Autumn 2023

visionary

Hope in sight®

Saving sight from scarring

Why your mitochondria matter

Peter's vision to beat glaucoma

CENTRE FOR Eye Research Australia

World Glaucoma Week
12-18 March 2023

Beating glaucoma together

Thanks to decades of research, we now have a great chance of preserving a person's sight if glaucoma is detected early enough.

It's why every year during World Glaucoma Week we join the global effort to share the importance of having regular eye checks. We also share our research towards finding better treatments and, ultimately, a cure for the disease.

And while we've made amazing progress, there is still so much more that needs to be done to help the 15 per cent of people with glaucoma who do not respond to current treatments.

In this edition of *Visionary*, you'll find stories from the people who have come together to search for answers.

Alongside our research, you can read about Peter Pitman, who took part in a clinical trial, and why research gives him hope for the future.

You'll also meet Jenny Turnbull, who has chosen to leave a gift in her will to CERA and learn why this is so important to her.

And there is also a story about you.

We've included the results of our 2022 supporter survey, which you may have completed last year, so you can learn more about other community members with an interest in fighting glaucoma and other eye diseases.

With all of us working together, I have no doubt we can collectively achieve new breakthroughs as we strive towards a world free from vision loss and blindness.

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THE UNIVERSITY OF MELBOURNE

the royal victorian eye and ear hospital

*All of the photography in this publication complies with COVID 19 restrictions. Some of the images were taken in 2019 before the pandemic.

Mitochondrial research: Associate Professor Ian Trounce and Dr Sushma Anand.

Photo: Anna Carlile

Why your mitochondria matter

Mitochondria are like microscopic batteries that provide most of the energy our cells need – and might be the key to new treatments for many eye diseases.

Found in every cell, mitochondria are tiny batteries that play an essential role in powering our bodies' systems – including sight.

"The heart and central nervous system – which your eyes are a part of – are completely reliant on mitochondria for energy," says Associate Professor Ian Trounce, Principal Investigator and Head of Mitochondria and Neurodegeneration Research.

Retinal ganglion cells, which make up our optic nerve – and transfer information from the eye to the brain – are among the most energy hungry.

"They're constantly firing – even when our eyes are shut," says Associate Professor Trounce. "It's like pushing electricity through a long cable for 1000s of kilometres."

When mitochondria stop providing enough power, our body's systems don't have enough energy to work properly – for retinal ganglion cells, this means vision loss.

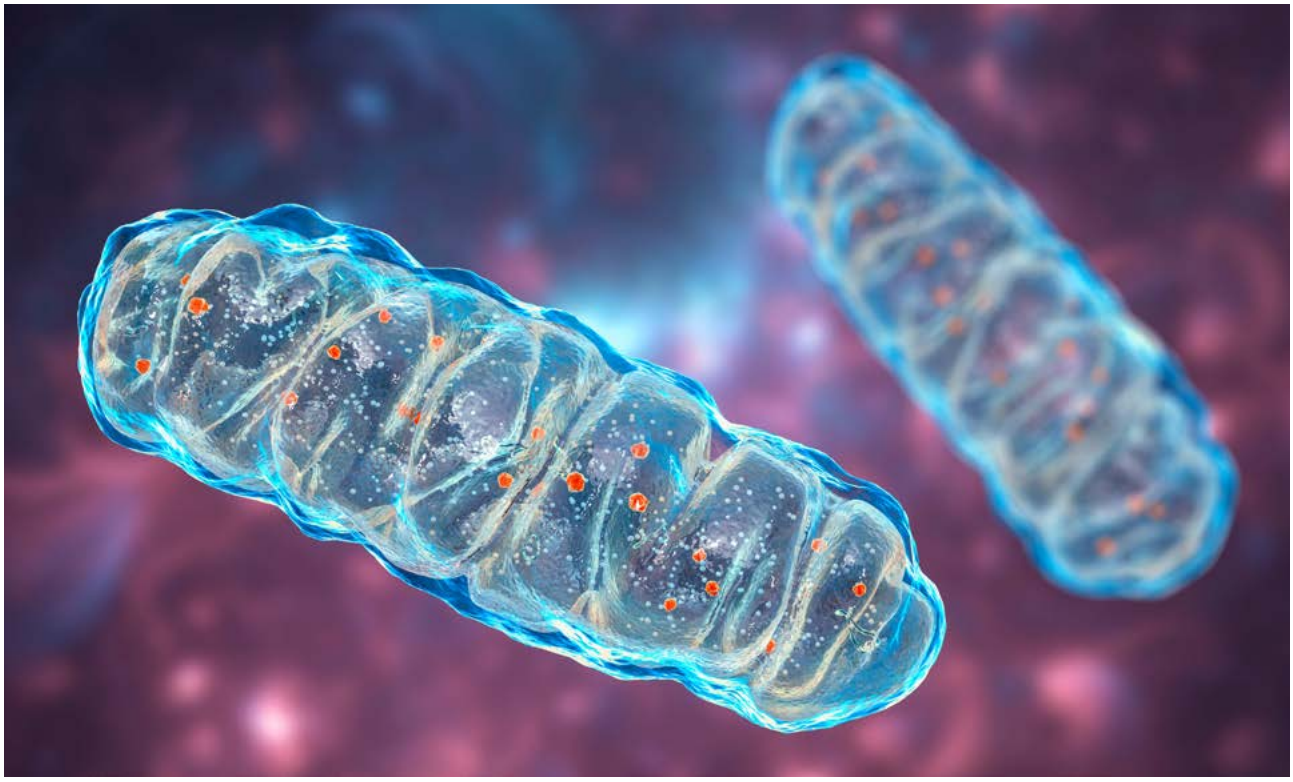
Learning why these little batteries stop working might provide clues to potential treatments for a range of eye diseases: from glaucoma and age-related macular degeneration (AMD), to rarer diseases such as Leber's Hereditary Optic Neuropathy (LHON).

