isolating them, coaxing them to grow into the desired cell type, and getting them to thrive after transplantation, we'll harness their power to protect, enhance, and restore vision.



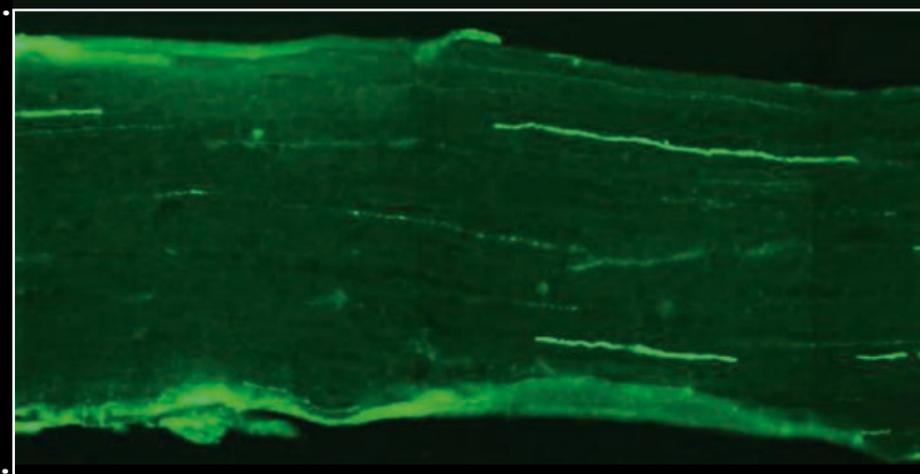
1
transplanted
retinal ganglion cells
take hold in the retina



2
they orient themselves
correctly and
respond to light



3
and they extend axons
down the optic nerve
to the brain





our vision predicts, protects, enhances, and heals with **genetics**

Discovering how to synthesize biologically active DNA

won Stanford Medicine a Nobel Prize in 1959 and ignited a revolution. We won another in 1980 for being the first to combine DNA from different species. We were the first to implant a foreign gene in an organism and get it to express

itself. And we were the first to use a person's full genomic sequence to predict risk for dozens of diseases. Gene therapies and gene mapping are crucial to our vision. And by leveraging Stanford's expertise, we'll use them not only to treat vision loss, but to predict and even preempt it.

We can edit parts of your genetic code to control the behavior of specific cells. For instance, as mentioned earlier, the axons that carry visual signals from your retinal ganglion cells down the optic nerve to the brain don't naturally regenerate after injury. But by tweaking the genes that code for certain cellular processes, we can coax axons to regrow.

Deleting a key gene called KLF9 is one approach we're using. KLF9 instructs retinal ganglion cells to produce a protein that suppresses the growth of

axons in healthy adults. DNA sequences constructed to suppress the expression of the KLF9 gene are delivered into cells by a specially engineered virus (see below). This new DNA tells the cell to stop producing the protein and the cell's axons start growing.

Another gene we can knock out inhibits the mTOR cell signaling pathway. Restarting mTOR with gene therapy is what made it possible to coax the optic nerves in those blind mice to regrow. Alternatively, we can use similar gene editing methods to shut

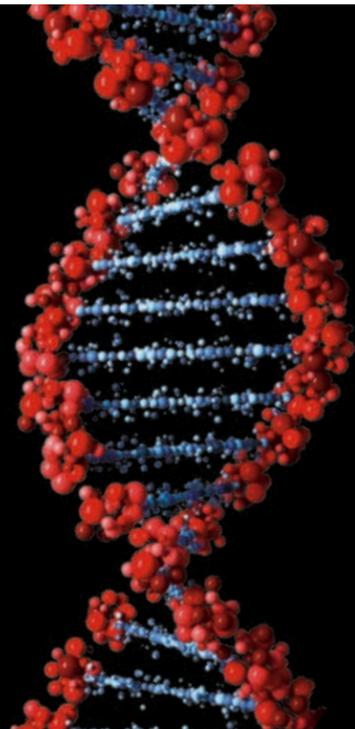
down the mTOR pathway and treat uveitis, a serious inflammation of the middle layer of the eye wall. Another approach we're pursuing combines gene therapy and microsecond laser pulses to precisely control treatment of retinal pigment epithelial cells in patients with macular degeneration.

