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DISCOVERY
THE DISCOVERY EYE FOUNDATION

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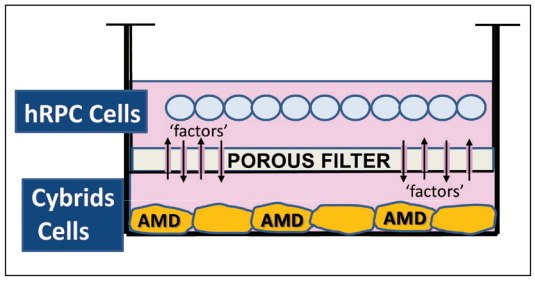
The Discovery Eye Foundation supports cutting-edge research related to sight-threatening eye diseases and their treatments.

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

DEF-Funded RP and AMD Projects Converge With Promise

Two hallmark DEF-funded projects are converging, providing great hope for those facing vision loss from retinitis pigmentosa (RP) or age-related macular degeneration (AMD).

The first project, headed by UC Irvine researchers Drs. Henry Klassen and Jing Yang, concentrates on putting human retinal progenitor cells into the eyes of those with RP in order to rescue damaged retinal cells. That project is currently in Phase II clinical trials, progressing toward FDA approval.



Tissue-culture model

According to DEF Research Director Dr. Cristina Kenney, if the project is approved by the FDA for use with RP, the next question is: What other diseases might these retinal progenitor cells be used for? That's where a second DEF-funded project comes in.

Kenney is working on a "personalized" cybrid cell model to screen agents that specifically target the mitochondria in AMD cells. To date, the researchers have different cybrid cell lines representing 60 different individuals with eye diseases. They are looking for novel mechanisms to protect AMD cells from dying.

Yang and Kenney are now working together to determine whether the retinal progenitor cells can be the agent that rescues AMD cybrids. "When we take the mitochondria from AMD patients and put them into healthy retinal cells, which makes cybrids, we have shown that these AMD cybrid cells will start to die. So we used that model to ask the question: How do we rescue them?" Kenney says.

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Colorful Collaboration to Treat Retinal Disease

A group of Discovery Eye Foundation–supported researchers is looking at testing color vision as a way to evaluate and treat age-related macular degeneration (AMD) and other retinal diseases.

"Color vision is affected with all varieties of retinal diseases, but it's not something that is routinely tested," says Dr. Andrew Browne, a clinical assistant professor of ophthalmology at the UC Irvine School of Medicine. "All the testing in clinical eye care revolves exclusively around black-and-white or white-and-white testing. The color-vision aspect is more about the quality of your visual experience, rather than the sharpness of your visual experience. We want people to see 20/20, but we want them to have a 'good' 20/20, not a 'bad' 20/20. There is a difference. There are people who are basically color-blind because of AMD or other diseases, but they see 20/20. You can be 20/20 and have poor quality vision and be very unhappy.

"It would be a significant step forward to have a test measuring color changes to detect early AMD."

"None of the therapies under investigation right now address this. Imagine living in an ashen, grey world versus living in a vibrant, highly saturated, colorful world. You can have crystal-clear vision, but the contrast and color can be washed out and ashen."

Browne has been collaborating with DEF Research Director Dr. Cristina Kenney and Dr. Kimberly Jameson of the Institute for Mathematical Behavioral Sciences at UC Irvine. Since one of the early signs of macular degeneration is the loss of color-vision perception, the laboratories are studying color vision in an effort to develop early diagnostics for people with AMD and other retinal diseases.

"It would be a significant step forward to have a clinical test measuring color changes to detect early AMD," Kenney says. "We believe measuring the loss of color perception may be the technique we are looking for to detect and follow AMD progression."

They are working to create simple, fast tools that can be self-administered on a tablet platform, such as an iPad, to evaluate parts of vision that are not now routinely tested anywhere in the world, in an effort to maintain or restore color vision. "Without tools that allow us to measure those aspects of vision routinely, we're not going to be addressing developing therapies to treat this," Browne says. "We want to restore the qualitative aspect of vision."

Meet the Researcher: **Mustafa Ozgul**

In secondary school in Turkey, Dr. Mustafa Ozgul learned to "see the big picture" when it came to research and science. It was an important skill, but not one that could have predicted his future expertise, which is in the smallest possible picture: nanotechnology.

Throughout medical school and his work at several universities in Turkey and the U.S., including University of California, Riverside, and California State Polytechnic University, Ozgul has been studying the use of nanotechnology to improve the delivery of drug therapies for various diseases.