The secrets might be hidden in the DNA of mitochondria.

Mitochondrial DNA

Most of our DNA is in the centre of our cells – the nucleus – and contains genetic information passed down from both our parents.

(Continued Page 4)



Tiny batteries: Mitochondria supply the energy our cells need.

However, mitochondrial DNA is stored outside of the nucleus and is only passed down from our mothers.

"Mitochondrial DNA is very important because it is made up of only 13 genes – but they are all essential for life," says Dr Isabel Lopez Sanchez, Head of Mitochondrial Biology and Disease.

Dr Lopez Sanchez is studying the mitochondrial DNA genetic changes that occur in LHON: a rare disease that damages the optic nerve and can cause the loss of central vision.

She says LHON is an ideal model to study the link between mitochondria and vision loss because it is caused by mutations in the mitochondrial DNA.

"By understanding LHON, we can learn more about other diseases, such as glaucoma."

LHON mutations affect only three of the 13 genes found in mitochondrial DNA, and only seem to impact retinal ganglion cells – similar to glaucoma.

In some people with LHON, having this mutation causes mitochondria to work less efficiently, eventually leading to cell death and vision loss.

New gene discovery

While one in 1000 Australians have a LHON genetic mutation, only about five people lose vision every year.

Dr Lopez Sanchez is looking at the difference between people who have a LHON mutation and lose vision, and those who don't.

She is exploring whether a gene found in the retina and retinal ganglion cells could be involved in cell death.

"We found a gene that's activated in people who lose vision that isn't activated in people who have healthy vision," she says.

Dr Lopez Sanchez is currently building a cellular model to understand the gene's purpose, which involves trying to activate the gene as it appears in people with LHON.

"It's a slow process because the gene we found doesn't want to be switched on or off, making it difficult to study," says Dr Lopez Sanchez.

"But, if our hypothesis is true, it could explain why some people with a LHON mutation lose vision and others don't."

Glaucoma genes

Learning about mitochondria can improve our understanding about many more diseases.

Associate Professor Trounce and his team are working to see if maintaining healthy mitochondria could slow down vision loss in glaucoma.

"By examining blood cells, we've established that mitochondria have some impairment in glaucoma patients," says Associate Professor Trounce.

Funded by the National Health and Medical Research Council, Associate Professor Trounce aims to identify the changes in mitochondrial DNA that may partly contribute to glaucoma.

Once these changes are found, his team, including Dr Sushma Anand, will investigate this link.

But first, they need retinal ganglion cell samples to study, and it's very difficult to obtain retinal ganglion cells from living donors without an invasive procedure.