But our vision extends far beyond gene therapies. As gene sequencing technology gets better, faster, and less expensive, we're using it to map the complex networks of interacting genes involved in diabetic

retinopathy and other degenerative eye diseases. Our goal is not just to understand the mechanisms driving these diseases, but to find genetic markers to predict risk in individual patients.

Gene-based treatment and prevention strategies like these are part of Stanford Medicine's program to create a new paradigm of lifelong wellness. Called Precision Health, it precisely tailors treatment and prevention strategies to each patient's unique biology and circumstances to stop disease before it starts.

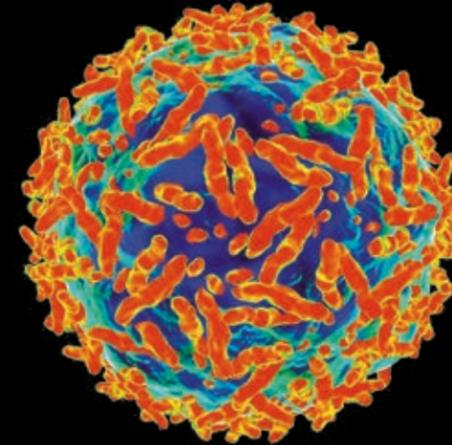
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identify the
gene or genes
you want
to edit



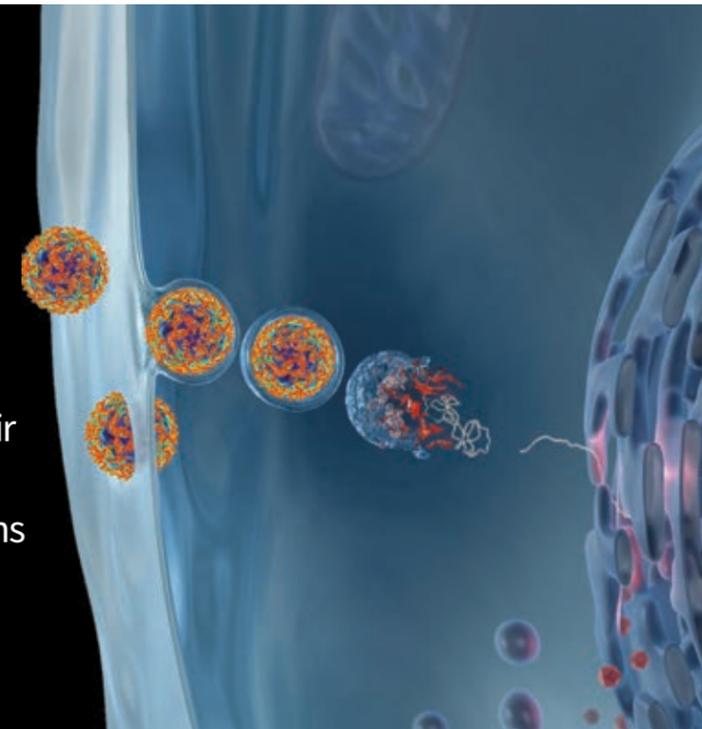
2
cut and paste
a new genetic
sequence using
a special complex
of molecules that
acts like scissors



3
load the edited
DNA into harmless
viral shells
(called capsids)
that only "infect"
specific cell types



4
inject the capsids
into the eye so
they can find and
enter the desired
cells to deliver their
payload of new
genetic instructions





our vision accelerates discovery with state-of-the-art **imaging**

Ironically, our inability to see is our biggest obstacle in translating discoveries into new therapies. Degenerative eye diseases can progress slowly, making it hard to tell if new treatments are working, which can drag clinical trials out for years. To speed things up, we need better imaging

tools—technologies Stanford has a long history inventing. We wrote the equations behind MRIs back in the 1950s. We were the first to image a single molecule, first to image gene expression in a live organism, and first to accomplish 3D imaging at the cellular level by making tissue transparent.

