CENTRE FOR
Eye Research
Australia

Hope in sight®

Annual Review 2021

Lighting the way

Our story

Vision is precious and no one should ever lose the gift of sight.

We're deeply committed to conducting eye research with real-life impact and finding ways to prevent people from going blind.

As an international leader in eye research, we use our world-class knowledge and expertise to achieve better treatments and faster diagnosis of eye disease.

Our goal is to prevent vision loss – and ultimately, find cures to restore sight. As true innovators, our scientists are on the brink of new discoveries every day.

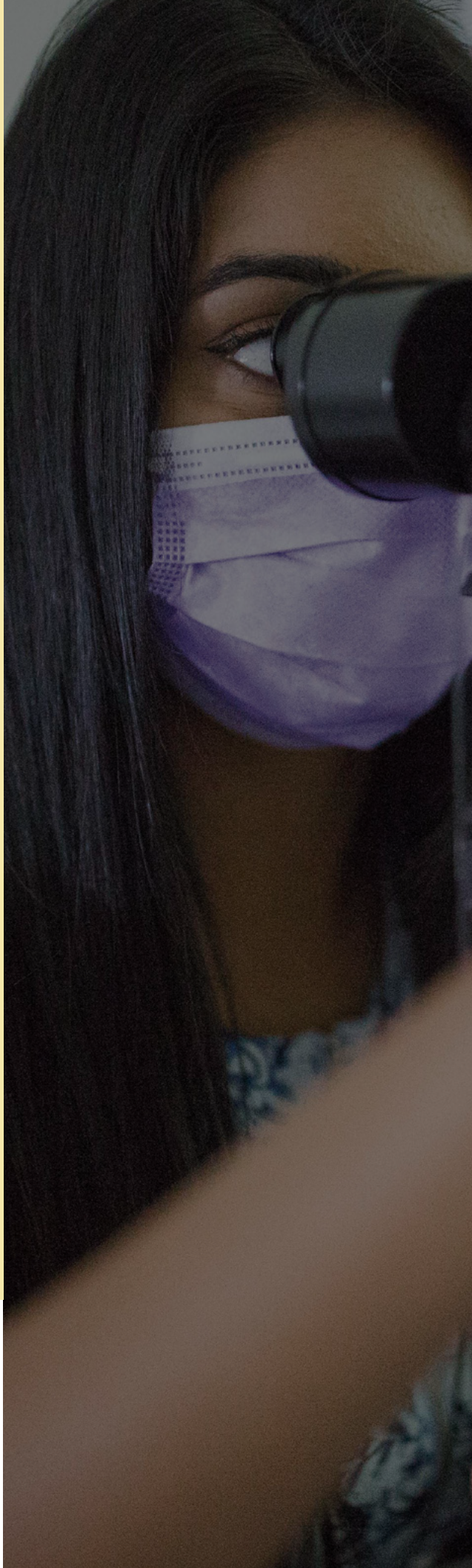
With your support we can continue this world-leading research and accomplish scientific breakthroughs previously deemed unattainable.

Our aim is to offer hope to people affected by vision loss and protect the sight of everyone in need.

With CERA, there's hope in sight.

CENTRE FOR
Eye Research
Australia

← **COVER: Sophie Thomas lives with Usher syndrome and is hopeful research will find a treatment for the condition.**



THE UNIVERSITY OF MELBOURNE

the royal victorian
eye and ear
hospital

Contents

↑ In focus: Clinical optometrist Bhaj Grewal at work.

Chair and Managing Director's message

Impactful medical research does not happen in isolation. It is a result of an extensive network of collaborators working towards a shared vision.

At the Centre for Eye Research Australia (CERA) this means joining forces with partners from universities, hospitals, industry, government and other research institutes to accelerate the pace of research, improve patient care and create a better health system.

It includes laboratory-based scientists working alongside clinicians to find therapies for diseases that are currently untreatable. It involves countless patients putting their trust in our researchers by agreeing to take part in clinical trials. Crucially, it also involves the many generous individual donors, visionary philanthropists, trusts and foundations whose support is essential to make our research happen.

Despite a challenging year, the strength of these collaborations enabled CERA to keep advancing vision research in 2021.

After an initial dip in 2020, clinical trials activity rebounded as we embarked on new studies to give Australians early access to potential new treatments.

Investing in innovation

We also continued to make strategic investments in the future of vision research – bringing new teams to CERA, undertaking critical planning to expand our research and strengthening our Innovation Fund.

Last year's sale of Oculo, CERA's first spin-out company, clearly demonstrates the benefits of translating great research ideas from the lab to the clinic.

Since it was incubated at CERA and spun out as a private company in 2015, Oculo - a secure digital platform which allows eye care professionals to share patient information - has had a huge impact on clinical practice.

Its sale is also benefiting the future of eye research. As a minority shareholder, CERA received a proportion of the proceeds which it will now use to invest in the next generation of vision researchers through a bigger and stronger CERA Innovation Fund that will support them to get 'blue-sky' research ideas off the ground.

In 2021, we established new discovery research programs in Visual Neurovascular Research and Genetic Engineering. We also broadened the scope of our clinical research, with new programs in Ocular Oncology and Clinical Biomarkers.

Our impact

Despite the difficult year, CERA continued to deliver cutting-edge new treatments for trial participants and attract competitive research funding.

Our retinal gene therapy researchers, in partnership with colleagues from the Royal Victorian Eye and Ear Hospital, delivered Australia's first trial of an experimental gene therapy for dry age-related macular degeneration.

They were also a part of another global study investigating the use of an antioxidant as a potential treatment to prevent vision loss from retinitis pigmentosa in people with Usher syndrome.

Successful clinical research projects like these rely on understanding what matters to patients and their families, as well as ensuring that they are well informed about the role of research.

CERA and the University of Melbourne conducted a world-first survey which asked patients with inherited retinal diseases about their views on potential gene therapies. These findings will provide a valuable resource for future trials, and we look forward to releasing the results later this year.

Our corneal researchers became founding partners in BIENCO, a pioneering national collaboration funded by the Medical Research Future Fund to develop a fully bioengineered cornea.

Researchers utilising artificial intelligence and detailed imaging techniques to improve the diagnosis of eye and cardiovascular disease received funding from the National Health and Medical Research Council's prestigious Investigator Grants scheme.

Thank you

It is satisfying to look back and see what we have achieved in 2021.

We appreciate the contributions of our partners at the Royal Victorian Eye and Ear Hospital, University of Melbourne, member organisations, industry partners and other research institutes who enable us to maximise the impact of our research.

We are also grateful for the continuing support of the Commonwealth and Victorian governments in helping medical research institutes weather the pandemic and thrive into the future.

We extend a heartfelt thank you to the many individual supporters and organisations who have stood by us in difficult times. It is truly humbling to have your ongoing support.

We also applaud CERA's incredibly talented and committed staff. Their dedication to making life better for people living with vision loss and their families is truly inspiring.

We look forward to continuing our work together to put hope in sight.

Olivia Hilton
Chair

Professor Keith Martin
Managing Director

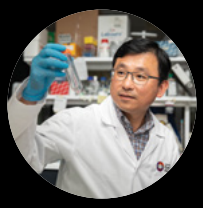
2021 snapshot

223

SCIENTIFIC PAPERS PUBLISHED

$5,931,505

IN GOVERNMENT GRANTS



NEW RESEARCH UNIT
GENETIC ENGINEERING

NEW RESEARCH UNIT
VISUAL NEUROVASCULAR RESEARCH

NEW RESEARCH UNIT
OCULAR ONCOLOGY

NEW RESEARCH UNIT
CLINICAL BIOMARKERS

$2,357,288

IN DONATIONS AND BEQUESTS

AUSTRALIAN-FIRST
GENE THERAPY TRIAL
FOR DRY AGE-RELATED
MACULAR DEGENERATION

OCULO SALE BOOSTS CERA INNOVATION FUND BY

$2,600,000

$1,956,691

IN PHILANTHROPIC GRANTS

LIONS EYE DONATION SERVICE TURNS

30

PROFESSOR ROBYN GUYMER AM INDUCTED TO VICTORIAN WOMEN'S HONOUR ROLL

COORDINATED CORNEAL DONATIONS FROM 317 DONORS

RETRIEVED...

634

DONOR CORNEAS

FOR...

539

CORNEAL TRANSPLANTS

INVESTIGATOR GRANT FOR DR ZHICHAO WU

INVESTIGATOR GRANT FOR DR LISA ZHU

Inspiring hope

Billy Morton is taking the challenge of living with vision loss in his stride.

The commerce student, 23, was diagnosed with a rare inherited retinal disease, choroideremia, in his teens.

