



DISCOVERY

THE DISCOVERY EYE FOUNDATION



The Discovery Eye Foundation supports cutting-edge research related to sight-threatening eye diseases and their treatments.

Supporting vision-saving research at the University of California, Irvine's Gavin Herbert Eye Institute since 2002.

Thanksgiving 2021

You CAN Teach an Old Drug New Tricks

Previously approved drug shows promise for dry AMD

Getting FDA approval for new treatments can take years or even decades. But what about repurposing drugs that have already been approved for other diseases? That's precisely the question DEF-supported researchers are asking about a new treatment for dry age-related macular degeneration (AMD) and other aging diseases, including Alzheimer's and Parkinson's.

Six years ago, DEF Research Director Dr. Cristina Kenney began collaborating with Parkinson's specialist Dr. Howard Federoff of the Department of Neurology at UC Irvine. DEF-supported researchers had previously shown that damaged

mitochondria are a significant factor in accelerating cell death in AMD, and Kenney developed a cybrid mitochondria model to study AMD. Federoff had set up a screening system to look at drugs previously approved by the FDA that might improve the health of mitochondria, whose demise also contribute to Parkinson's and Alzheimer's. Of more than a thousand drugs screened, he identified 13 that could rejuvenate mitochondria. Kenney's cell-culture models and Federoff's system were a match made in research heaven.

Together, the researchers homed in on one drug, which Federoff named PU-91, because it was the 91st drug he'd tested. "When we added PU-91 to our AMD cybrids, the cells lived longer, they functioned better, the damage to the mitochondria was decreased,

While there is currently one type of treatment for wet AMD, there is no treatment at all for the dry form of AMD. An oral treatment for dry AMD is a game-changer.

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Old Drug, New Tricks

(continued from front)

and it really improved the health of the mitochondria,” Kenney says. “PU-91 is a drug called fenofibrate, which has been used for years to treat high cholesterol. When this drug is modified slightly, it helps sluggish mitochondria regain their health. We’re taking a drug that has been used for many years with FDA approval, and we’re repurposing it for a new target and new types of diseases.”

Benefits of repurposing

Tremendous savings of time and money are to be had by repurposing a known drug rather than starting with a drug people have never used before. Perhaps most importantly, because it’s been used for so many years in patients, the known drug has

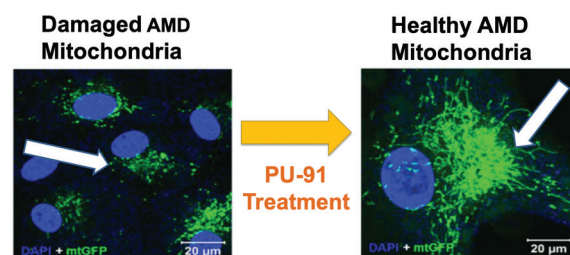
a proven safety track record. PU-91

has an additional advantage in that it is taken orally.

While there is currently one type of treatment for wet AMD — an

injection — there is

no treatment at all for the dry form of AMD. An oral treatment for dry AMD is a game-changer.



After treatment with PU-91, the AMD mitochondria are greatly increased in number and are healthier (green dye). Blue stains nucleus of cells.

The research is going so well that a company has been formed specifically to bring this drug to market for dry AMD. “As we become more successful, this type of drug can also be used for neurodegenerative diseases that have damaged mitochondria, such as Parkinson’s disease and Alzheimer’s disease,” Kenney says. “Potentially, it might even be used for something, such as glaucoma, that causes cell death of the retina ganglion cells in the eye. There are a lot of potential uses for it.”

Bench to bedside

DEF currently is supporting ongoing studies to optimize PU-91’s formulations for maximum effectiveness in patients with AMD. “It’s exciting, because this is the goal for translational researchers,” Kenney says. “Take what you’re doing at the bench and bring it to the bedside.”

Meet the Researcher: Anderson Vu

While Southern California native Anderson Vu wasn't doing so well in his college economics and accounting classes, he *was* doing well in general chemistry. So well, in fact, that he changed his focus to STEM (science, technology, engineering and math). When he graduated from University of California, Santa Barbara, in 2013 with a degree in zoology, he took a job in a hospital laboratory. One night, the emergency medical department called for supplies, and Vu was lucky enough to watch a hands-on medical procedure, called "thoracentesis" (a procedure to remove fluid from the area around the lungs) firsthand. That was the night he decided to become a surgeon.