With the same technology astronomers use to peer into the heart of the galaxy, we're now able to look into a patient's eye and see the retina in unprecedented detail. Called adaptive optics, this technology compensates for the blur caused by the distortion of light waves as they pass through Earth's atmosphere—or for our purposes—the vitreous fluid, cornea, and lens of the human eye.

The resolution of the resulting images is astonishing. As you can see in the photos below, individual pho-

toceptor cells are clearly visible. With adaptive optics, we'll be able to track and predict the slow progression of degenerative eye diseases, cell by cell. We'll also be able to see how well new therapies are working with far greater speed and precision, which means we'll be able to get them to patients faster.

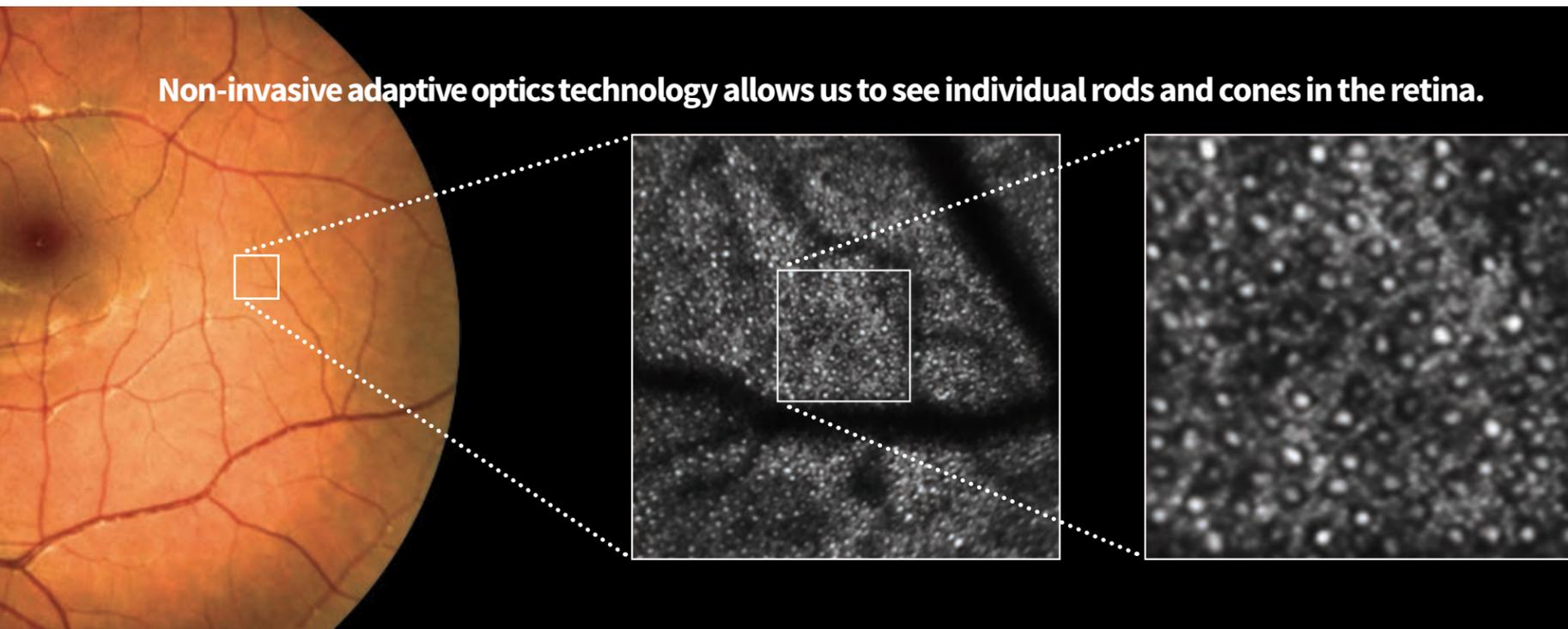
We're also using a familiar technology in a new way. Optical Coherence Tomography (OCT) scans have been a routine part of eye exams for years. These scans capture high-resolution 3D images of the retina

like the colorful ones below. Because they capture far more information than is typically used, and because so many are performed every year, OCT scans are a goldmine of untapped information.