Dr Anand, supported by the CASS Foundation, is developing a process to grow the cells in the lab using a technique called direct programming.

She says these cells will include the mitochondrial mistakes known to cause optic nerve diseases.

"Through this method, we hope to find out why retinal ganglion cells are affected in glaucoma and other eye diseases, such as LHON."

Dr Anand takes specific skin cells, called fibroblasts, and then replaces their native mitochondria with ones that contain different DNA.

From here, she uses direct reprogramming to encourage the fibroblasts to become retinal ganglion cells.

"This takes two weeks to one month, allowing us to complete several experiments already," says Dr Anand.

"The cells are showing the expected shift from skin cell characteristics to that of the affected nerve cell in the eye, which is the first step."

If Dr Anand's cellular model is successful, it will be much easier to learn more about what exactly goes wrong in the mitochondria.

"When we understand why mitochondria stop working, it's the first step in understanding what we need to do to keep them healthy – and in the longer term this could lead to new treatments that prevent vision loss from diseases of the optic nerve," she says.

World Glaucoma Week Appeal

➜ Support our work to find new sight-saving treatments for glaucoma.

➜ **You can donate on the form enclosed with this edition of *Visionary*, or online at cera.org.au/donate**

Photo: Anna Carlile

Leaving glaucoma in the shade

Peter Pitman hopes today's research will plant the seed for better glaucoma treatments in the future.

A green thumb and good vision served Peter Pitman well as a horticulturalist and garden designer.

Now in his 70s, Peter loves nothing more than being outdoors and tending to plants, often with his beloved wife Joan by his side.

Roses remain a firm favourite of Peter's, and good eyesight is essential to successful pruning that will keep them in full bloom.

"You need to know where you're cutting," Peter says.

"You don't want to leave any dead wood, so you need to cut it right on the notch."

Staying healthy

A commitment to health and fitness from an early age – including a stint as a VFL umpire – enabled Peter to keep doing what he loves.

"I think we take our natural health for granted," he says.

Peter didn't experience any health or vision problems until his 60s, when he required urgent surgery on a detached retina.

A couple of years later he was diagnosed with glaucoma when a routine eye check found very high pressure in his left eye.

Losing sight

Glaucoma occurs when the optic nerve, which carries visual information between the eye and brain, is damaged.

The most common cause is too much fluid pressure inside the eye, which builds up over time and causes injury.

Glaucoma is often called the 'silent thief of sight' because many people don't notice the early loss of peripheral vision, and by the

time they experience symptoms, irreversible damage has occurred.

Peter considers himself lucky the disease was picked up early, but after a lifetime of good health, he was not used to taking regular eye drops to keep it in check.

That's why he jumped at the chance to take part in a clinical trial at CERA investigating a potential new treatment.

"I wasn't sure the research would be able to help me – but I thought it might make a difference to someone in the future," says Peter.

↑ *Clinical research relies on volunteers like Peter Pitman (left and above with Professor Keith Martin).*

Clinical research

The trial, led by CERA Managing Director and glaucoma researcher Professor Keith Martin, is just one of many projects investigating the causes and potential new therapies for glaucoma at CERA.

Professor Martin says people living with glaucoma, such as Peter, play a vital role in eye research.

"We are truly grateful for their time and the enormous trust they place in our teams by trialling new treatments or taking part in other clinical research, including natural history studies, which track the progress of disease."

Professor Martin is also leading pre-clinical research to develop a gene therapy for glaucoma, and collaborating with Dr Flora Hui to test the ability of vitamin B3 (nicotinamide) to protect the optic nerve from damage.

Professor Martin says the combination of lab-based and clinical scientists gives CERA a unique ability to conduct research that makes a real difference.

He says boosting clinical trials at CERA over the next few years will be a key priority to give more people with eye diseases access to cutting-edge, new treatments.

Supporting research

Peter Pitman is grateful to have taken part in the clinical trial and appreciates the care shown to him by Professor Martin and the Clinical Trial Research Centre team.

He says the experience has given him a new-found appreciation of scientific research and his sight.

"You don't think about how important your sight is until there's a chance you won't have it."

World Glaucoma Week Appeal

➜ Help our research team find life-changing therapies so more people with glaucoma like Peter can see clearly.