A can-do attitude and supportive family have helped him deal with an uncertain prognosis and keep pursuing all the things he wants to do in life.

Choroideremia mostly affects young men. It usually starts with night blindness followed by a progressive loss of peripheral vision throughout adulthood – but it affects everyone differently and it’s difficult to predict how quickly someone will lose their sight.

Currently, there is no treatment or cure for the disease.

In 2021, the Morton family threw their support behind CERA’s Hope in Sight Giving Day to raise money for vital gene therapy research.

“When Billy was first diagnosed the idea of a treatment just wasn’t on the radar – in a decade the research has really moved forward,” says Billy’s father Andrew Morton.

Meanwhile Billy is taking every day as it comes. “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.”

Read more about the Morton family’s support of Giving Day on page 16.

← **Sight savers: Andrew, Billy and Beth Morton's fundraising efforts are supporting CERA researchers.**

Gene therapy first

A clinical trial – the first of its kind in Australia – is investigating if the administration of a one-time treatment could slow vision loss from dry age-related macular degeneration.

Gene therapy research provides two great hopes - the potential to treat previously untreatable diseases, and durable treatments that may place a far lighter burden on patients over time.

In 2021, CERA researchers and a surgical team from the Royal Victorian Eye and Ear Hospital joined forces for groundbreaking trials of an investigational gene therapy to treat geographic atrophy secondary to dry age-related macular degeneration (AMD).

Gene therapies aim to introduce functioning genes into the human body to treat or potentially cure a disease.

As opposed to lengthy courses of drugs, the HORIZON and EXPLORE Phase II clinical trials are investigating a potential treatment which could require only a single application to be effective.

The trials are testing both 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 at the Royal Victorian Eye and Ear Hospital, Dr Tom Edwards has performed the surgeries to deliver the treatment.

The joint capability of CERA's world-class researchers combined with the expertise and facilities of the Royal Victorian Eye and Ear Hospital, all housed under the same roof, has made it possible to make these clinical trials available to patients in Melbourne.

Dry AMD

AMD is one of the leading causes of blindness in Australia. Around one in seven Australians over the age of 50 have the early signs of AMD, and it is the leading cause of legal blindness across this demographic.

AMD occurs when the tissue at the back of the eye that absorbs light begins to die, leading to holes or blurry spots in central vision. If the condition progresses to its later stages, it can lead to severe vision loss.

There are two kinds of late-stage AMD: wet and dry. While there are treatments available for wet AMD, there are currently no approved treatments to prevent the damage of late-stage dry AMD.

"Gene-based therapies are exciting because they have the potential to target the root cause of many blinding eye diseases, at the nano-scale of DNA," says Dr Edwards.

"The extreme pace of technology development has meant that for eye diseases previously deemed incurable we are increasingly hopeful of developing treatments that may slow vision loss."

The investigational gene therapy that is part of the current trial is designed to increase production of the complement factor I (CFI)

protein with the aim of restoring balance to an overactive complement system, a part of the immune system. When overactive, the complement system has been linked with inflammation and damage to healthy parts of the macula.

The treatment is administered surgically underneath the retina using a cannula as thin as a human hair, which is precisely guided into position using advanced microscopy equipment.

The treatment is designed to only be administered once.

Following the surgery, patients are being carefully monitored by CERA's clinical researchers for any changes to their vision through the trial period.

"It would be a tremendous breakthrough if this treatment proved successful," says Dr Edwards.

"Not only would it be terrific for those who participated in the trial, but for the wider community of patients and family members who are affected by late-stage dry AMD," says Dr Edwards.

"They would have hope of a treatment that could slow progression of central vision loss."

↑ **Groundbreaking: Surgeons Dr Tom Edwards and Associate Professor Penny Allen performing the Australian-first surgery.**

Treatments in sight

A clinical trial at CERA is investigating a potential treatment that could slow vision loss in people with Usher syndrome.

"I'm so lucky," Sophie Thomas enthuses, enough to raise an ear of her seeing-eye dog Yarra.

It's a phrase Sophie, 45, uses a lot sitting in her inner city apartment describing living with Usher syndrome, a rare genetic condition responsible for hearing loss or deafness, gradual vision loss and, sometimes, balance problems.

Part of Usher syndrome is a hereditary eye disease called retinitis pigmentosa. The disease affects the retina, the light-sensitive layer at the back of the eye. It has no cure.

Born with severe hearing loss, Sophie has also been progressively losing her vision since her mid twenties.

But she says she is lucky to be surrounded by so many "amazing humans" – husband, family, friends, her boss and work colleagues, volunteers and ordinary kind people in the street – all making her life, and the lives of many others impacted by vision loss, a lot easier.

Sophie, a group business services manager at Clicks IT Recruitment, says her employer has "gone along this journey of vision loss with me for the past 15 years".

"They have been fantastic and always given me every support I needed - from making sure I had all the equipment I needed to do my job to asking staff to keep their bags off the floor to reduce tripping hazards," she says.

Sophie is also enthusiastic about a clinical trial at CERA investigating whether an antioxidant oral tablet can slow vision loss from retinitis pigmentosa.

"I am so excited about this trial," she says. "I am very passionate about any research that may slow down or even prevent vision loss from this terrible disease – if not for me, then for future generations of people who have Usher syndrome.

"I know I won't get the vision I have lost back, but if they discovered a tablet that could stop me losing more vision, I would be super happy."

Clinical trial

The world-first clinical trial exploring if the antioxidant tablet called N-acetylcysteine amide (NACA) will slow down vision loss caused by retinitis pigmentosa is being led by principal investigator Dr Jonathan Ruddle, a Melbourne eye surgeon and CERA researcher.

It is hoped the antioxidant tablet could mitigate or even stop 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.

↘ **Enthusiastic support: Sophie Thomas, with seeing-eye dog Yarra, is hopeful clinical research may find a treatment for vision loss associated with Usher syndrome.**

Nearly 50 Australian adults – 12 from Victoria – are participating in the two-year trial at four sites nationally. Some participants are being given the oral tablet that may protect against oxidative stress, while others are being given placebo tablets.

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.

Sophie is extremely excited about what this trial might mean for people experiencing the condition.

"I was disappointed that I couldn't join this trial in finding a cure for this horrible disease, but I am very keen to join any future trial phases or other trials," she says.

CERA Clinical Trial Coordinator Bhaj Grewal says people in their forties like Sophie have adapted to their vision loss, and so it can be very alarming when they start losing more vision.

"Hopefully for people like Sophie in their forties we can find a treatment that will maintain the vision they have for the rest of their lives," she says.

"And for people in their twenties hopefully it's even more positive where we can really slow down the process, so they don't experience such dramatic vision loss."

Understanding gene therapy

The results of a survey to gauge awareness of gene therapies among people with inherited retinal disease will help inform future patient care.

Just a few years ago, a person diagnosed with inherited retinal disease (IRD) would have been told to prepare for a future living with progressive, irreversible vision loss.

But advances in research into treatments for IRD, particularly gene therapy, are moving fast. So fast that public knowledge of breakthroughs is not keeping up.

As more gene therapies for IRDs become available it's critical that people have a good understanding of what might be available to them.

Understanding awareness

To find out how well the issues are understood in the IRD community, researchers from CERA and the University of Melbourne joined forces to survey people with IRD.

The survey, led by Associate Professor Heather Mack and Associate Professor Lauren Ayton, gauged respondents' understanding of the potential of gene therapies, and their views on issues like genetic testing, treatment costs and clinical trial participation.

Associate Professor Mack says they were absolutely delighted with the level of engagement from the IRD community, with 681 responses. Of these, 42 were parents or caregivers of children with IRD.

"Another unexpected side benefit was that the survey itself increased awareness about gene therapy treatments among the IRD community – raising awareness and giving hope," she says.

Key findings

Only 28 per cent of survey recipients reported having "a good knowledge" of gene therapy.

More than 70 per cent said they would take up gene therapy if it was available to them, but the vast majority didn't know exactly what it involved. Despite this, 40 per cent saw no barriers to receiving gene therapy.

The results will be used to design targeted support and education programs for both clinicians and for people with IRDs.

Most importantly, Associate Professor Mack said the survey sent a powerful message to the IRD community: "This is for you; we are working for you, and we are interested in your thoughts and questions about these new treatment options being developed for you."

The survey was funded by Retina Australia and a National Health and Medical Research Council fellowship to Associate Professor Ayton.

Researchers are also grateful to Vision Australia, Retina Australia, UsherKids, Cure Blindness Australia, the Royal Australian and New Zealand College of Ophthalmologists and the Australian Inherited Retinal Disease Registry and DNA Bank for distributing the survey.

