Spring 2021

visionary

Hope in sight®

Hope in Sight GIVING DAY

14 October 2021

Join BILLY in the **race** to **beat BLINDNESS**

DONATE to find cures for Inherited Retinal Disease

CENTRE FOR Eye Research Australia

HOPE IN SIGHT GIVING DAY

Research puts hope in sight

When I began my career as an eye surgeon in 1996, I could not have imagined the pace of innovation that we are now seeing in 2021.

Retinal conditions – like inherited retinal diseases (IRDs) and age-related macular degeneration (AMD) – were considered untreatable and likely to consign people to a life of impaired vision or even blindness.

Fast forward 25 years and thanks to research the outlook has changed dramatically.

A global research effort has resulted in vision-saving treatments for people with 'wet' AMD. And now the race is on worldwide to find new treatments for 'dry' AMD – including a gene therapy, which is part of a clinical trial here at CERA (Page 8).

In 2021, vision researchers are on the brink of discovering new treatments for IRD. Already, a gene therapy has been approved to treat a rare form of retinitis pigmentosa and about 40 trials of potential treatments for other conditions are under way around the world.

On World Sight Day – **Thursday 14 October 2021** – CERA is holding its second **Hope in Sight Giving Day** to raise funds for gene therapy research. For every dollar you donate we receive $3 in matched donations from our generous partners at the National Stem Cell Association of Australia and CERA Foundation.

This year Billy, 22, who is living with an IRD called choroideremia, is sharing his story to raise awareness of the life-changing potential of gene therapy research (pages 3-5).

Your donation will support Dr Raymond Wong who is developing a gene therapy to 'switch on sight' by regenerating vision-sensing photoreceptor cells (Page 6).

Please save the date – **14 October** – and together we can put hope in sight.

Keith Martin

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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.

Billy's focus on the future

Photo: Andrew Morton

Billy Morton was diagnosed with a rare genetic eye disease in his teens. Today he's taking challenge of living with vision loss in his stride.

When Billy Morton is not studying or working, you'll find him blazing a trail alongside the Yarra River.

The 22-year-old runs around 80 kilometres a week, prioritising his regular exercise in a schedule that also includes university commerce studies, part-time work and – outside of lockdown – hanging out with friends and playing social netball.

"Running is more than physical. It definitely helps take my mind off of things, and gives my mind a good break," he says. "It gives me a sense of independence and freedom."

In his early teens Billy was diagnosed with choroideremia, a rare genetic eye disease that causes degeneration of the layers of the retina, the light-sensitive cells at the back of the eye which are essential for vision.

Choroideremia, which usually affects young men, often starts with night blindness in childhood or the teen years, followed by a progressive loss of peripheral vision throughout adulthood which eventually results in tunnel vision – and sometimes, as people get older, full loss of central vision.

There is currently no treatment or cure for choroideremia. But so far, the disease has not stopped Billy from doing the things he wants to. He doesn't have a driver's licence but other than that his life is similar to many others his age.

"Sometimes I have to use my mobile phone to see in dark places like clubs or cinemas – but I can use the light on my mobile phone and I'm often with friends," he says.

(Continued Page 4)

Left: A young Billy in 2009 with his cousin, Paralympian Sam Harding, who also has choroideremia. Above: The Morton family Andrew, Billy, Tess, Beth and Sofia.

Billy's best mate since high school, Callum Blackburn, says he often forgets his friend has a vision problem.

"It's not something we talk about," he says. "It's not that Billy is trying to hide it – but he just gets out there and makes the most out of every situation. It's only sometimes when it's dark and there might be an obstacle in the way that he'll reach out for someone's shoulder."

Navigating uncertainty

Choroideremia carries an uncertain prognosis – and it's hard to predict how quickly someone's vision will decline. People with the disease experience progressive vision loss throughout life – but it is different for everyone and for some people the rate of vision loss is faster and more severe.

Billy's parents Andrew and Beth recall keeping a night light on in the bathroom when the children were small and noticed that Billy found it very difficult to see at night.