➜ **You can donate on the form enclosed with this edition of *Visionary*, or online at cera.org.au/donate**

Photo: Anna Carlile

Saving sight from scarring

CERA researchers are investigating whether gene therapy could be used to combat scarring after glaucoma surgery.

Glaucoma surgery is a highly effective way of preserving sight, but like most treatments, it comes with challenges.

The medicine that is currently used after surgery, which reduces scarring, is toxic and carries a risk of vision loss.

Now researchers from across CERA are working to investigate if gene therapy can be used to combat scarring instead.

"We want to go straight to the source of scarring," says Dr Jennifer Fan Gaskin, Head of Ocular Fibrosis Research and Consultant Ophthalmologist at the Royal Victorian Eye and Ear Hospital.

Dr Fan Gaskin is working with Associate Professor Guei-Sheung (Rick) Liu, Head of the Genetic Engineering Research Unit, and Associate Professor Raymond Wong, Head of the Cellular Reprogramming Unit, to pinpoint the genes involved the scarring process and develop a potential gene therapy to prevent scarring.

Dr Fan Gaskin is also working with CERA's Head of Macular Research Professor Robyn Guymer AM, investigating macular degeneration and corneal scarring, in the hope the treatment could eventually be applied to other eye diseases.

"Scarring is not just a problem with glaucoma surgery, it is a source of disease for almost every part of the eye," Dr Fan Gaskin says.

Scar tissue

When medicated eye drops and laser surgery aren't an option for patients with glaucoma, filtration surgery is the next choice to reduce eye pressure and help preserve eyesight.

In the procedure, surgeons create an extra 'drain' in the eye to release excess fluid, reducing pressure and protecting the optic nerve from further damage.

Dr Fan Gaskin says the body naturally forms scar tissue, which can block the drain and cause it to fail.

"We have to use very strong anti-scarring medication that is quite toxic and not specific to the cells we are targeting."

The medication can weaken the healthy tissue around the new drain, which can eventually cause leakage and open the area to infection.

"At worst, this can lead to a total loss of eyesight," she says.

Identifying scarring genes

To help Associate Professor Wong pinpoint the genes involved in scarring, Dr Fan Gaskin and her team will take healthy cells from glaucoma patients before they undergo filtration surgery.

"We will take a biopsy of the tissue that typically goes on to scar after surgery and sequence the genes to identify the specific genes involved in the scarring process," says Dr Fan Gaskin.

"Then we manipulate the cells in the lab to encourage scarring and see what happens to the genes."

Gene therapy collaboration: Dr Jennifer Fan Gaskin and Associate Professor Guei-Sheung (Rick) Liu.

Associate Professor Wong and his team look at the gene changes to determine which one is involved in scar formation.

"It's very likely this approach will allow us to target the genes that are important in the scarring process," says Associate Professor Wong.

Editing genes

Using CRISPR gene editing, Associate Professor Liu's team plans to edit the gene that promotes the scarring process to prevent scars from forming excessively.

"This could potentially result in a more effective, targeted and longer-lasting treatment than the currently used drug," says Associate Professor Liu.

In the future, a potential gene therapy could be delivered via an injection to the eye as part of the treatment.

While the research is still early, Associate Professor Liu is cautiously optimistic as gene therapy has been successful in treating other eye diseases.

"If this is successful, we can move our research from the lab to the clinic," he says.

World first: Dr Luis Alarcon-Martinez aims to observe blood flow in the optic nerve.

Photo: Anna Carlile

Looking behind the eye

Powerful imaging techniques are allowing us to see living tissue in the optic nerve and the damage caused by glaucoma at a scale never seen before.

Seeing the intricate structures and processes that power our vision as they occur in the eye can help scientists develop new treatments to fight disease.

Dr Luis Alarcon-Martinez, Head of the Visual Neurovascular Research Unit at CERA, is using two-photon microscopy techniques to investigate the optic nerve at a scale not previously possible.

"It's very exciting because this novel microscope's setup will enable us to see optic nerve fibres damaged by glaucoma in extremely high detail," says Dr Alarcon-Martinez.

"This will hopefully provide insights into why glaucoma causes this damage in the optic nerve."

Your optic nerve is like a cable: transmitting electrical signals from the eye to your brain, where they're interpreted as images.