It was a path that led to a meeting with DEF Medical Director Dr. Anthony Nesburn and DEF Research Director Dr. Cristina Kenney. At the time, Kenney's lab at the Gavin Herbert Eye Institute at University of California, Irvine, was working with peptides to find a treatment for the dry form of age-related macular degeneration (AMD).

"There is currently no FDA-approved drug to treat the dry form of age-related macular degeneration, which affects approximately 85%–90% of patients with AMD," Ozgul says. "Previous studies show that the humanin peptide protects cells, but it is found in lower levels in older people."

A peptide is a compound consisting of two or more amino acids linked in a chain. Humanin is a small peptide composed of 24 amino acids. Kenney, who has been researching mitochondria in people with AMD, tested treating damaged mitochondria with a more powerful version of the peptide, humanin-G, and found that the peptide improved the health of the damaged eye cells.

"The power of this peptide is tremendous, but no one had figured out exactly how it works or how to deliver it," Kenney says. "Currently, you can't eat it, and you can't inject it. One of our biggest problems was to figure out a realistic delivery system."

When the researchers met, Kenney was trying to find a way to stabilize and administer synthetic humanin-G, which degrades at normal body temperature. One such path was looking at nanoparticles to contain the humanin-G and allow it to be injected for slow release to treat diseases such as AMD and glaucoma, as well as Alzheimer's and other aging diseases.

The perfect addition to the team, Ozgul became an assistant project scientist at the Gavin Herbert Eye Institute. With his help, the researchers are now studying the use of nanotechnology to form nano-sized capsules that would hold the peptide. These capsules would allow for the stabilization and long-acting release of humanin-G.

"Our preliminary data show that the nanoparticles improve the long-acting release properties, and we believe the treatment can help cells recover and stop the progression of dry AMD," Ozgul says. The team has completed basic cell-culture studies and is currently working on animal studies. The next step will be human studies.

None of this would be possible without DEF. "DEF funding allowed us to develop the nanotechnology and stabilization formula for humanin-G," Ozgul says. "I am so grateful DEF was interested in our project. Because of their support, we are getting closer every day to our long-term goal, which is a treatment for the dry form of age-related macular degeneration."

YOUR DONATIONS AT WORK

Thanks to the generosity of our donors, DEF was able to purchase a game-changing instrument: the Incucyte Live-Cell Analysis System. The Incucyte screens cells 24/7, automatically collecting vital information and letting researchers analyze data quickly — reducing the time for detailed analyses from months to days.

"We are now able to screen 400 samples at one time," says DEF Research Director Dr. Cristina Kenney. "Additionally, we can screen the cells over days and weeks to determine how they respond to drugs and medications. Now we can gather the long-term results in 'real-time' without harming the cells or ending the experiment. This approach has provided invaluable information about the drugs and agents we are testing. It streamlines our analyses, which can now be done around the clock."

Kevin Schneider, PhD, placing cells into the Incucyte.

The automated information gleaned from the Incucyte helps fast-track scientific discovery. It is helping guide DEF-supported researchers to more rapidly determine what drugs or agents have positive and negative effects on diseases, such as age-related macular degeneration and diabetes, in an effort to discover treatments and cures.

Projects Converge

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Kenney and Yang developed a tissue-culture model, where the retinal progenitor cells are grown in one part of a chamber, and the AMD cybrids are grown in another part of chamber, surrounded by culture medium. There is a porous separator between the two chambers through which the cells can communicate.

"We are finding that the retinal progenitor cells produce a factor that protects the AMD cybrids," Kenney says. "This provides promising evidence that these proprietary retinal progenitor cells that are being tested for treating RP also may be helpful in AMD patients.

"DEF has been supporting both these retina-related projects for quite some time, and it's very exciting to see them coming together to potentially treat both RP and AMD."

$100,000 Bequest Makes Mark for Vision Legacy

Carol from Wisconsin started giving $25 a year to DEF in 2009. During the following decade, she incrementally increased the amount up to $200 a year. Then, in 2021, she left DEF a very generous — and unexpected — gift.

"We were so surprised and grateful to receive a bequest from Carol for $100,000, which was 3.5% of her estate," says DEF Medical Director Dr. Anthony Nesburn. "It was very generous of her to leave a legacy that will continue supporting eye research in perpetuity."

Like members of DEF's Vision Legacy society, Carol named DEF in her will. It's an easy and meaningful way to ensure your generosity makes a vision-saving difference beyond your lifetime. You can even use your gift to target a particular project, such as AMD, keratoconus or stem-cell research. If you have already named DEF as a beneficiary in your estate plan, please let us know. Call (310) 623-4466, or visit www.discoveryeye.planningyourlegacy.org for assistance in joining this important and appreciated group.