"We would be at basketball and notice that he would miss rebounds or things that happened on the court, or knock things over," says Beth.

Choroideremia runs in families, passed on via a genetic mutation in the X-chromosome. Women who carry the mutation often have very mild, or no symptoms at all.

Billy's cousin Sam Harding, a competitor in the athletics in this year's Tokyo Paralympics, had been diagnosed with the disease as a child. Armed with this knowledge, the Mortons headed to eye specialists and for genetic testing.

"Even though we knew Sam had choroideremia, initially Billy's diagnosis was a shock," says Beth.

"We certainly knew there was a problem – but didn't realise the great impact that it had on Billy's peripheral vision and anticipate it will get worse.

"But from that point we carried on – and when he was first diagnosed Billy had good vision and it didn't affect his schooling."

At his secondary school, Xavier College, Billy focused on the positives. When his sight made playing basketball difficult, he started rowing.

"Billy is always talking about what he is doing, not what he can't do," says his dad,

Andrew Morton. "He is very focused on what he wants to do, he is interested in politics and economics and cares about social justice."

After Year 12 – inspired by a talk at Xavier – Billy and Callum took a gap year to volunteer in a school in Sri Lanka.

Motivated by that time, he now aspires for a career as an economist and would like to work in government.

"I am fascinated by how the decisions that are made at an economic level can make a difference for people," says Billy. "It is also a career where I don't have to rely on my vision and that I can still do if I lose my sight in my 40s."

Changing the future

Billy is currently part of a natural history study between CERA and the University of Melbourne to learn more about people with choroideremia and other inherited retinal diseases (IRDs).

Until recent years, because of the lack of treatments, there has been little research into how the disease progresses or a likely prognosis for patients.

But now with rapid advances in gene and cell therapy research, propelled by the emergence of cutting-edge technologies like CRISPR gene editing, there is hope for the future.

Natural history study leader Associate Professor Lauren Ayton says her team aims to create a database of people with information about their vision, their genetic profile and if they are want to take part in clinical trials.

"This means that when new treatments and trials come up, we will have people ready to take part," she says.

Hope in sight

Andrew Morton says that when Billy was first diagnosed there was no prospect of a treatment.

"The idea of a treatment just wasn't on the radar. In a decade the research has really moved forward."

Beth says watching her nephew Sam's vision loss progress gave the family some idea of what Billy's prognosis could be – but research was offering hope to families.

"It gives you hope that there may be some deterioration that will be halted, that would be really amazing."

Like many young people, Billy is concerned about the future and says he's 'not super-optimistic' about the state of the world.

"Despite this there are so many things going on that are incredibly exciting that make me hopeful and optimistic. When you look at things like gene therapy and the way the science is moving– things like data and AI – there are so many great examples about how these technologies are being used to make a difference.

"For now, I just make the most of every day and appreciate what I have without worrying about the things I can't control.

"Hopefully there will be research that will benefit me, but, if not, it is exciting to know that it could make a difference for other people."

➜ For details on taking part in CERA's natural history study contact IRDgroups@unimelb.edu.au

➜ **Register to donate on Hope in Sight Giving Day at charidy.com/HopeinSight**

Photo: Anna Carlile

Switching on sight

Dr Raymond Wong is using cutting edge technologies in his quest to restore the retina's light-sensing cells and tackle blindness.

More than 126 million photoreceptors form part of the complex layers of cells that make up the retina at the back of our eye.

The tiny light-sensing cells are an essential part of the vision process – picking up light and sending it from the retina to the brain via the optic nerve, enabling us to see.

Photoreceptors rely on a series of complex genetic signals to function properly. But when these signals misfire, or the cell is damaged, irreversible vision loss and blindness can occur.

Globally, more than 190 million people have retinal diseases where the death of photoreceptor cells leads to a loss of sight. These include rare inherited retinal diseases (IRDs) like retinitis pigmentosa or Stargardt's disease and more common conditions, with a more complex genetic profile, such as age-related macular degeneration (AMD).