↑ Gene survey team: (from left) Researchers Nicole Tindill, Dr Myra McGuinness, Associate Professor Lauren Ayton, Dr Ceecee Britten-Jones, Associate Professor Heather Mack.

Shedding light on LHON

CERA researchers are working to crack the code of the rare genetic eye disease LHON.

From exploring genetic causes in the lab to assessing the disease's impact on Australian families, CERA researchers are striving to solve the mysteries of Leber's Hereditary Optic Neuropathy (LHON).

LHON is a rare genetic disease that affects the optic nerve. It is caused by changes in the DNA of the mitochondria – the powerpacks that provide energy to our cells.

However, it carries an uncertain prognosis as even though family members may have the same genetic mutation their vision will not be impacted in the same way.

Most people with the mutation will not lose their vision – but some may experience sudden, irreversible vision loss, sometimes in the space of days or weeks.

"Because LHON is very rare some eye specialists may never have encountered a patient with the disease," says CERA's Principal Investigator of Mitochondrial Biology and Disease Dr Isabel Lopez Sanchez.

However, she hopes that understanding of the disease and its impact will be heightened by a new study on the prevalence of LHON in Australia and work underway in the labs at CERA.

New data

In 2021, Dr Lopez Sanchez and Professor David Mackey from the Lions Eye Institute, led a study published in the *American Journal of Human Genetics* which for the first time revealed the number of Australian families impacted by LHON and their risk of going blind from the disease.

It found that 96 Australian families are affected by the disease with 355 Australians currently living with it.

Traditionally known as a young man's disease, the study confirmed LHON can also affect women, older adults and younger children.

It was previously thought around 50 per cent of males carrying the LHON gene risked losing their vision, and for females it was 10 per cent. But instead the study found that 17 per cent of males and five per cent of females carrying the LHON gene risked losing their vision.

Dr Lopez Sanchez says the study would provide researchers with a comprehensive database of people they can invite to take part in future clinical trials or studies aiming to prevent or treat vision loss.

Discovering genes

Dr Lopez Sanchez's research is also investigating a gene that appears to be up to 20 times higher in people with the LHON mutation who have lost their vison, compared to those who have the mutation but have maintained their sight.

Dr Lopez Sanchez identified a "mystery" gene when analysing the blood and saliva samples of people with the LHON gene mutation.

She is now investigating the role of the gene and how it impacts on vision.

"Could it be that LHON carriers who have higher levels of this gene lose their vision, while LHON gene carriers with lower levels of the gene don't?" she says.

Her research has moved to the next phase where she is making cell models to see if the mystery gene is causing vision loss.

Editing DNA

Another CERA researcher is also focused on unlocking the genetic causes of devastating vision loss from LHON.

Dr Sandy Hung from CERA's Clinical Genetics Unit is using a base editing system to target and change the point of mutations in the DNA sequence.

Her goal is to engineer and develop tools to repair or correct faults in the genes that can cause the disease to progress.

"Revolutionary discoveries in genetic engineering lay down the path for us to develop tools to modify DNA and find a way to 'edit and correct' the mistake in the gene that causes LHON," she says.

Funding support

The study into the risk of vision loss from LHON was funded by the Ophthalmic Research Institute of Australia, the Mito Foundation and National Health and Medical Research Council.

Dr Lopez Sanchez's lab-based research is funded by a Perpetual IMPACT Philanthropy Program.

Dr Hung's work is supported by the Ophthalmic Research Institute of Australia and Mito Foundation.

↑ **Genetic puzzle: Dr Sandy Hung and Dr Isabel Lopez Sanchez are looking for the genes that cause LHON.**

Sowing the seeds of optimism

The possibilities offered by science and medical research are a source of inspiration for Billy Morton.

Billy, 23, was diagnosed with the inherited retinal disease choroideremia in his teens.

In 2021, his family shared their story to raise vital funds for CERA's gene therapy research as part of our Hope In Sight Giving Day.

Choroideremia, which typically starts with night blindness in childhood, followed by a progressive loss of peripheral vision in adulthood, carries an uncertain prognosis. There is currently no treatment.

"When you think about gene therapy and the way the science is moving there are so many great examples about how these technologies are being used to make a difference," says Billy.

"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 others."

Inspired by Billy's story and the chance to triple their impact with matched funding of $50,000 from both the National Stem Cell Foundation of Australia and CERA Foundation, our supporters dug deep.

In less than 24 hours, they raised more than $191,000 for Associate Professor Raymond Wong's cellular reprogramming research which aims to "switch on sight" by regenerating damaged cells.

Senior Manager, Philanthropy Ryan McCarthy says CERA is extremely thankful to Billy and the Morton family. "We are also incredibly grateful to the National Stem Cell Foundation of Australia and CERA Foundation for their support," he says.

↑ **Bright outlook: Billy Morton is excited by the possibilities of research.**

John and Joan's lasting legacy

John and Joan Garden's generous bequest to eye research will benefit vision research into the future.

Joan Garden lived a full life despite her vision problems.

The popular flight attendant, who later worked as a trainer at Myer's CBD stores, lived with a benign brain tumour for many years.

It affected the sight in her left eye, so Joan – who also had issues with her other eye – wanted to support eye research to help others.

After she died in August 2018 at the age of 79, her brother John ensured her wishes were carried out.

Both had attended CERA community information forums to learn more about our programs.

When John, who had also worked for an airline, died in September 2020, at the age of 88, he left a significant donation to CERA on behalf of Joan.

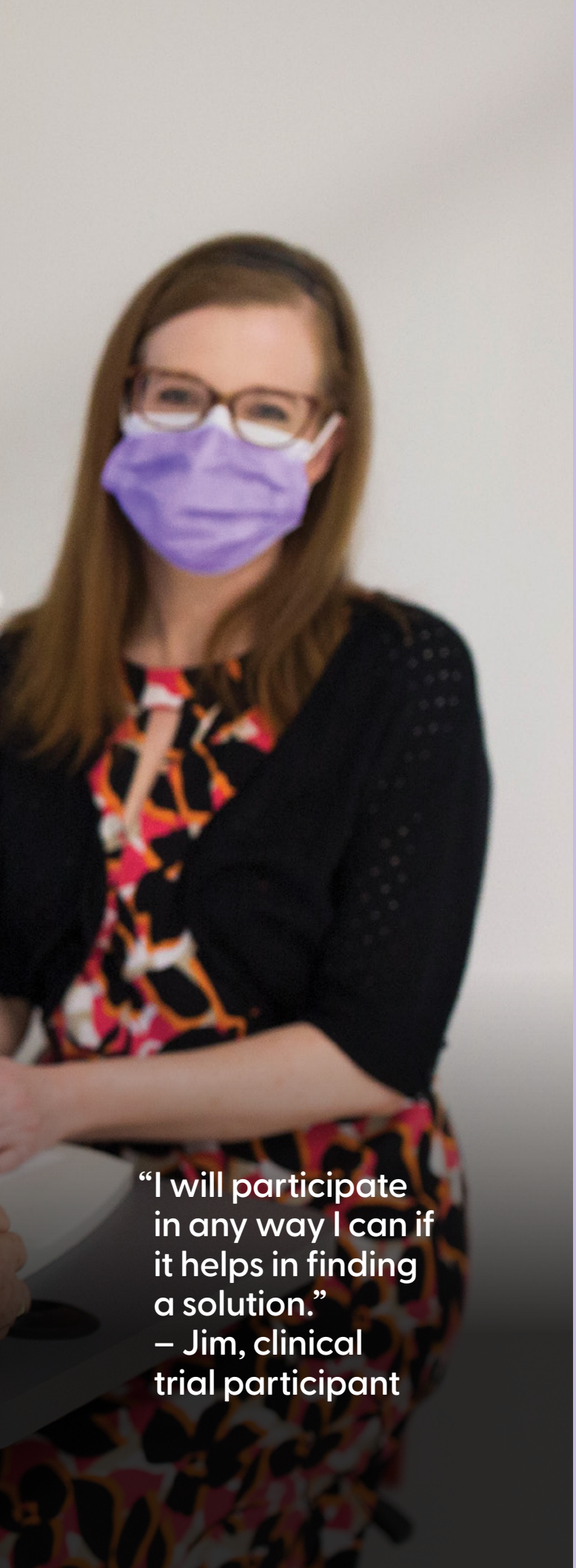
It was a generous gesture from siblings who lived rich and fascinating lives during the heyday of air travel.

While Joan's health declined in later life, she and John remained active in the community and enjoyed gardening at their home.

Both will be remembered for their generosity and community mindedness.