In glaucoma, these signals are disrupted.

The disease attacks the retinal ganglion cells, which make up the optic nerve, leading to vision loss.

It is not known exactly how retinal ganglion cells are damaged in glaucoma, but one of the biggest risk factors is high intraocular pressure (IOP).

Zooming in

While not all patients with glaucoma have high IOP, many show irregularities in the blood vessels of their eyes – something Dr Alarcon-Martinez is keen to investigate.

"A problem we face in glaucoma research is that we don't have imaging techniques to visualise the optic nerve at very high resolution," says Dr Alarcon-Martinez.

Two-photon microscopy is an imaging technique that allows the visualisation of living tissue at depths unachievable with other microscopes.

The team recently developed a world-first two-photon microscopy image set up to see the blood flow in the retina of living organisms – leading to the discovery of previously unseen structures.

Thanks to an Australian Vision Research grant, Dr Alarcon-Martinez's team will now use this technology, combined with special microsurgery techniques, to access the optic nerve in a living organism.

They will then attempt to compare the blood flow in a healthy optic nerve against that of a glaucoma-affected optic nerve.

"Two-photon technology has been around for a long time, however, we are the first to adapt it for these purposes," says Dr Alarcon-Martinez.

Hope for gene therapy

Dr Alarcon-Martinez says, if successful, the insights provided by the imaging could be applied to future trials of gene therapies such as those being developed by Professor Keith Martin, CERA Managing Director and Head of Glaucoma Research.

Professor Martin is leading a collaboration between the University of Melbourne and the University of Cambridge to investigate potential gene therapies to strengthen the optic nerve and protect it from damage.

To achieve this, the research team are studying a molecule that may hold the answer to improving the 'transport system' within the nerve fibres of the eye.

Professor Martin says he is excited by the potential this imaging technique could offer.

"The ability to visualise the optic nerve in such high detail may enable us to better understand how the optic nerve degenerates in glaucoma and how it can be repaired," he says.

"In turn, this could help us determine which gene therapies are most likely to be effective in human clinical trials."

Broader impact

While in its early stages, the research could provide preliminary data that may one day lead to developing therapies that preserve optic nerve health – and support existing strategies for lowering intra-ocular pressure.

"If we're successful, it could have a huge impact on glaucoma and other diseases related to the optic nerve," says Dr Alarcon-Martinez.

This includes other eye diseases such as age-related macular degeneration, as well as many neurodegenerative diseases such as Alzheimer's and Amyotrophic lateral sclerosis, the most common form of motor neuron disease.

Dr Alarcon-Martinez says hopefully in the future the technology could help assess the impact of trauma on vision.

"We may even be able to examine the eye injuries suffered by military personnel who have received trauma to their optic nerve caused by explosions."

Having your say

We're grateful to everyone who took part in our 2022 *Supporter Survey*. Your insights will help shape the information, events and communications we provide in 2023.

CERA's generous community of supporters have spoken out about their passion for eye research in the findings of our latest *Supporter Survey*.

Gifts in Wills Lead Bron Sugden thanked the 667 people who responded to the 2022 survey.

"Your insights will be invaluable in helping us provide timely, relevant information to our supporters in a range of ways that suit them," she says.

"Many of you are passionate about supporting eye research because of a personal experience with the disease.

"Feedback from the survey will ensure we keep you up to date with the latest in eye research and the impact your support makes."

Survey results

Personal experience continued to be an important motivator for those supporting research.

And with more than 85 per cent of survey recipients indicating they are over 55 – including 53 per cent who are 74 or older – there is a strong interest in eye diseases that affect older people.

Like our previous survey in 2019, glaucoma (48 per cent) and age-related macular degeneration (44 per cent) continued to be the two eye diseases of most interest to our supporters.

There was also strong interest in cataracts (25 per cent) and diabetic eye disease (17 per cent).

The percentage of participants interested in inherited retinal disease (19 per cent), which typically starts at a younger age, more than doubled since 2019.

The survey demonstrated our donors' strong commitment to continuing to support CERA, with more than two thirds indicating they were very likely or extremely likely to donate again.

Almost 80 per cent said it was easy or very easy to donate to CERA.