"Currently there is no cure for blindness once the photoreceptors are lost, " says Principal Investigator Dr Raymond Wong, who leads Cellular Reprogramming research at CERA.

"Our team is working on developing a new gene therapy that could help regenerate photoreceptors and treat a wide variety of degenerative retinal diseases."

Advancing therapies

In recent years, there have been rapid advances in gene therapy research that has led to hope of many new treatments for IRDs, which for decades were considered untreatable.

Conventional gene therapy for retinal diseases aims to halt photoreceptor loss by using safe viral vectors to introduce genes into the eye – either replacing faulty genes with healthy copies, or to introduce a protective gene to prevent cell damage.

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Reprogramming cells: (from left) Daniel Urrutia Cabrera, Dr Raymond Wong and Crystal Nguyen.

These potential treatments are highly targeted towards the genetic profile they are treating – patients will need to be individually matched to the right therapy.

Dr Wong and his team are taking a different approach.

Armed with expertise in several innovative technologies, including cell reprogramming, transcriptomics and CRISPR gene activation, Dr Wong's team are investigating ways to develop a gene therapy which could regenerate photoreceptor in a broad range of retinal diseases.

Reprogramming cells

All cells within the retina have a precise genetic profile, and the genes they express, to function normally.

Professor Wong and his team are looking to take the profile that makes photoreceptors function successfully – and use it to 'reprogram' another group of cells in the retina known as Müller glia.

In humans, many millions of Müller glial cells help maintain the structural and functional stability in other cells of the retina.

They are of particular interest to researchers because they have stem-cell like qualities – and in other species – like zebra fish and chicken they have the natural ability to regenerate the retina.

"We use transcriptomics – a read out of the gene expression in the cell – to determine the important sets of genes in the human retina, in particular the photoreceptors," says Dr Wong.

"We then grow Müller glial cells in the lab, and use CRISPR gene activation technology to switch on different sets of genes in the cells to turn them into photoreceptors".

Currently, the research is in pre-clinical stage, being tested on cells in the lab and animal models – with early progress backed by the National Health and Medical Research Council and generous philanthropic support from Retina Australia and the Kel and Rosie Day Foundation.

On Hope in Sight Giving Day, backed by matched funds from the National Stem Cell Foundation of Australia and the Centre for Eye Research Australia Foundation, CERA is raising funds to further accelerate the pace of Dr Wong's research.

"Funds raised from our generous supporters have been critical to getting our research to this point," says Dr Wong. "Every dollar we receive on Giving Day will further accelerate the pace of our investigations and move us closer to our goal of developing a treatment which could potentially restore sight."

Hope in Sight Giving Day – 14 October 2021

Every dollar you donate means three dollars will go to support Dr Raymond Wong in the race to beat vision loss and blindness. CERA thanks our generous partners at the National Stem Cell Foundation of Australia and CERA Foundation for their support.

Register to donate now at charidy.com/HopeinSight

Australia's gene therapy first

Photo: Mathew Lynn

CERA researchers and surgeons from the Royal Victorian Eye and Ear Hospital have joined forces to deliver Australia's first investigational gene therapy for 'dry' age-related macular degeneration.

Three Victorians with dry age-related macular degeneration (AMD) have undergone pioneering gene therapy surgeries to trial an experimental treatment for their eye disease.

The patients are part of Australia's first clinical trials of an investigational gene therapy for a form of AMD known as dry AMD or geographic atrophy.

Their involvement is also contributing to important research into the disease – for which there is currently no treatment or cure.

The patients are part of the Phase II clinical trials – HORIZON and EXPLORE – testing the safety and effectiveness of an investigational gene therapy developed by UK company Gyroscope Therapeutics.

CERA Principal Investigator of Retinal Gene Therapy and vitreoretinal surgeon Dr Tom Edwards performed the first surgeries to deliver the investigational gene therapy between March and May this year.

Over the next 18 months, up to 20 patients are expected to receive the investigational treatment as part of the trials.