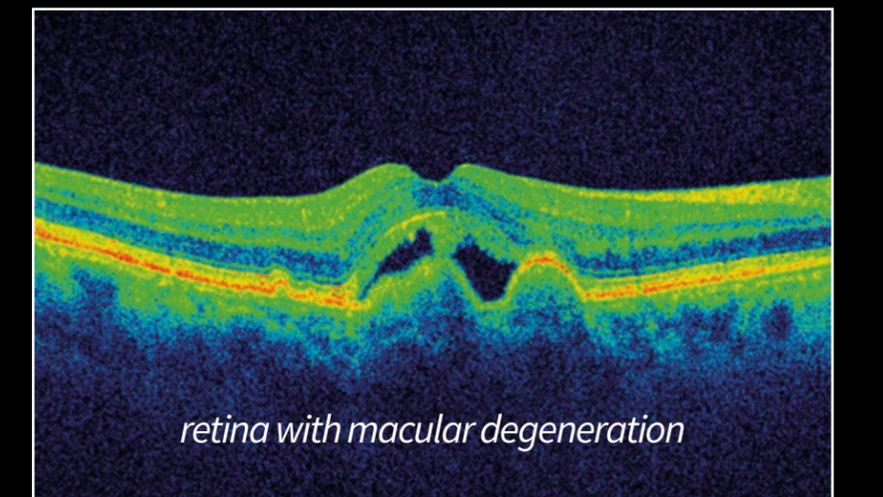
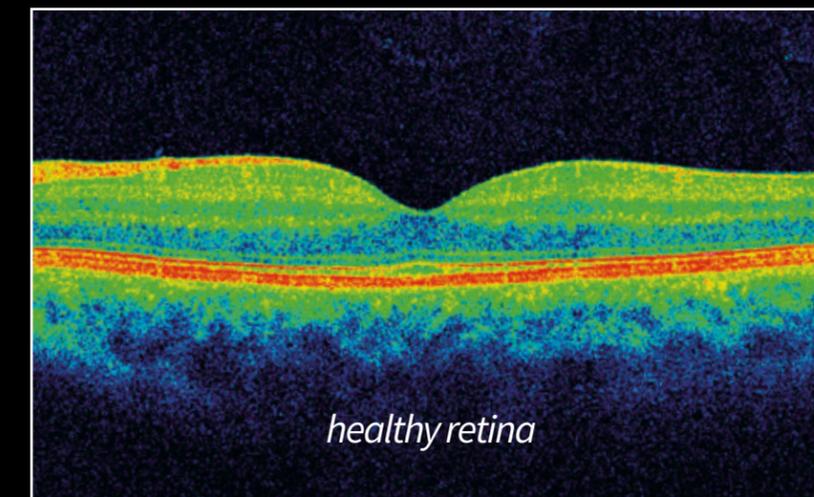
So we're analyzing data from thousands of scans taken of patients with both wet and dry age-related macular degeneration. Using machine learning to compare OCT scans from patients who develop the more serious wet form of the disease with those who don't, we're perfecting an algorithm to predict

disease progression. We hope to not only illuminate the causes of macular degeneration, but anticipate the change from dry to wet (or mild to severe) so we can intervene before serious damage is done.

We can now see individual photoreceptors firing in real time using these technologies and others. With this level of accuracy, we won't just speed up clinical trials. We'll predict and even prevent eye diseases before they start—and make Stanford Medicine's vision of Precision Health a reality.



