50 1970 2020 ANNIVERSARY

DISCOVERY
THE DISCOVERY EYE FOUNDATION

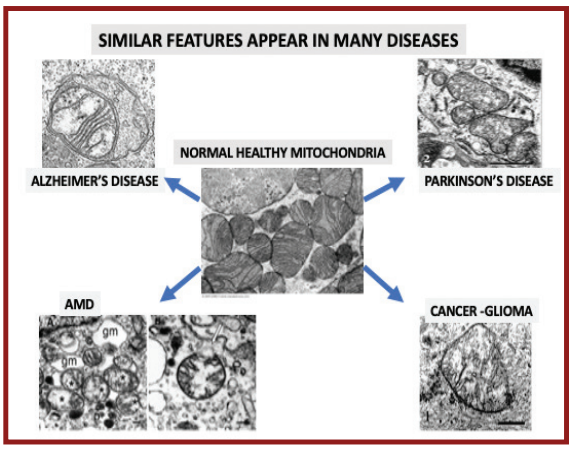
Thanksgiving 2023

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 Funding Leads to Shift in Treating Age-Related Diseases

DEF is at the forefront of a whole new way of looking at the treatment of age-related diseases — diseases that can be ascribed to failing mitochondrial energy production. Research is progressing with the goal of identifying drugs that improve mitochondrial health and their energy production.



The older way of viewing and treating age-related diseases was to treat the ailing organ, be it the heart, kidney, liver or brain. But age-related macular degeneration (AMD) and Alzheimer's disease, for example, involve many pathways, all dependent on failing energy production. DEF-supported researchers have been collaborating on a drug known as PU-91, also called fenofibrate, which rejuvenates failing and sick mitochondria to restore normal energy production.

PU-91 is an oral drug that already has been approved by the FDA for other purposes. Most recently, we have learned that PU-91 targets the master regulator of mitochondrial energy production. DEF Research Director Dr. M. Cristina Kenney has been working on this project with Parkinson's specialist Dr. Howard Federoff, formerly of the Department of Neurology at UC Irvine. DEF-supported researchers had previously shown that damaged mitochondria are a significant factor in accelerating

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8635 West Third St., Suite 390W
Los Angeles, CA 90048
(310) 623-4466
contactus@discoveryeye.org
www.discoveryeye.org
www.discoveryeye.org/blog

Meet the Researcher: **Fatima Elghazali**

California native Fatima Elghazali loves the creativity associated with doing research. “I like thinking outside the box, discussing new things with my mentors and new ideas,” she says. “I love when the experiments go right — finding out something’s possible when it wasn’t possible before.”

During her last year as an undergraduate at University of California, Irvine (UCI), Elghazali began “shadowing” Dr. Olivia Lee, an associate clinical professor of ophthalmology at the UCI School of Medicine. Lee introduced her to DEF Research Director Dr. Cristina Kenney.

“Dr. Kenney would ask me about my research, and I would ask her questions about the patients she was seeing,” she says.

Those conversations fed a collaboration between Lee’s and Kenney’s labs, on a project using Schirmer diagnostic tear strips in a novel way. Elghazali began working to isolate proteins to see if they can identify biomarkers and inflammatory cytokines associated with various ocular diseases to aid in treatment plans and disease diagnoses. It is an effort that may be helpful in the early diagnosis of keratoconus.

Elghazali applied to a post-baccalaureate program at the National Institutes of Health (NIH). She was accepted but struggled with the cost of moving across the country. Kenney encouraged her to apply to DEF’s Excellence in Research Scholar Program to help fund her travel. Using her Schirmer project experience, Elghazali won a DEF grant that allowed her to accept her place in the NIH program, where she is spending a “gap year” while applying to medical school.

“It’s been a blessing and honor to be able to do this,” Elghazali says.” I was struggling to gather the funds for this move, and it was amazing to get the support from DEF. Without it, I would not have been able to come to the East Coast to pursue research at our nation’s leading research facility. It helped fuel my next step as a scientist.”

Mario Antonini Leaves Visionary Legacy

Mario Antonini, a longtime board member and supporter of DEF, died this year at the age of 91.