About AMD

AMD occurs when debris develops in the central retina (or macula), the tissue responsible for taking light and turning it into vision. Over time the cells in the retina

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Dr Tom Edwards and colleagues at the Eye and Ear Hospital took part in pioneering surgery to deliver an investigational gene therapy.

slowly die leaving gaps, or holes, in the vision. About one in seven Australians over 50 has the early signs of AMD, in stages called early and intermediate AMD. These stages can lead to severe vision loss if they progress to the late stage of the disease.

There are two forms of late stage disease – wet and dry. Wet is where blood vessels bleed in the back of the eye.

Dry AMD , the other form of late stage AMD, - is an irreversible degeneration of retinal cells, causing a gradual and permanent loss of central vision.

Research has led to the development of treatments which can effectively manage the wet form of AMD but there are no treatments for the dry form of late AMD.

CERA's Principal Investigator of Retinal Gene Therapy Dr Tom Edwards says it can be a devastating diagnosis.

"In the advanced, late stage form of AMD, it can rob people of their ability to read, drive or even see the faces of loved ones," says Dr Edwards.

Investigational Gene Therapy

The investigational therapy aims to introduce a corrective gene to dampen overactivity in a part of the immune system that has been linked to inflammation and damage to healthy eye tissue.

The investigational product consists of a non-infectious virus that acts as a delivery vehicle for the gene therapy to the correct area of the eye.

It is administered in an operating theatre, using a canula as thin as a human hair to deliver a small amount of fluid containing safe viral particles filled with the corrective gene underneath the retina.

To ensure maximum precision, a foot pedal and advanced microscopy equipment is used to guide the canula into position.

After the surgery, patients' vision will be monitored by CERA's clinical researchers and undergo a series of rigorous visual assessments throughout the trial period.

An eye on the future

Dr Edwards says the current collaboration between CERA and the Eye and Ear, highlights Melbourne's unique mix of infrastructure, clinical and research skills for ocular gene therapy.

"It's an exciting time for patients, researchers and clinicians. The collaborative relationships here in Melbourne provide a great example of Victoria and Australia's potential to become a world leader in developing and trialling gene therapies to prevent vision loss and blindness," he says.

"We have a specialist eye hospital in the Eye and Ear, a world top-five eye research institute in CERA and the nation's highest concentration of biomedical researchers and biotech companies."

More information

For more information on the HORIZON trial [NCT04566445] or the EXPLORE trial [NCT04437368] visit Gyroscope Therapeutics or **clinicaltrials.gov**

CERA is currently conducting a variety of AMD clinical research projects. Contact **amd-studies@cera.org.au** or register on our website **cera.org.au/take-part-in-research**

Future vision

Associate Professor Penny Allen and her team have achieved a major milestone in their research to develop the bionic eye.

The Australian bionic eye has captured the world's attention after a landmark clinical trial at CERA showed that it's capable of improving functional vision in blind patients.

A bionic eye works by stimulating visual impulses in people who have lost their sight. It gives a 'sense of vision' by producing flashes of light called phosphenes that can help patients detect edges, shapes and movement.

The Australian bionic eye comprises an electrode array that is inserted surgically into the eye, coupled with external components that capture images and translate them into electrical signals.

This second-generation device improves on the original prototype, trialled in 2012. It includes a larger field of vision to improve navigation and a portable design to test the device outside the lab for the first time.