↑ **Lasting legacy: Bequestors John and Joan Garden lived full lives despite her vision problems.**

Eye on the future



Jim Langdon is an avid traveler – since 2005 he and his wife Clare have been on road trips across Europe and Canada as well as cruising the Mediterranean, Japan, Alaska and the Baltic.

“Everybody asks which one is our favourite and it's difficult to answer because there's that many good ones,” says Jim.

“The Rockies were terrific, and on our last trip in 2019 we did a tour of Croatia that was brilliant.”

Jim was first diagnosed with age-related macular degeneration in 2014, and although his vision has declined he still keeps busy. He regularly gets together with his three daughters and eight grandkids, aged between eight and 18, who all live relatively close to his home in Melbourne’s east.

He has also volunteered for a clinical trial to study the potential effectiveness of a device designed to treat AMD by increasing blood flow to the eye. The selection process included having an angiogram to see the blood vessels at the back of his eye.

Jim hopes that the results of the trial will make a difference for the future.

“I actually quite enjoy working with CERA’s researchers. They're good people, and while what they are researching may not help me, it might help my grandkids and other people that have the same problems,” says Jim.

“I will participate in any way I can if it helps in finding a solution.”

← **Looking forward: Jim Langdon with Senior Research Coordinator Lauren Hodgson.**

Breathing easy

CERA's Macular Research Unit is investigating links between sleep apnoea and age-related macular degeneration.

There are not many factors that can help identify someone at risk of developing age-related macular degeneration (AMD), and even fewer that can be modified.

Age and family history are the biggest risk factors by far, but apart from stopping smoking there is not much that a person can do to reduce their personal risk of developing the disease.

Discovering new risk factors, especially those that can be changed, has the potential to implement new strategies to intervene and prevent vision loss.

The search has led CERA Deputy Director and Head of the Macular Research Unit Professor Robyn Guymer AM to look at sleep apnoea, an often undiagnosed condition that is believed to affect as many as a quarter of Australians over 65 years of age.

"Sleep apnoea is a very common, often undetected problem in our community, and it's common in the same group of people who develop age-related macular degeneration," says Professor Guymer.

"We don't currently ask questions in our eye clinics about sleep apnoea, which seemed like a missed opportunity."

Professor Guymer says the two conditions may have a physiological link.

In sleep apnoea, the throat muscles relax which obstructs airflow and reduces the amount of oxygen the body is able to absorb during the night. As oxygen plays a key role in the restorative process the retina goes through overnight, sleep apnoea could accelerate the progress of AMD.

"If we are able to find an association between having sleep apnoea and AMD then currently available treatments for sleep apnoea, such as continuous positive airway pressure (CPAP), may be a potential treatment," says Professor Guymer.

"This is opposed to having to develop a new drug, for example, which takes years to develop."

Looking for a link

Research by Professor Guymer, with medical student Wendy Fang and visiting researcher Dr Palaniraj Rama Raj, has already uncovered some early indications of a link based on the results of patient surveys.

While the very early findings are promising, more work needs to be done to confirm the association.

"While we've asked several hundred people the validated questionnaires, the questions themselves are not perfect for detecting those likely to have sleep apnoea," says Professor Guymer.

Her team is now working on more objective ways to determine if there is an association between those who actually do drop their oxygen levels at night and AMD.

Researchers in the Macular Research Unit are now providing patients with pulse oximeters to take home and wear over several nights to record actual oxygen levels in their blood.

"We record the number of times the oxygen levels drop below a normal level during sleep and how low it drops," says Professor Guymer.

Future work will also include looking to see if the association is with all AMD or particular subsets, such as the critical phenotype of reticular pseudodrusen (RPD).

"We're trying to understand the core problem of RPD, a particular deposit that occurs in only about a quarter of people with AMD but is highly prevalent in the late form of disease when vision loss occurs," says Professor Guymer.

"If there were some more evidence to support an association, the next step might be to do formal sleep studies to consolidate the screening tests."

Professor Guymer's work on sleep apnoea and AMD is supported by funding from of the National Medical Health and Research Council's Synergy Grants Program.

These grants are designed to fund programs that aim to solve problems which cannot be solved by an individual researcher or a single group. This particular grant has brought together the researchers from CERA, WEHI and the University of Melbourne.

↑ **On the pulse: Wendy Fang and CERA Deputy Director Professor Robyn Guymer AM examining a pulse oximeter.**

Local treatment, major impact

CERA's partnerships with suburban ophthalmic practices are improving access to clinical trials.

As an active 75-year-old diagnosed with wet age-related macular degeneration, Jill Edwards found it took some time for her to focus on the ball while playing tennis in the days when she was having her regular eye injections to manage the condition.

"It wasn't that I couldn't see the ball, I was just misjudging the distance," Jill says.

When the opportunity came up to participate in a clinical trial for new treatment for wet AMD she jumped at the chance.

Instead of receiving eye injections every few weeks, Jill is trialling a slow-release treatment that is placed inside a device that has been surgically implanted in her eye.

The device needs to be topped up only once or twice per year, saving her from more frequent eye injections.

Jill also says she is no longer experiencing difficulty focusing after her injections.

"Now, with the new treatment, the lack of focus doesn't seem to be happening," she says. "I can see straightaway."

Rather than travelling into East Melbourne, Jill is having her progress monitored at Retina Specialists Victoria in Rowville. The clinic is part of a network of suburban clinics partnering with CERA in delivering clinical trials in ways that are more convenient for participants.

Senior Research Fellow Associate Professor Sanj Wickremasinghe, who is monitoring Jill's progress at Rowville, says the network is providing greater access to trials for patients.

"A lot of the patients tend to be older and might not feel confident coming all the way into the city," he says.

"Or if they have a family member coming in with them, they don't have to find parking in the city for the day. Many are much more comfortable coming to a local practice."

During the COVID-19 pandemic suburban visits have resulted in a much smaller number of appointment cancellations.

It has also increased knowledge of clinical trials among clinicians in the area.

Since expanding its footprint to suburban clinics in 2019, the CERA Clinical Trial Research Centre has run trials for a range of conditions, including diabetic macula oedema, another condition that requires regular monitoring.

"Anything that reduces the treatment burden, which is the hope of these new drugs, will be a game-changer for patients," Dr Wickremasinghe says.

↑ Local tests: Dr Sanj Wickremasinghe and clinical trial participant Jill Edwards at his Rowville clinic.

Searching for new clues

CERA's newest research unit, led by Dr Zhichao Wu, is using groundbreaking technology to search for new markers of eye disease that could transform clinical care.

By the time a person shows obvious symptoms of an eye disease, it is highly likely the condition has already reached an advanced stage.

This is particularly true for vision loss. Once a person notices their sight has begun to decline, irreversible damage may have already occurred.

"I'm an optometrist, and it is surprising just how often sight-threatening eye diseases are identified in the context of a routine eye check" says Dr Zhichao Wu, Principal Investigator and Head of CERA's new Clinical Biomarkers Research team.

"In glaucoma, people can sometimes turn up with half their field of vision lost. This is something that we should have been able to pick up much earlier."

If earlier signs of disease can be accurately detected, it might be possible to start treatments sooner in order to save sight.

Dr Wu's new team is combining clinical expertise, new imaging techniques and the latest advances in artificial intelligence to try to find these telltale signs sooner than is currently possible.

New signs

A biomarker is an indicator of normal or abnormal biological processes that can be measured. Common biomarkers include monitoring cholesterol or blood pressure to measure heart disease risk.

Biomarkers serve a range of critical functions, from the diagnosis of a disease to predicting its worsening. They can also be used to assess the effectiveness of treatments, and help us understand more about the mechanisms of disease.

Unfortunately, biomarkers that can help accurately predict who will develop vision loss from glaucoma and age-related macular degeneration are yet to be discovered.

However new technology has the capacity to change this. By combining new devices capable of scanning the eye in greater detail than previously possible with the latest in artificial intelligence technology, it may be possible to see and identify new biomarkers for these diseases.

Research grant

In September 2021, Dr Wu was awarded a National Health and Medical Research Council Grant to fund this work to investigate age-related macular degeneration.

"Part of my research will involve using artificial intelligence to pick up new disease biomarkers in AMD from the rich, but complex, modern eye imaging data," says Dr Wu.

"This could help us tease out who amongst the one in seven Australians with the early stages of age-related macular degeneration are at the highest risk of vision loss, but also ultimately help us better understand the causes of AMD too."

Glaucoma collaborations

Dr Wu and the Clinical Biomarkers Research team's work also aims to tackle glaucoma, using a similar method to better predict a person's individual rate of glaucoma progression.

"The new imaging will allow us to get a more complete, detailed picture of the nerve tissue inside the eye, and we will exploit pattern recognition technology to help detect the signs of progressive glaucoma damage at an earlier stage," says Dr Wu.