We can predict the progression of macular degeneration using artificial intelligence and routine OCT scans.





our vision leverages the world's most advanced **technology**

Silicon Valley gives Stanford an unbeatable advantage.

No other university can attract finer innovators—scientists and engineers with a deep understanding of today's tools, and the passion and ingenuity to invent tomorrow's. The atmosphere here crackles with start-up excitement. Risks

are taken and envelopes are pushed. It's no accident laser retinal surgery got its start at Stanford in 1964. Today, the same goes for artificial corneas and light-powered retinal implants. And that's only the beginning. Soon we'll be using nanotechnology and bioprinting to fight blindness.

The tech revolution started on Stanford's campus more than 60 years ago, and we've been at the forefront of it ever since. Here, engineers, physicists, chemists, data analysts, programmers, and others—from both academia and industry—collaborate to create the future.

We work on the cutting edge of medical technology. Because the eye is a uniquely accessible organ, the field of ophthalmology has always been at the forefront of technological innovation. When we pioneered

laser retinal surgery back in the 1960s, we opened the door to everything from laser neurosurgery to tattoo removal. And the innovations just keep coming.

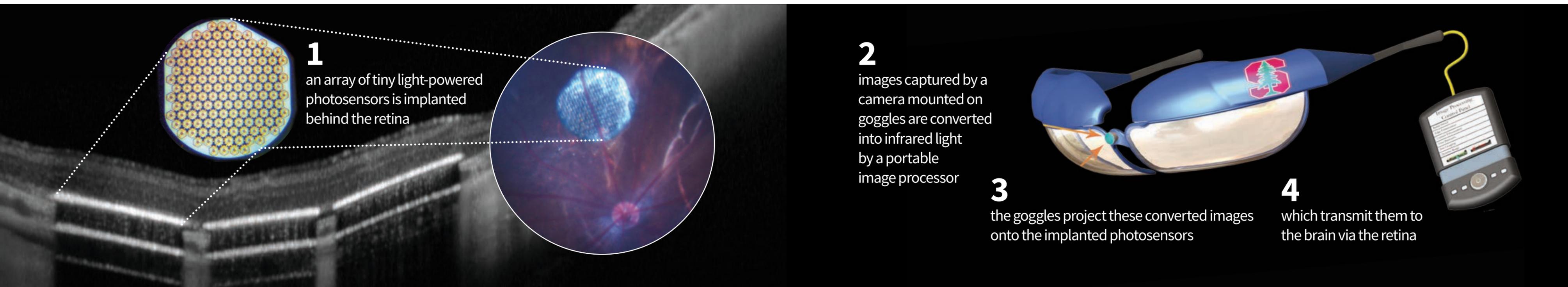
Since then, we've invented many laser technologies. Ultrafast lasers that rejuvenate diseased tissue without damaging nearby healthy cells. Scanning lasers that instantly cauterize the leaky blood vessels of macular degeneration and diabetic retinopathy. Even OCT-guided laser systems for cataract surgery. But our vision goes far beyond lasers.

Bionic light-powered retinas are just one example. As you see below, we're replacing missing photoreceptors with tiny silicon chips that transmit image data from video goggles to retinal neurons and down the optic nerve to the brain. Clinical trials are launching, and patients blinded by degenerative eye diseases may soon be able to recognize faces and even read.

We're also using magnetic nanoparticles to control the precise shape and placement of transplanted stem cells in the eye, and soon we hope to use them

as precision drug delivery vehicles. We're using tissue engineering to create artificial corneas. And soon we hope to use 3D bioprinting to produce everything from sheets of retinal stem cells ready for transplantation to complete retinas.