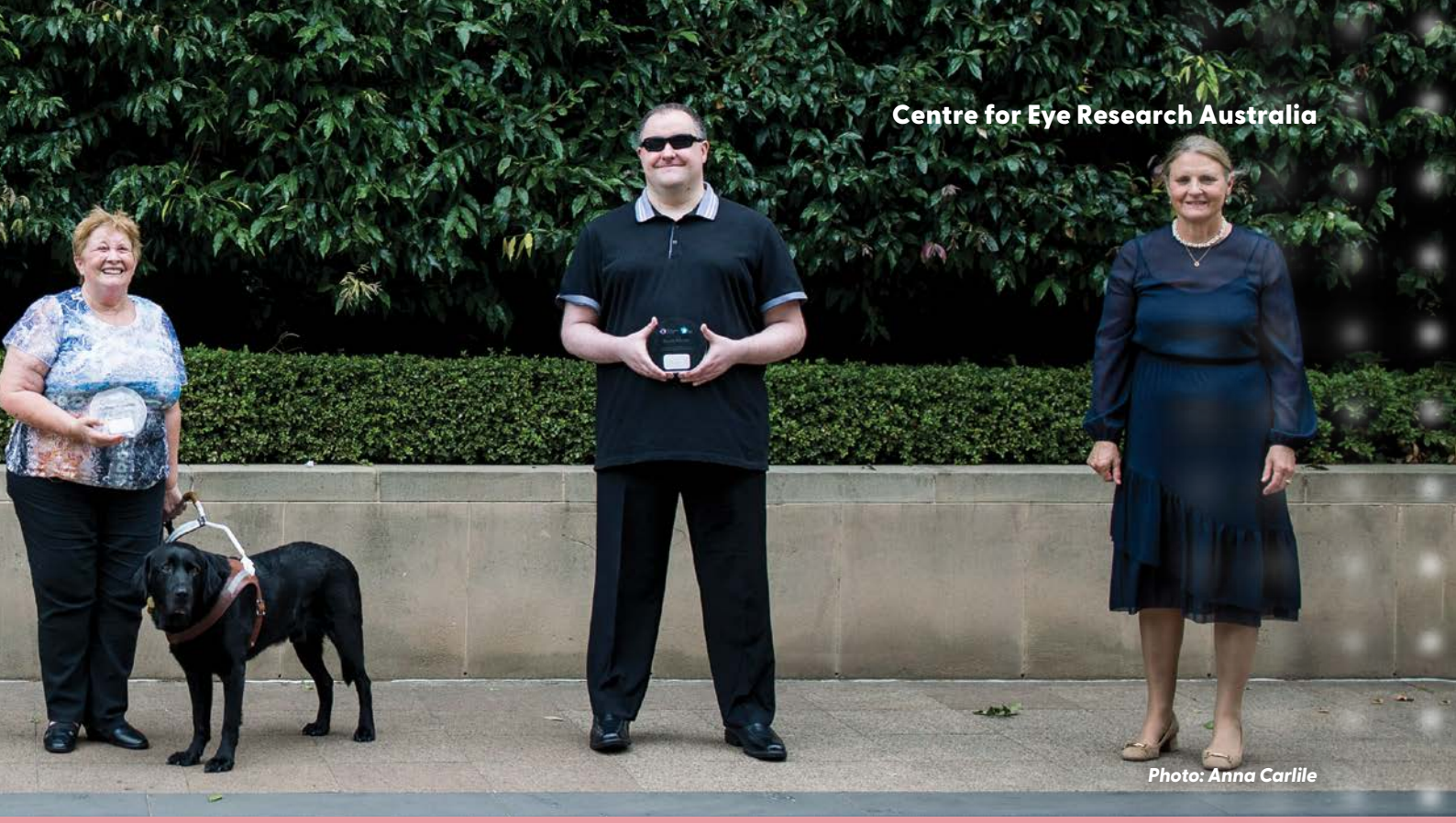
Four Victorian participants took part in the rigorous two-year trial to assess the new device's safety and whether it could produce the phosphenes that would help them navigate and locate objects. The National Health and Medical Research Council and commercial partner Bionic Vision Technologies (BVT) funded the trial.

All participants have severe vision impairment from an inherited eye disease called retinitis pigmentosa. Patients with this condition are perfect candidates for a bionic eye.

While they have lost the cells that produce sight, they still have nerve tissue that can be stimulated to produce visual impulses. For the trial volunteers, participation was a chance to contribute to a better future for other people who have lost vision from retinitis pigmentosa.

Making history

"I saw being involved as a history-making opportunity for vision impaired people," says participant Colleen Knowles.



Before the trial, participants could only perceive light and dark. They could not detect objects and hadn't been able to navigate independently for at least 15 years. But after several months of training to learn how to interpret the electrical signals from the bionic eye, all four could perceive – and navigate – the world around them.