The project will see his team collaborating with CERA's Ophthalmic Neuroscience Unit, led by Associate Professor Peter van Wijngaarden and Dr Xavier Hadoux, who are using hyperspectral imaging to detect conditions such as Alzheimer's disease and diabetic retinopathy.

Dr Wu's new work will build on his collaboration with Professor Robyn Guymer AM's Macular Research Unit.

In recent years Dr Wu's work has played a key role in the team's significant breakthroughs in understanding age-related macular degeneration.

↑ **Biomarkers team: Orthoptist Nora El Sayed, Dr Zhichao Wu and optometrist Sandy Rezk are CERA's new Clinical Biomarkers Research Unit.**

↑ Improving diagnosis: Dr Rod O'Day is developing new ways to identify cancer in the eye.

Improving eye cancer care

Victoria's first Ocular Oncology Research Unit is investigating new ways to improve diagnosis and treatment of melanomas of the eye.

Dr Rod O'Day, Honorary Principal Investigator of CERA's new Ocular Oncology Research Unit, is working with clinical and basic researchers to improve diagnosis and treatment of eye cancer.

Like skin, the eye can develop a freckle or mole called a choroidal nevus. While these growths, which affect as much as six per cent of the Australian adult population, are almost always benign, they can grow into malignant melanomas.

The new unit is investigating new ways to improve diagnosis and treatment of these melanomas.

"Our aim is to help diagnose potentially fatal cancers earlier, when treatment can save lives," says Dr O'Day, a consultant ophthalmologist at the Royal Victorian Eye and Ear Hospital.

"Current multimodal imaging can accurately distinguish between a benign mole and a melanoma, but this requires having access to expensive pieces of equipment and the experience to interpret the results.

"We are focusing on educating optometrists in how to diagnose and manage tumours using the imaging technology they currently have in place and in developing better techniques to help them pick up on the early warning signs of a malignant tumour."

Dr O'Day is working with CERA Deputy Director Associate Professor Peter van Wijngaarden, to use hyperspectral imaging to help characterise tumours at the back of the eye.

The hope is that this technique can more precisely mark out the borders of lesions and monitor change and growth more accurately.

"We also want our treatments to be less invasive and cause less damage to the eye," says Dr O'Day.

Current treatments require either removal of the eye or radiotherapy, which results in significant vision loss for over half of patients.

Crucial to this work, says Dr O'Day, will be integrating basic and clinical research into the routine care of patients with eye cancers at the Eye and Ear, where he works closely with Dr John McKenzie and Dr Daniel McKay in the Ocular Oncology Unit.

Collaborating with medical and radiation oncologists at Alfred Health, Peter MacCallum Cancer Centre and across Australia will also be critical to ensuring patients have access to clinical trials and new treatments.

Dr O'Day is also excited about possible collaborations with CERA scientists to investigate the potential of artificial intelligence, new ways of looking at single cell RNA, and other research areas to help drive better outcomes for patients with eye cancer.

Artificial intelligence reveals true age

Dr Lisa Zhuoting Zhu is using AI to identify a person's true biological age from a simple photograph of the retina.

It is often said that the eyes are a window to the soul, but it is becoming increasingly apparent that they may also serve as a window to the rest of the body.

"The retina, located at the back of the eye, is a unique site where the small vessels and neuronal tissues can be visualised directly," says postdoctoral research fellow Dr Lisa Zhu.

"Previous studies have shown that retinal vessel changes, such as a vessel bleeding, and retinal disease, such as age-related macular degeneration, are predictors for future systemic diseases."

Additionally, tissues in the eye are similar to those in the brain, heart and kidney – meaning that damage to these tissues might suggest problems throughout the body.

Armed with this knowledge, Dr Zhu is using artificial intelligence to determine "retinal age", an estimate of a person's risk of a range of diseases from a scan of the retina.

Her research is supported by an Investigator Grant awarded by the National Health and Medical Research Council.

Biological age

"Although many diseases are more likely to affect the elderly, we can find considerable numbers of elderly people who maintain good health, suggesting the ageing process cannot be well tracked by chronological age alone," says Dr Zhu.

"Instead, a better measure is biological age, which is a measurement of how genetics and environmental factors affect a person's health."

While there are already several ways to measure a person's biological age, they are typically expensive or invasive, making them difficult to use in everyday practice.

With the world's ageing populations placing a heavy burden on global healthcare resources, developing simple and practical health screening methods is increasingly important.

To develop the retinal age measure, more than 19,000 retinal images from the UK Biobank Study and the chronological age of each person were used as inputs for a state-of-the-art machine learning system developed by the team.

The machine learning system was able to identify small signs, imperceptible to human experts, that reveal a person's biological age. Importantly, those people with a biological age higher than their chronological age showed higher rates of mortality.

"Patients could maximise the benefits of having their regular eye check by not only detecting eye disease, but also quantifying their individual ageing process," says Dr Zhu.

The next steps of her research, which is funded by the NHMRC for the next five years, will focus on refining the model with bigger, more diverse data sets that are more representative of the world's population.

↑ New insight: Dr Lisa Zhuoting Zhu is using AI to take a snapshot of a person's overall health.

Breaking new ground

Long before a new medication or medical device can be used in the clinic, a significant amount of research happens in the lab.

Discovery research is critical to improving our understanding of the complex processes that enable us to see, as well as why they stop working.

And that pre-clinical research is often the first step in the discovery of new treatments and cures for eye disease.

CERA's unique ability to participate in every stage of research, from the lab to the clinic, is at the heart of our commitment to innovation.

In 2021 we strengthened our commitment to discovery science, welcoming new basic research teams - Genetic Engineering and Visual Neurovascular Science.

We also bolstered the long-term sustainability of our CERA Innovation Fund, with a major investment to ensure it can support the next generation of innovators in eye research.

In 2021, the fund backed diverse research projects in genetic engineering, gene therapy and mitochondrial research.

While the clinical implementation of these projects might be many years away, their efforts now are crucial to the discovery of future treatments.

← **Thinking big: Research assistant Layal El Wazan from CERA's new Genetic Engineering Research Unit is helping create the next generation of gene therapies.**

Investing in innovation

Proceeds from the sale of CERA's first spin-out company are supporting eye research innovators.

Oculo is a secure platform that allows eye health professionals to share patients' eye imaging, referrals and clinical correspondence.

The technology was developed at CERA by former Managing Director Professor Jonathan Crowston and Dr Kate Taylor before it was spun out into a separate company in 2015.

Today an estimated 70 per cent of eye care professionals in Australia and New Zealand are using the platform to securely share patients' eye imaging, referrals and clinical correspondence. It was central to the management of over one million patients for Australia's diabetes eye health program, KeepSight.

Throughout Oculo's expansion, CERA remained a minority shareholder. After the company was sold to Finnish ophthalmic diagnostics company Revenio in 2021, CERA leadership decided to utilise revenue earned from the sale to establish a dedicated, sustainable pool of funding to support innovative vision research.

A total of $2.6 million will be used to expand on the scope and remit of CERA's Innovation Fund, which was first established from the generous philanthropic support of the estate of the late Ruth Chitty in 2017.

The injection of funds will secure the long-term future of the Innovation Fund, giving researchers with bold ideas and "blue-sky" projects access to funding for research projects that need an early kickstart.

Supporting bold ideas

It will also support researchers who want to take their ideas from the lab to the clinic to improve patient care – with extra funding for patent applications, seed funding for start-ups and other early operating costs for companies incubated at CERA.

CERA Managing Director Professor Keith Martin says it's fitting that the sale of Oculo has been used to keep strengthening innovation at CERA.

"Since it was founded at CERA by Jonathan Crowston and Kate Taylor, Oculo has made an enormous positive impact on patient care," he says.

"We want to keep encouraging that culture of innovation at CERA – and back our researchers to come up with creative ideas.

"We also want to give start-up companies spun out of CERA the best chance of success, so that they can move their research from the lab to the clinic where it can make a real difference for people with eye disease.

"I'm looking forward to CERA supporting the next generation of innovators to advance their translational research and make a big impact on eye care in the future."

2021 Innovation Fund

In 2021, research projects supported by the CERA Innovation Fund included research by:

- Dr Tom Edwards to develop a potential new gene therapy
- Dr Isabel Lopez Sanchez to investigate mitochondrial optic nerve degeneration
- Associate Professor Rick Liu to develop CRISPR RNA base editing
- Associate Professor Ian Trounce to examine mitochondrial RNA.

CERA thanks Dr Katherine Jackman from Brandon BioCatalyst for helping select the recipients of the 2021 Innovation Fund.