At St. George's University School of Medicine in Grenada, Vu found he quite liked the thrill of trauma surgery. Then one day, he had the opportunity to watch cataract surgery. "I observed how meticulous they could be," Vu says. "I found the intensity of cataract surgery and surgical trauma to be quite similar, and I really enjoyed it."

When his sister, an optometrist, took him to her company's holiday party, Vu met an ophthalmologist who made him promise to do an ophthalmology rotation during his fourth year of medical school. It was during that rotation that Vu found he loved eye surgery's emphasis on very fine techniques and its relation to surgical and visual outcomes — he was hooked.

Vu met DEF Research Director Dr. Cristina Kenney when he was looking for a position at UC Irvine's Gavin Herbert Eye Institute. He came to work in the lab of Dr. Andrew Browne in 2020,



and it wasn't long before Vu was given DEF's Outstanding Research Award.

Vu earned the award for furthering a project that had been started by a previous student, who was looking at how a new type of software for testing visual acuity compared against the gold standard: the eye chart. Theoretically, the software was supposed to be more accurate, but

patients did worse on the software exam. Vu's award-winning proposal sought to build on this work and find the reason patients did worse on a supposedly superior test.

Eye-chart letters or symbols, also called optotypes, are used as the primary visual acuity test to track the progression of ophthalmology disease. Vu is now examining which optotypes give the most accurate assessment of a patient's vision.

"Accurately measuring visual acuity is a vital — and sometimes overlooked — step in all patient-oriented eye research," Kenney says. "Every new breakthrough comes down to showing that a discovery saves or improves vision, so being able to accurately measure that vision is essential. That's why DEF is so excited to support Dr. Vu's project."

"I am thankful we have organizations like DEF that support small-time researchers like myself," Vu says. "I've had great guidance from Drs. Browne and Kenney. They have mentored me in ways that are unlike anything I've ever experienced. I'm glad there is room for researchers who are also looking at ways we can change testing paradigms for the better."

Melanie Peters Thorne and her Collectible Car

Melanie Peters Thorne's brother gave her a 1929 Model A Ford in 1980. Five years ago, the avid car collector and Santa Fe resident decided to have it restored. It came back from the restorer on her birthday four years ago, a beautiful buttercup yellow, with no gas in the tank. Thorne and her husband were filling the car, when the spigot came loose, drenching her in gasoline. When she realized the toxic gas had affected her vision, she visited ophthalmologists and opticians nearby, all of whom told her there was nothing wrong. But she was seeing double and triple of everything.

A longtime donor to Discovery Eye Foundation, Thorne turned to DEF Medical Director Dr. Anthony (Tony) Nesburn. He identified the issue and referred her to the experts who could help her. Subsequently, she had cataract surgery on her left eye. She could see again.

When it came time for surgery on her right eye, her hardened lens resisted removal, causing a problem. "When the patch



came off, it was like looking through a muddy swamp," Thorne says. "The floaters were so big, I was naming them after continents." Surgery to clean up the vitreous debris followed, clearing most of the floaters.

Three years later, Thorne says, "Life is normal, life is great!" Her eyes are stable; she uses her left eye for distance and her right eye for close-up vision. She and her husband play tennis at least three times a week and "play cars" once a week — this involves their Ferraris and a car group called the "Santa Fe 500."

In addition to providing ongoing financial support to DEF, Thorne is a member of Vision Legacy,

which means she has included DEF in her estate plan. She also has donated blood for DEF Research Director Dr. Cristina Kenney's research, and she recruits others to do the same.

"It was Tony who figured out my eye problem, and I am very grateful," Thorne says. "DEF is on the cusp of making so many discoveries that will be instrumental in finding help for people with horrible diseases, such as macular degeneration. One of the great things about DEF's research is they share their findings, which has helped with breakthroughs for other diseases, including COVID. It is important that DEF's research continues. I know there are answers out there."



What Will Your Legacy Be?

DEF's Vision Legacy society offers an easy and meaningful way to make a vision-saving difference beyond

your lifetime. You can even use your estate gift for a

specific project, such as AMD, keratoconus or stem-cell research. For more about joining this important group, call (310) 623-4466, or visit www.discoveryeye.planningyourlegacy.org.