"The first time we went outside I actually got a shock to know that there were so many trees on the nature strip!" says Colleen. "I've now become a people watcher. I'm checking things out all the time.

"It's been amazing to navigate around certain objects and find something on the table instead of knocking it over and breaking it."

Enriching lives

The bionic eye trial showed that it was safe and enriched the patients' lives in many ways. One gained more enjoyment from live theatre because he could gauge people's location. Another could more easily locate tools and machinery in woodwork class.

Associate Professor Penny Allen, CERA's Principal Investigator on the Bionic Eye Project acknowledges the "huge collaborative effort" it took to produce these ground-breaking results but credits the participants' dedication as a key factor.

"We are so grateful for the support they have provided," she says.

Where to next

In late 2020, BVT received $1 million funding from the Medical Research Future Fund to further develop the device's visual processing.

Learnings from this important clinical trial will be used by BVT for the next phase of bringing the bionic eye to more people with blindness.

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Team effort: (from left) Dr Matt Petoe, Bionics Institute; participants Sam Kuzu, Mark Boyd, Colleen Knowles (with guide dog Freeman), Scott Nixon and Associate Professor Penny Allen. Participants are holding plaques thanking them for taking part in the research.

Noah's Usher story

As a new clinical trial investigates a potential treatment to slow vision loss from Usher syndrome, Shelley Alderman shares her son Noah's experience of living with the condition.

When Noah Alderman had a routine hearing test on the day after he was born, his parents were given news no parent wants to receive – their baby had been born with moderate to severe hearing loss.

"That was quite a shock," recalls his mother, Shelley.

"He was our first baby, it's just a routine test, and you are told they haven't passed. Obviously, we went through all the emotions with that."

Just over two years later, there was an even greater shock in store – one that explained the hearing loss and also had serious ramifications for the little boy's vision.

Noah was diagnosed with Usher syndrome, a rare genetic condition that is responsible for hearing loss or deafness, gradual vision loss and, sometimes, balance problems. There is no cure.

Waiting game

Now aged three, Noah, who wears hearing aids to help with his hearing, has normal vision, but is expected to start losing his sight during his teenage years – although how fast or severely that will happen is unknown.

"The doctors try to give you a timeline, but for every person it's different," Shelley explains. "They say he will first have night vision loss and then his peripheral vision will start to deteriorate. But there's no set path. It's just a waiting game, really."

The diagnosis of Usher syndrome came when Shelley was 30 weeks pregnant with daughter Olive.

While Olive was found to not have Usher syndrome, her older brother was found to have type 2 of the condition.

Waiting game: Noah Aldermann, 3, who has Usher syndrome, with his baby sister Olive and, right, with parents Shelley and Will.

Photos courtesy of Usher Kids Australia and Emily King Photography.

The disorder, which is passed from both parents to a child through faulty genes, is grouped into three main types. Types vary according to age and severity of symptoms.

Retinitis pigmentosa

Associated with Usher syndrome is a hereditary eye disease called retinitis pigmentosa. This is what will cause Noah's vision loss.

The disease affects the light-sensitive layer at the back of the eye known as the retina. It has no cure.

While there is no treatment for retinitis pigmentosa, a new research project is in search of one.

CERA are part of a world-first clinical trial investigating whether an antioxidant oral tablet can slow down vision loss from retinitis pigmentosa in people with Usher syndrome.

Oxidative stress

The trial is being led by Principal Investigator Dr Jonathan Ruddle, a Melbourne eye surgeon.

Dr Ruddle explains people with retinitis pigmentosa develop a harmful problem called oxidative stress in the eyes.

"Oxidative stress causes damage to the photoreceptors (cells that help you see), and this can ultimately lead to vision loss," he says. "We're hoping that the antioxidant tablet we are giving people will slow down that vision loss. It would be life-changing for people."

Clinical trial

Nearly 50 Australian adults with Usher syndrome are being recruited to take part in the trial.