↑ **Supporting innovation: (from left) Dr Tom Edwards, Dr Isabel Lopez Sanchez, Dr Katherine Jackman from Brandon BioCatalyst, CERA Business Development Manager Dr Shereen Tan, Associate Professor Rick Liu and CERA COO Leah Borsboom.**

Next generation gene therapy

CERA's new Genetic Engineering Research Unit is using cutting-edge technology to pave the way for simpler, longer lasting and more effective eye disease treatments.

Gene therapy research offers the potential to slow the progression of diseases that cause gradual blindness, and possibly one day cure them. The research is complicated and painstaking but also rewarding.

CERA's new Genetic Engineering Research Unit, led by Associate Professor Rick Liu, is investigating a next generation of gene therapies, where treatments can be switched on and off in the eye on demand.

Associate Professor Liu's team's research is developing simple tools that can precisely tailor treatment by controlling the amount of therapeutic protein expressed when needed. Treatment can be turned on with a simple eye drop.

"Our switchable gene therapy research provides an elegant solution that allows the gene therapy to better control and help tailor therapies to eye conditions," he says.

"We are currently developing this technology for the long-term management of diseases such as diabetic retinopathy and wet age-related macular degeneration, by stopping the abnormal growth of blood vessels in the back of the eye."

Associate Professor Liu says these therapies could apply to a range of other eye conditions.

"Although the method requires further refinement before human trials could start, it lays the groundwork for moving forward with this type of technology in multiple settings," he says.

"In the next five to 10 years, we hope to see this technology move to the clinical stage."

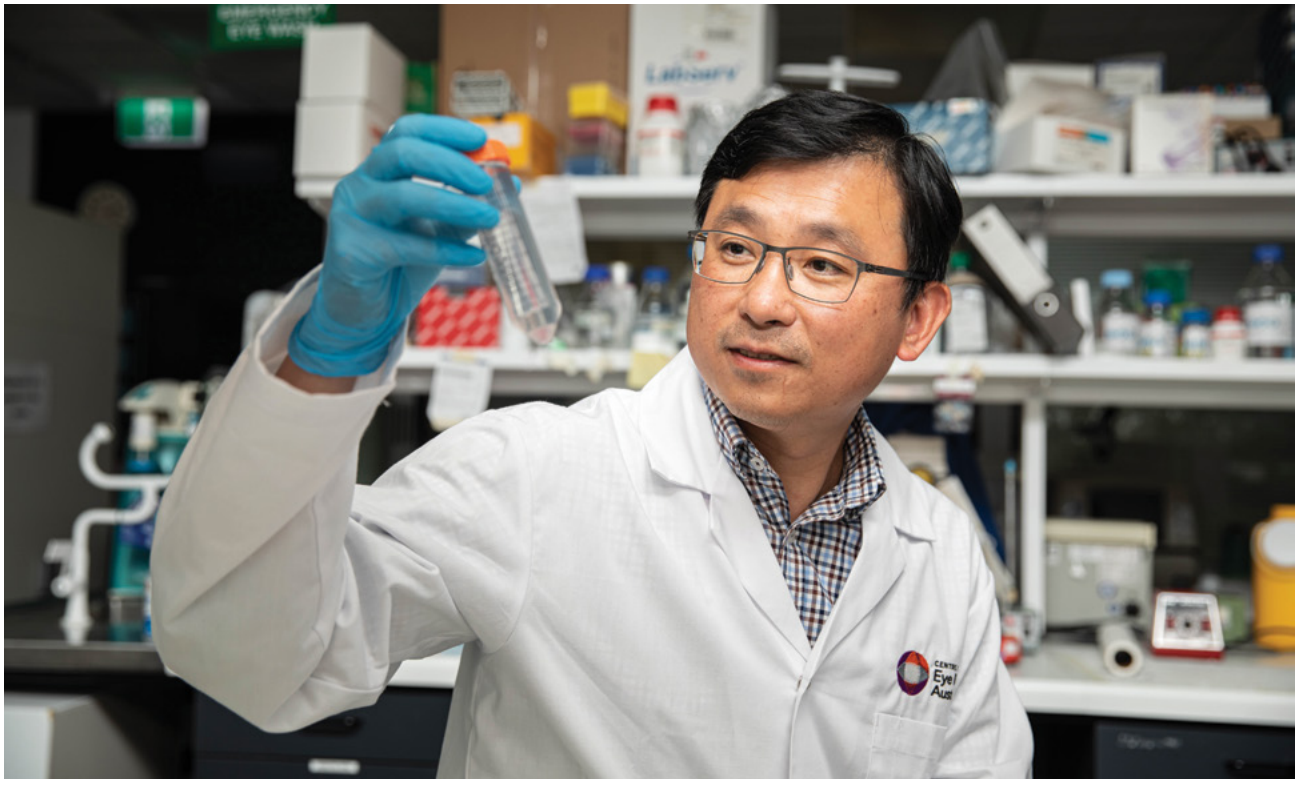
Laying the groundwork

Associate Professor Liu completed his post-doctoral studies at CERA and the University of Melbourne before embarking on retinal gene therapy research.

In 2017, he moved to the University of Tasmania where he established an ophthalmology research laboratory at the Menzies Institute for Medical Research. His team investigated ways to clear hurdles that impeded the clinical application of gene therapies for eye diseases.

Apart from looking to the next generation of gene therapy, his research has also contributed to improving the understanding of complex and rare eye diseases at a molecular level and enhanced public awareness about gene therapy.

In 2021 he returned to CERA, and his new team is set to focus on editing genes that cause eye disease with CRISPR gene editing technology and improving drug administration through nanotechnology.



New frontiers

"Our work on the latest gene editing technology will allow us to address a wide range of degenerative retinal diseases by correcting the faulty gene in the patient's retina cells and make it normal again," Associate Professor Liu says.

"It can potentially delay or cure these eye diseases.

"We can now also use gene editing technology to modify genes associated with eye diseases such as diabetic retinopathy and glaucoma, to potentially providing better ways to manage them."

The research aims to create new therapies that are durable and controlled simply, eliminating the need for frequent eye injections.

Some of the work involves nanomedicine, which applies tiny particles to transport drugs to places they wouldn't otherwise be able to reach on their own.

This technology could enable the development of eye drops that are "stickier" and more effective than traditional drops, meaning less frequent administration and possibly greater therapeutic effect.

↑ **Next generation: Associate Professor Rick Liu is focused on new gene therapies.**

Decades of support and achievements

Andrew Michelmore AO has been a champion of CERA for over 20 years and seen dramatic leaps forward in eye research.

Andrew Michelmore's diagnosis with vision loss was both sudden and unexpected.

"I remember sitting with an optometrist in 1992 and the door to their practice was open; I could see right down their corridor and up the street," Andrew says.

"And I thought 'gee, I can see much less through the field in my right eye than I can with my left eye'."

After sharing this experience with a rowing partner, who also happened to be an ophthalmologist, he was urged to get checked for glaucoma.

"At that stage I'd lost half of the vision in that eye, and I didn't even realise it," Andrew says.

"I would have been 40 when I went in. I didn't know about glaucoma and I thought: people need to know more about this disease."

Andrew, a former champion rower with a long career in the metals and mining industry, was inspired to support research when he experienced dramatic advances in research firsthand.

"I had surgery done on my right eye first," he says. "What they did on my left eye 18 months later used a totally different material. It is remarkable what has been achieved in the last 20 years."

When he asked his surgeon, former CERA researcher Associate Professor Julian Rait OAM, how he could contribute to research to help people in the future, he was pointed in the direction of CERA.

"I've been a great beneficiary of research, and I'm fortunate to be able to contribute, so I do. And hopefully other people will too."

Andrew is passionate about what the future holds and is particularly excited by stem cells, cellular reprogramming and the potential offered by artificial intelligence.

CERA Managing Director Professor Keith Martin says contributions like that of Andrew's have a significant impact on the work that can be done at CERA.

"Individual philanthropic contributions really accelerate medical research and development," says Professor Martin.

"Contributions like Andrew's allow our researchers to chase big ideas and do the kind of research that does not always fall within the funding criteria of Federal Government grants.

"It has been a pleasure getting to know Andrew, and I'm looking forward to sharing with him many more achievements CERA researchers are making."

Andrew says he is also excited for what the future holds.

"I just keep saying to people, I just have to live long enough to allow the technology to catch up to deal with what comes next," he says.

↑ Strong supporter: Andrew Michelmore AO with Professor Keith Martin.

Watching the retina in realtime

One of CERA's newest research teams is aiming to revolutionise our understanding of the complex communication system in the retina.

Dr Luis Alarcon-Martinez was part of an international team which uncovered previously unseen mechanisms which control the blood flow of the retina.