Silicon Valley's vibrant biotech community is vital to our vision. No other place on earth offers such technological and intellectual capital. Working with the best minds in biotech, we'll create new solutions and get them to patients faster than ever.





our vision streamlines clinical trials so patients get help **faster**

Twelve long years. That's the *average* amount of time it takes to develop a new drug in America. For degenerative eye diseases like glaucoma and macular degeneration, it can take many more years—years that the millions who face permanent blindness can't afford to wait. With one of

the only FDA-approved drug manufacturing facilities in academia, along with the most advanced research and imaging technologies, we'll transform today's plodding, one-size-fits-all approach into one that is nimble, precise, and customized to the biology of each individual patient.

Why does it take so long to develop new therapies?

Today's outdated clinical trials systems, byzantine regulatory requirements, and difficulties finding enough eligible volunteers all make translating discoveries into new therapies a glacial process. And, as mentioned earlier, the slow progression of many ophthalmic diseases holds things up even further.

We owe it to patients facing blindness to speed up this process. The Center will accomplish exactly that

by accelerating every stage of therapy development, from discovery to delivery.

It all begins in a new lab with specialized equipment to analyze ocular structure and visual function. This state-of-the-art facility will enable our researchers to not only discover novel treatment approaches, it will allow them to quickly determine which candidate therapies exhibit the most promise in pre-clinical studies so they can advance to human testing.

We'll produce those therapies at our own facility, which complies with the FDA's good manufacturing practice (GMP), strict standards that ensure safety and consistency in therapies produced for human use. Stanford is one of just a few universities with a dedicated GMP facility, and it gives us a huge head start in the race to get new therapies to patients.

We'll quickly see how well therapies are working with advanced imaging technologies like adaptive

optics. The incredible precision of these non-invasive technologies will overcome the hindrance of slow disease progression to speed things up further.

Finally, the Center will attract world-class faculty with the regulatory expertise to increase both the number and the speed of our clinical trials. With these outstanding scientists, facilities, and technologies, we'll set a new global standard for taking therapies from the lab to the clinic faster than ever.



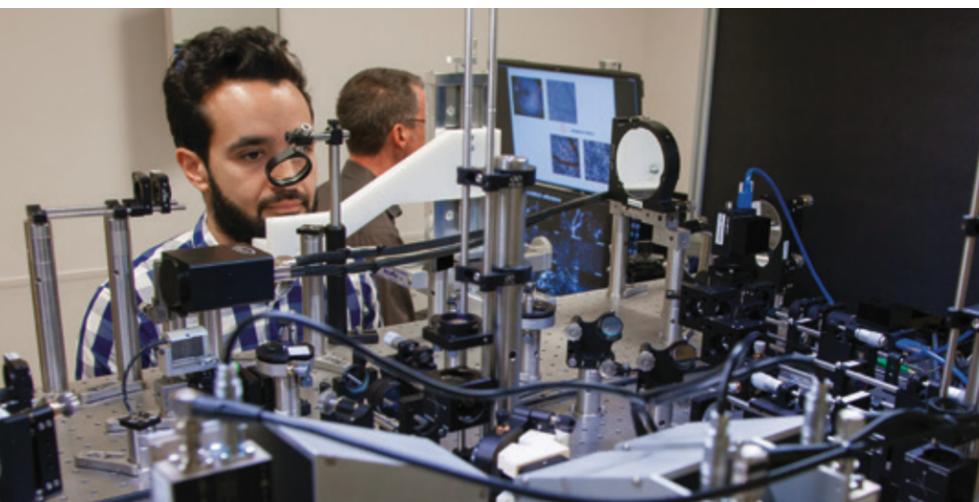
1

novel therapies are developed in our labs



2

treatments are manufactured in our GMP facility



3

cellular-level imaging accelerates clinical trials



4

patients get new therapies faster



our vision brings together the world's best **to end blindness**

My husband Sash truly appreciated the beauty of life. Whether he was sailing the seas of Maine and Florida, collecting modern art, building businesses and careers, or simply enjoying good food and wine with family and friends, Sash believed in savoring all life has to offer. He taught me and all those around him to drink in the beauty of life—while we still can.



When I discovered I had macular degeneration,

something was. The work he's doing in regenerative medicine, his worldwide collaborations with the best vision researchers, and his drive to develop better therapies and get them to patients quickly convinced me to help him.