The only child of Italian immigrants, Mario was born in Michigan and later moved with his family to California. While attending Stanford University for undergraduate and MBA degrees, he counseled his father, who had been a tile-setter and auto-plant worker, on how to run his masonry manufacturing business. Though he wanted to be an investment banker, Mario returned home to help in the family business and to complete his Army ROTC service.

Building Angelus Block into an industry-leading business in Southern California took tremendous dedication, and Mario was very proud to bring a third generation into the business: his son, Edward Antonini, and his daughter, Marla Antonini Richmond. He was even prouder to have seen his grandson, Matthew Richmond, become the fourth generation to enter the family business.

"Dad was the ultimate definition of the American success story," Edward says. "He was a true capitalist and the epitome of a self-made man. His passion and love for his business was usually his top priority, and he poured everything into making it a success."

Prone to bronchitis as a child, Mario was treated by exposure to UV light — with no eye protection. "As an adult, he surmised that that treatment gave him very early cataracts, as well as glaucoma," Marla says. "He had both by the time he was 30, along with a lifetime of eye problems."

DEF Medical Director Dr. Anthony Nesburn became his ophthalmologist, beginning a decades-long friendship. Mario began financially supporting DEF in 1987, eventually joining the board of directors.

"Mario was an active and involved DEF board member for at least 10 years," Nesburn says. "With his business background, he was always the voice of reason about financial and other matters. In addition, he was a steadfast friend and a model patient."

"Dad was not overly generous with his time or money to people or causes that he did not have the utmost respect and trust in," Edward says. "He was extremely, extremely selective. So, it's a testament to his trust and belief in DEF that he was so dedicated to the organization."

Mario left a substantial bequest to DEF, ensuring his legacy of support would continue to save sight long into the future.

VISION FOR THE FUTURE

When you join the DEF Vision Legacy Society, you make a profound impact on the gift of sight for generations to come.

It's easy to join **Vision Legacy**:

- Include DEF in your will and living trusts.
- Designate DEF as a beneficiary.
- Explore IRA charitable rollover options.
- Contribute through donor-advised funds.
- Create a charitable gift annuity.
- Establish an endowment.

For more information, visit discoveryeye.mylegacygift.org.

Treating Age-Related Diseases

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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. They 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 cybrid cell lines, the cells lived longer, they functioned better, the damage to the mitochondria decreased, and it dramatically improved the health of the mitochondria," Kenney says. "PU-91 was used for years to treat high cholesterol and triglyceride levels, and it has high marks for safety."

When this drug is modified slightly, it helps sluggish mitochondria regain their health. The researchers are now repurposing it for new mitochondrial targets and additional diseases, such as dry AMD. The next step is pre-clinical studies to optimize the delivery system for peak efficacy of PU-91.

"If we treat and rejuvenate a cell's mitochondria and energy production, we should be able to treat all these diseases with one drug rather than many different drugs. It's really a breakthrough."

"This represents a whole different way of thinking about aging and aging diseases," Kenney says. "In the past, disease has been defined by the organ it affects. But mitochondria and energy production play a role in all these diseases. Rather than thinking someone has heart disease or kidney disease, we can think of them as having metabolic pathologies that are directly related to mitochondria.

"Cancers, diabetes, AMD, heart disease and Parkinson's all affect different organs, but what they have in common is abnormal metabolism caused by abnormal mitochondria. So if we treat and rejuvenate a cell's mitochondria and energy production, we should be able to treat all these diseases with one drug rather than many different drugs. It's really a breakthrough."

IN MEMORIAM

Discovery Eye Foundation's longtime CFO, Gracie Rogoff, died suddenly in September.

Gracie began her association with DEF in 1985 as executive assistant to DEF Medical Director Dr. Anthony Nesburn in the ophthalmology research laboratories at Cedars-Sinai Medical Center.

Kind, giving and empathic, Gracie was the backbone of DEF. She was passionate about the organization's mission, and she dedicated her life to upholding and furthering it. Gracie reveled in giving to others and to making people smile.

The entire DEF community will miss Gracie tremendously.