The study, called *Safety and Efficacy of NPI-001 Tablets versus Placebo for Treatment of Retinitis Pigmentosa Associated with Usher Syndrome (SLO RP)*, is sponsored by Nacuity Pharmaceuticals and will follow the participants for two years.

For Shelley and husband Will, the research fuels hope that effective treatment might be found by the time Noah is a teen.

"We're going to prepare Noah for the chance he might lose his vision," says Shelley. "But if a treatment comes to fruition that will stop his world from going dark, that would just mean the world to us and would be amazing for so many people with retinitis pigmentosa."

More information

The clinical trial is also being conducted at Save Sight Institute, Sydney Eye Hospital; Lions Eye Institute, Perth, and Queensland Eye Institute, Brisbane.

For details on how to take part, email **IRD@groups.unimelb.edu.au**

For more details on the clinical trial visit **clinicaltrials.gov/ct2/show/NCT04355689**

CERA thanks the Alderman family and Usher Kids Australia for their assistance with this story.

Jacquie's foresight helps others

CERA is incredibly grateful for the contribution of late supporter Jacquie Stephens who has left a lasting legacy for vision research.

Jacquie Stephens was so determined to make a difference that in her late 80s, she asked if she still 'qualified' to donate her eyes for research if they had cataracts.

A generous benefactor to many charities, Jacquie had a strong interest in medical research, in particular diabetic retinopathy, stem cell research, age-related macular degeneration and glaucoma.

When she passed away, aged 90, Jacquie left a generous bequest to CERA, along with donations to many other charities including the Royal Victorian Eye and Ear Hospital and Guide Dogs Victoria.

An only child, Jacquie was always strong, forthright and in many ways ahead of her time with her views of life and the wider world.

Born in Dimboola on the cusp of the Great Depression, her family later moved to Melbourne. Jacquie worked as a personal assistant and travelled Australia and the world, living in London at one stage.

She loved the arts, particularly theatre, opera, orchestral performances and ballet.

Jacquie, who didn't marry and lived most of her adult life in Malvern, loved people and animals. She made the first of 20 CERA donations in 2001.

Fondly remembered: Jacquie Stephens was a strong supporter of eye research.

Soft spot

While she also donated to WEHI and the Florey Institute of Neuroscience, Jacquie had a soft spot for CERA.

She remained engaged and attended bequest nights until early 2019, even after a fall. Jacquie told CERA that she knew people with AMD, glaucoma and diabetic retinopathy.

Supporting CERA was important to her because "with an ageing population we need to be as prepared as possible to deal with emerging problems".

When CERA Donor Relations Advisor Elaine Levine met Jacquie at a research event she was immediately drawn to her warmth and sharp wit.

"She invited me to lunch at her home where we shared more stories about her life and travels," Elaine says. "I will miss her presence at our future events and will remember her fondly."

If you're considering leaving a gift in your will to advance CERA's research, please call **1300 737 757** for a confidential discussion. You can also learn more at **cera.org.au/leave-a-gift-in-your-will**

Centre for Eye Research Australia

Wednesday, 13 October 2021, 7pm

Hope in Sight online forum

Dr Carla Abbott
Retinal research

Associate Professor Lauren Ayton
Retinal research

Dr Tom Edwards
Retinal gene therapy

Professor Robyn Guymer AM
Macular research

Professor Keith Martin
Glaucoma research

Dr Raymond Wong
Cellular reprogramming

Associate Professor Peter van Wijngaarden
Ophthalmic neuroscience

On the eve of World Sight Day, our panel of experts will be on hand to answer your questions about the latest in vision research.

Register at cera.org.au/events

Hope in Sight Giving Day

HOPE IN SIGHT
GIVING DAY

Donate on 14 October 2021 and TRIPLE your impact

Join Dr Raymond Wong's team in the race to beat vision loss and blindness.

Help us raise $150,000 for gene therapy research. Every dollar you give will be tripled by our generous partners at the National Stem Cell Foundation of Australia and CERA Foundation.

$30 → $90
$50 → $150
$100 → $300

Donate at charidy.com/HopeinSight

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