While 28 per cent said their donation made "a great deal" or "a lot" of difference to eye research, Bron stresses that even smaller donations make a significant impact over the longer term.

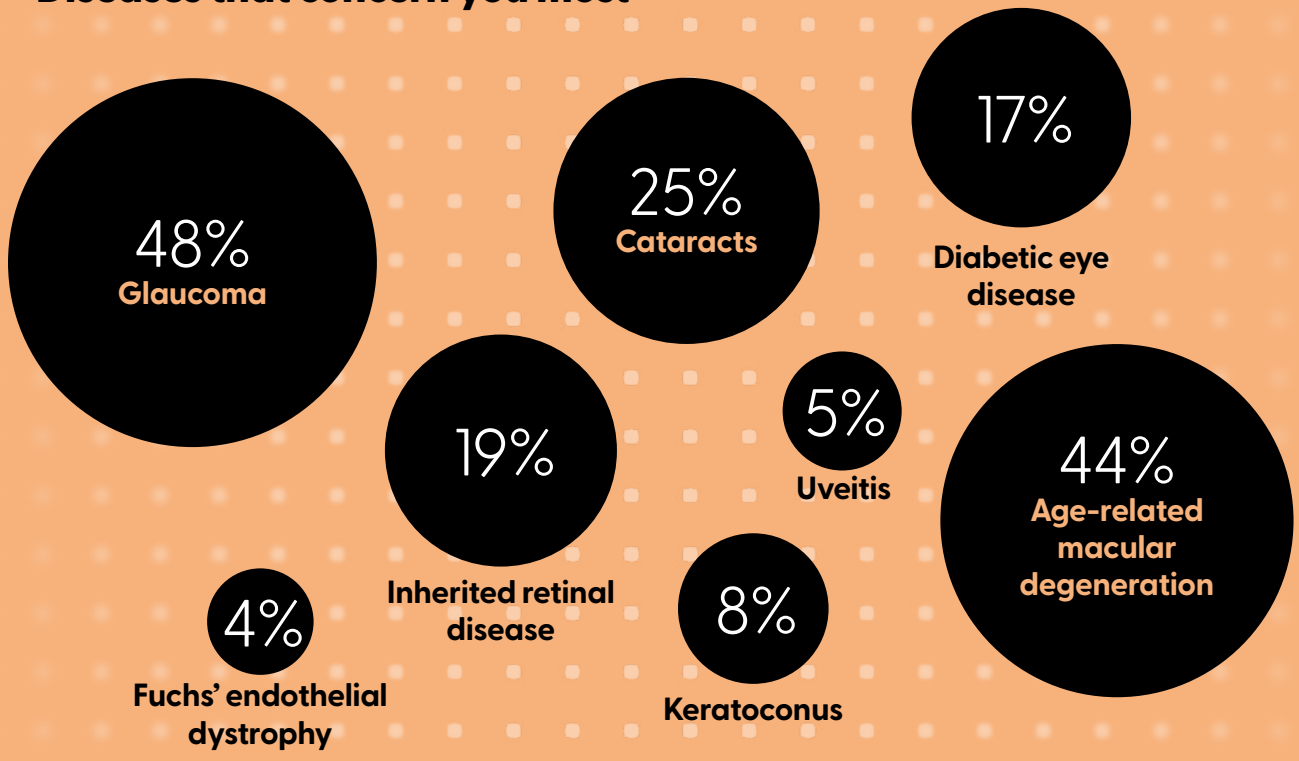
"Every donation adds to the one before, and contributes to the one after. What may seem small at the time, increases exponentially.

"Please know your donation will make a significant impact on the lives of those who will benefit from our research.

"We are particularly grateful to those supporters who requested information on giving monthly by becoming a CERA Luminary.

"We are also honoured that many of you have indicated you will leave a gift in your will to CERA."

Diseases that concern you most



Figures exceed 100% as respondents nominated more than one disease.

While we recently welcomed supporters back for our first in-person community forum in over two years – it's clear the pandemic has changed the way supporters want to receive information.

While most people favoured in-person events, or a mixture of in person and online, 29 per cent said they preferred to attend online events.

The vast majority (71 per cent) said these events should focus on 'learning about the latest in eye research', while 42 per cent wanted 'information on keeping your eyes healthy'.