One of life's cruelest ironies is that just when we're wise enough to truly appreciate its beauty, we start losing the ability to see it.

I've been lucky so far, but many of my friends and

I realized I could lose my sight, and with it, the ability to enjoy so much of that beauty. And I was shocked to learn that treatment options are so limited. This is also true for retinitis pigmentosa, glaucoma, and many other degenerative eye diseases. They told me, "All you can do is take vitamins and wait and see."

Well, Sash wasn't one to sit around and wait and neither am I. I knew I had to do something, and after getting to know Jeff Goldberg, I knew what that

millions around the world are losing their sight at a time when they most deserve to revel in the view. Jeff and I want to change that forever. That's why we're building this center at Stanford in Sash's honor and why we need your support. Together, we'll work to make sure everyone can witness life's astonishing beauty for as long as they're living it. **Please join us.**

Mary M. Spencer



your vision will make it possible to accomplish **our vision**

Philanthropic visionaries like you are making this bold initiative to tackle macular degeneration, glaucoma, and other incurable eye diseases a reality. Your gifts to the Mary M. and Sash A. Spencer Center for Vision Research will fuel the most innovative ophthalmic science and accelerate the

development of desperately needed new diagnostics and therapies. By bringing together the best researchers from across Stanford and around the world, you'll be bringing real hope to people facing blindness. With *your* vision, we'll give millions back *their* vision.

investments in vision research

We are optimistic about the future and ready to transform vision research and treatment. Gifts to the following areas will enable Stanford to mobilize the best people and most innovative science in a concerted multidisciplinary effort to end blindness.

Disease-Specific Research | varying gift amounts

To treat and prevent macular degeneration, glaucoma, retinal dystrophies, corneal diseases, and other eye and vision disorders, early stage research is critical to quickly move discoveries from the lab to patients. Your gifts will help stimulate innovative ideas and projects that otherwise might go unexplored, enabling investigators to generate early results that can attract additional funding from federal and other sources. Typically, the cost of a research project can range from several hundred thousand to more than one million dollars, but gifts of all amounts are appreciated and help to move research forward.

Endowed Vision Center Directorship | \$4 million

Strong visionary leadership is essential for the Center to attract top researchers, foster meaningful collaborations across multiple disciplines, drive innovation, and achieve scientific breakthroughs. This directorship will provide research funds and salary support for the faculty leader of the new Center.

Endowed Professorships | \$4 million each

Endowed professorships are the highest honor the University can bestow upon a faculty member. They give senior faculty the freedom to pursue their most promising and creative ideas and are a vital means of recruiting and retaining world-renowned researchers and physicians. New endowed professorships will advance several key areas of vision science and medicine, including retinal degenerations, optic neuropathies, corneal diseases, neuroscience, cell and gene therapy, and therapeutic and diagnostic device engineering.

Endowed Faculty Scholars | \$2 million each

Some of the most innovative research at Stanford is done by early- or mid-career faculty who redefine the boundaries of their disciplines and create new research paradigms or clinical innovations. Endowed faculty scholar awards will recognize and support these outstanding investigators, empower them to pursue high-risk, high-reward research, and help them develop into tomorrow's leaders in vision research and patient care.

Fellowship Funds | \$1.2 million to endow a fellowship; \$60,000 or more for expendable use

Fellowships allow us to attract and train the most talented graduate and postgraduate students in the field of ophthalmology. These funds support young investigators, enabling them to pursue new projects under the oversight of the best faculty mentors. Gifts to these funds will prepare a new generation of scientists to continue our quest to improve the lives of those suffering from eye disease.

Director's Research Fund | gifts of any amount

Gifts to this fund enable us to take advantage of exciting research opportunities as they arise. They support the most promising new projects across a range of ocular and vision diseases and help us translate discoveries made in the lab into treatments delivered in the clinic.

contact US

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WE ARE ALL PART OF THE EQUATION



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