He is now utilising that expertise in Australia where he is heading CERA's new Visual Neurovascular Research Unit, conducting ground-breaking discovery research at the intersection of visual and brain sciences.

The research could help unlock new treatments and prevent vision issues from conditions such as glaucoma, age-related macular degeneration, diabetic retinopathy, and retinopathy of prematurity.

About the retina

The retina is made up of millions of cells, including retinal ganglion cells which enable us to see by transmitting electrical signals to the brain via the optic nerve.

Just like any other cell, retinal ganglion cells need a healthy supply of oxygen and nutrients, carried by blood vessels, in order to function properly.

"We are looking at neurovascular processes: how the neurons, the nerve cells in the retina, are communicating with blood vessels to ask for nutrients," says Dr Alarcon-Martinez.

"We know that interruption of blood supply is found in retinal and other neurodegenerative diseases.

"But until recently, we had almost no idea of how or why this happens."

New mechanisms

In a study published in *Nature* in 2020, Dr Alarcon-Martinez and colleagues from the University of Montreal laid the groundwork for a better understanding of the mechanisms that control blood flow in the retina.

Embedded within the capillaries of the vascular system are a type of cells known as pericytes, cells that can control the amount of blood passing through the capillaries by dilating or contracting them.

Using cutting-edge two-photon microscopy, Dr Alarcon-Martinez and colleagues were able to observe these processes in living organisms in realtime at unprecedented levels of resolution: that of single nerve cells and capillaries.

Looking at the retinas of living mice, they showed that pericytes project very thin tubes – "nanotubes" – to communicate with one another and supply blood where it is most needed.

Importantly, the study also showed that capillaries lose their ability to regulate blood supply when these nanotubes are damaged, with detrimental effects on the functioning of the retina.

Eye diseases

Diseases such as glaucoma or age-related macular degeneration are common conditions, affecting an estimated 350 million people worldwide and over two million Australians.

Dr Alarcon-Martinez says it's incredibly exciting to have discovered a mechanism which could potentially help prevent vision loss or blindness for so many people.

He also points out that many degenerative conditions that affect the brain, such as Alzheimer's disease, have eye symptoms that can occur before the onset of disease.

"This means that our work could potentially also improve our understanding and treatment of these other neurodegenerative disorders."

↑ **Sharp focus: Dr Luis Alarcon-Martinez is uncovering new ways to see the eye.**

Future research for the Visual Neurovascular Research Unit will focus on gaining a better understanding of the dynamics between nanotubes, neurons and vessels.

"There is much that we still need to clarify," says Dr Alarcon-Martinez.

"We don't know yet if impaired communication between neurons and vessels is a cause or consequence of disease. And we have yet to figure out what it is that damages nanotubes in the first place."

Dr Alarcon-Martinez says CERA provides the ideal environment to study these processes.

"The great strength of CERA is that it produces outstanding work across all three types of research: basic, translational, and clinical. This means that we can progress things faster from pre-clinical research through to patient trials and treatment."

Reconnecting nerve transport systems

Professor Keith Martin is leading research to reconnect damaged nerve transport systems that cause vision loss.

The nervous system is the information superhighway of the human body, ferrying electrical signals through nerve cells in the form of electrical signals all the way from head to toe.

When the nervous system is damaged, these signals can be interrupted or only partially received, resulting in symptoms ranging from numbness or paralysis to blindness.

Despite being vastly different conditions, both glaucoma and dementia affect the nervous system. In glaucoma, an interruption of signal transmissions along the optic nerve leads to vision loss and blindness, while in dementia the build-up of tau proteins in the brain disrupts communication between the cells responsible for memory and cognitive function.

If these pathways can be repaired and the signals that they ferry restored, then it could be possible to reverse the symptoms of both these debilitating conditions.

Published in 2021, research led by Professor Martin and Dr Tasneem Khatib from the University of Cambridge has shown that a new approach to gene therapy might make this possible.

Information overload

Gene therapies work by using a safe virus to repair or replace a malfunctioning gene in the human body. Typically, these types of therapies need to be used in highly specific circumstances.

"Currently many gene therapies are targeted at rare diseases caused by a single genetic fault, where a missing or damaged gene can be replaced to treat the condition," says Professor Martin.

"More common neurodegenerative diseases like glaucoma or dementia are much more complex and caused by a range of genetic and other contributing factors."

However, pre-clinical research undertaken by Professor Martin and Dr Khatib tackles the disease in a new way.

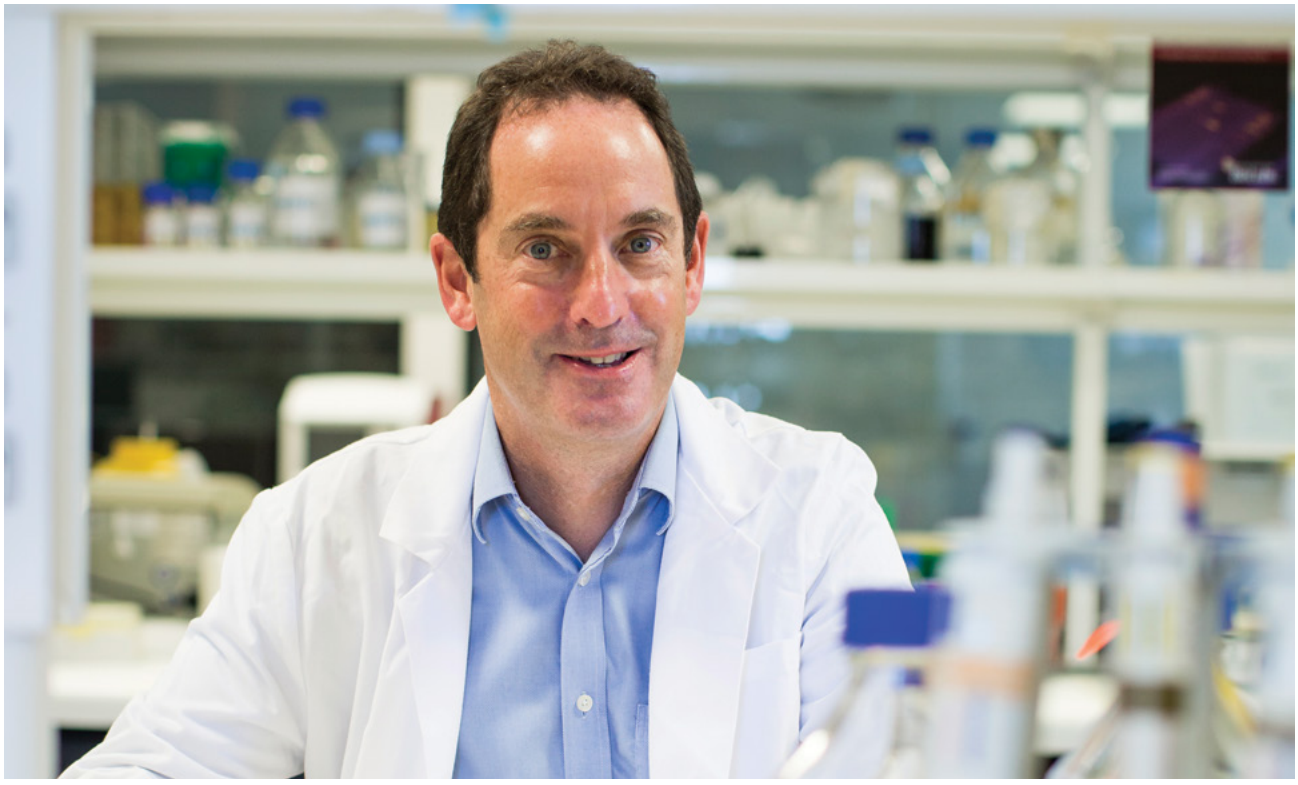
Gene therapy

Instead of replacing or repairing a single faulty gene, the team used a gene therapy to enhance the body's production of two molecules which are both thought to improve the function of axons – the long, slender projections of nerve cells that carry electrical signals which are damaged in glaucoma and Alzheimer's.

The two molecules - brain derived neurotrophic factor (BDNF) and tropomyosin receptor kinase B (TrkB) - were combined into one treatment and trialled in pre-clinical models to test its effectiveness in treating glaucoma and cognitive decline due to dementia.

It is hoped that this combination of molecules will encourage axions to regrow, which might restore their function.

Results showed an improvement in optic nerve activity after receiving the therapy



as well as signs of improved vision among glaucoma preclinical models.

There was also a slight improvement in short-term memory seen among dementia pre-clinical models, which the team plan to test in a larger study to confirm the effect.

Crucially, the approach also appeared to lead to a sustained therapeutic effect, which is an important consideration for treating chronic degenerative diseases.