"We are extremely humbled by the many kind comments we received and appreciate the ongoing support of our donors," says Bron.

"We could not do our research without them."

What you told us

"CERA has kept me feeling more hopeful with the latest in eye research, especially in the last few years, with the hope of gene therapy regarding retinal eye disease."

"This has given me reason to keep positive and hope in my later years there will be something to look forward to."

"This is a genuine organisation doing research on the cutting edge and getting real results."

"I am enjoying the benefit of treatment for wet AMD which CERA helped bring online. I love to hear reports of progress, or otherwise, in the projects undertaken by CERA."

A legacy of sight

Jenny Turnbull has always had a passion for helping others in need. A glaucoma diagnosis almost 30 years ago inspired her vision to leave a lasting legacy.

In her own words, Jenny Turnbull has a "blessed life" and she isn't letting glaucoma get in the way of that.

Fortunately, her glaucoma was diagnosed early and treatment has slowed progress of the condition but, for many people, this isn't the case.

That's why Jenny has chosen to leave a gift to CERA in her will – to help transform the diagnosis and treatment of eye diseases in the future.

"I'm very grateful for the life I've had from birth till the present day – and happy to leave a legacy that might benefit future generations," Jenny says.

↑ *Gift of sight: CERA is grateful to Jenny Turnbull and Janet Cliff.*

Early life

Born in East Malvern, Jenny grew up in a happy household in Oakleigh with her mother, father, sister and two brothers.

"We had many happy holidays and day trips in our little Austin 7 – a matchbox on wheels," Jenny says.

After completing her teaching certificate, aged 18, Jenny was the first in her family to leave home and worked in the country for a few years.

"I was posted to Marino – a far-flung country town in the western district," she says.

After travelling around Europe and the UK for 12 months, Jenny arrived back in Melbourne in 1961, where she worked as a vocational counsellor.

"I really enjoyed helping people get back into the workforce, and I continued to work in rehabilitation until I retired," she says.

Diagnosis no barrier

Jenny's mother was diagnosed with glaucoma in the 1960s, but Jenny didn't quite understand the significance of this until a visit to the optometrist in 1994 led to her own diagnosis.

Not long after, Jenny began donating to CERA.

"I had benefited from having a very good specialist and, because glaucoma's hereditary, I thought family could get it in the future, and I could give something towards research," says Jenny.

Now 85, Jenny's glaucoma has progressed, and needs to be monitored, but it certainly hasn't stopped her from doing what she loves.

"I enjoy theatre, I love being down at the beach and just being able to appreciate things through sight," Jenny says.

Never a dull moment

After charting her own path for many years, Jenny now shares a home with her friend Janet.

Since meeting Janet 44 years ago, her life has become busier than ever.

"If anything comes up, there's two of you to do it – like volunteering at the Sydney Olympics and the Melbourne Commonwealth Games," says Jenny.

Or playing her beloved tennis with friends.

"Janet and I enjoy playing socially without the pressure of having to win that point," she says.

A lasting legacy

The two often attend CERA's community forums to get the latest updates from researchers on glaucoma and other eye conditions.

"I think CERA is an excellent organisation: they're transparent and keep you informed about their work – it's exciting how quickly they're moving with things."

Jenny and Janet recently made a joint decision to update their wills and leave a gift to advance eye research.

"Any donation, small or large, will be very much welcome because what they discover through research will help a lot of people," Jenny says.

"If I can make some small contribution, I'm helping future generations."

Help create a future free from vision loss

Gift in Wills Lead Bron Sugden says CERA is deeply grateful for Jenny and Janet's support.

"By remembering CERA in their wills, Jenny and Janet are creating a legacy of hope for people affected by vision loss and are helping protect sight for generations to come," she says.

"Legacy gifts enable our researchers to understand the causes of eye disease, inform disease prevention and improve diagnosis and treatment."

If you'd like to know more about how a gift in your will could make a difference, please visit **cera.org.au/shine**

For a confidential discussion, call our Philanthropy Team on 1300 737 757 or email **giftsinwills@cera.org.au**

Be a star that shines on

With a gift in your will to CERA, you leave a legacy of sight for future generations.

For more information
Visit **cera.org.au/shine**
Email **giftsinwills@cera.org.au**
Call **1300 737 757**

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