"We reckoned that replacing two molecules that we know work effectively together would help to repair this transport network more effectively than delivering either one alone, and that is exactly what we found," says Dr Khatib.

The results provide hope that a treatment capable of reversing the damage done in glaucoma, Alzheimer's, and many other complex neurodegenerative diseases could soon be on the horizon.

"Although the research is in early stages, it shows promise for developing gene therapies for many of these common diseases to complement existing therapies," says Professor Martin.

The research was published in the journal *Science Advances* in April 2021, and was funded in the UK by Fight for Sight, Addenbrooke's Charitable Trust, the Cambridge Eye Trust, the Jukes Glaucoma Research Fund, Quethera Ltd, Alzheimer's Research UK, Gates Cambridge Trust, Wellcome Trust and the Medical Research Council (UK).

↑ **Repairing pathways: Professor Keith Martin is leading an international research collaboration.**

Constructing the cornea

Collaboration between experts from the University of Melbourne and CERA has led to technology that is expected to revolutionise corneal surgery.

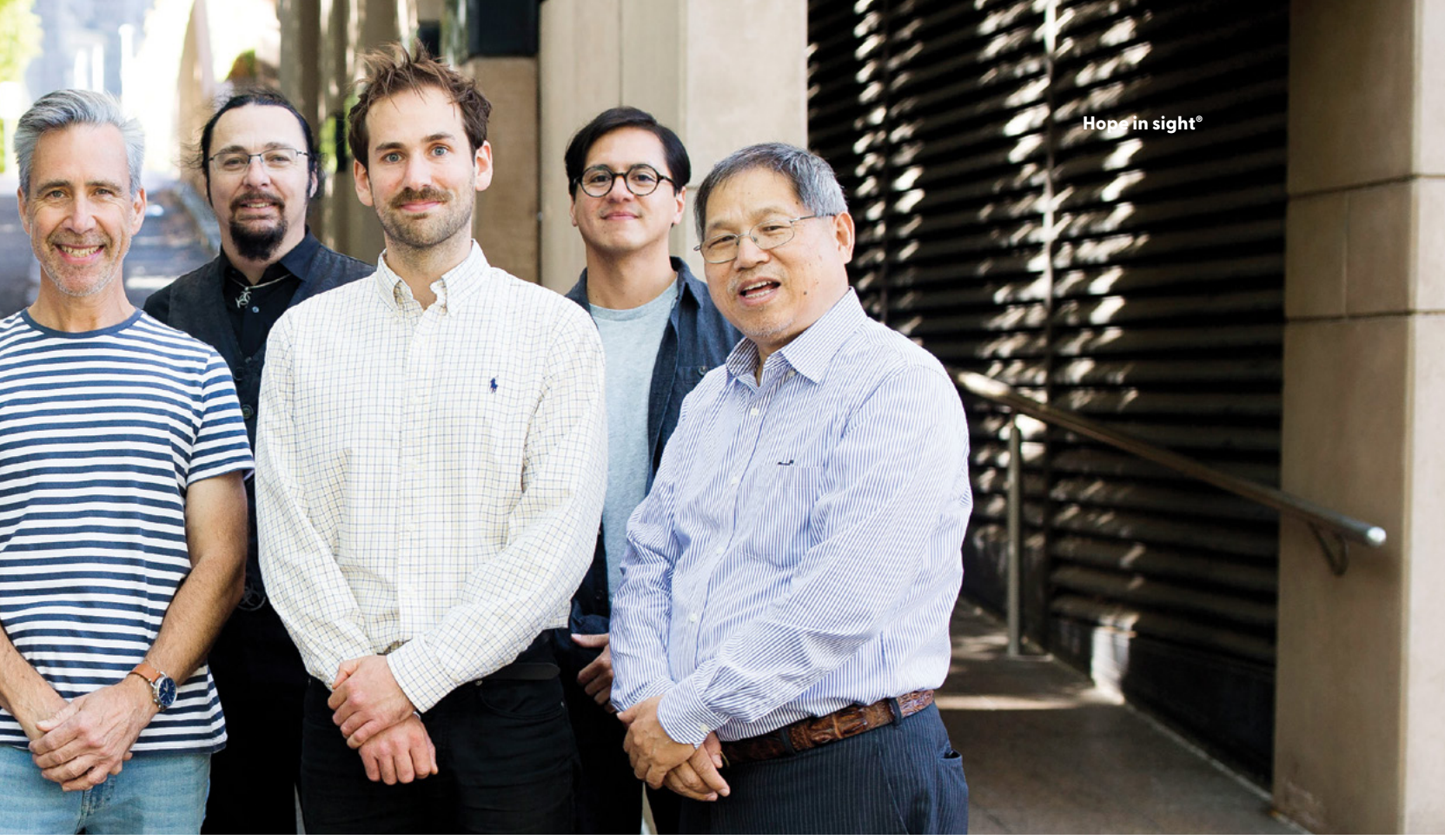
Several years ago, the possibility of improving how corneal surgery is performed brought together corneal researcher Professor Mark Daniell and chemical engineer Professor Greg Qiao, Associate Dean (Research Training) in the Faculty of Engineering & Information Technology at the University of Melbourne.

Their collaboration is on track to improve surgical outcomes for patients. It has also played a critical role in a new national effort to create a fully bioengineered cornea.

The cornea is the clear window at the front of the eye that lets light in. It is crucial to good vision, but injury and disease can make it turn cloudy, leading to blindness.

Because the cells that make up the middle and inner layers of the cornea will not heal on their own, a transplant from a donor is the only option to restore sight.

Unfortunately, corneal transplant techniques that replace the endothelium layer, the innermost layer of the cornea, are difficult to perform. Donor endothelium tissue easily curls up like a scroll, and only a limited number of surgeons are comfortable handling the difficult material.



To make this surgery easier, Professor Daniell, Professor Qiao and researchers from CERA and the University of Melbourne have developed a hydrogel scaffold that holds the corneal tissue flat, making it far easier to manoeuvre into place.

"There is a checklist of five qualities we require in a scaffold; it must be tough, transparent, transportable, biocompatible and biodegradable," says Professor Daniell.

"After a lot of trials, we have finalised its characteristics and proven its safety in the laboratory, and in our models."

The team have also partnered with EverSight, the largest non-profit community-based eye bank network in the US, on the next stages of commercialising the project.

The Victorian Government has also supported the project via the Victorian Medical Research Acceleration Fund. It is expected that human trials will begin as soon as next year.

National effort

The team's work is also contributing to a new, national effort to create a fully artificial cornea that could replace the need for donor tissue.

The BIENCO consortium also involves the University of Sydney, the University of Wollongong, the Queensland University of Technology and the South Eastern Sydney and Illawarra Area Health Service.

The group is funded by a Medical Research Future Fund Grant under the Australian Government Frontier Health and Medical Research Initiative.

If the group is successful in building a fully bioengineered cornea it may solve a global shortage of donor tissue.

↑ **Extensive collaboration: L-R: Professor Mark Daniell, Dr Paul Gurr, Dr Heather Machin, Professor Greg Dusting, Jason Palmer, Dr Karl Brown, Dr John Finnegan, Dr Jamie Ruiz-Montenegro Villa, and Professor Greg Qiao.**

Lead researchers

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BSc, MSc, PhD

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Bionic Eye Project
MBBS, FRANZCO

Associate Professor Lauren Ayton
VENTURE Study
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Dr Lisa Zhuoting Zhu
Ophthalmic Epidemiology
MD PhD

For more details about our researchers visit cera.org.au

Our Board

We extend the deepest appreciation to our Board members who give their time and expertise to provide strategic direction and governance to CERA.

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BBus (Mkt) (Hons)

Simon Brewin
Royal Victorian Eye and Ear Hospital
BBus, Grad Dip HSM, MBL, FCHSM, GAICD

Professor Andrew Cuthbertson AO
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Wendy Miller
BA LLB (Hons)

Professor John Prins
University of Melbourne representative
MBBS, PhD, FRACP, FAHMS

Alternate Directors

Llewellyn Prain
BA (Hons) LLB (Hons) GAICD (for Simon Brewin)

Professor Jenny Wilson-Berka
BSc (Hons) PhD (for Professor John Prins)

Associate Professor Peter van Wijngaarden
MBBS (Hons), PhD, FRANZCO (for Professor Keith Martin)

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Chief Operating Officer and Company Secretary
LLB (Hons), GAICD

Tena Cheng
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LLB, BSc

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Deputy Director, Principal Investigator Ophthalmic Neuroscience
Associate Professor of Surgery (Ophthalmology), University of Melbourne
MBBS, PhD, FRANZCO

Abridged financials

CONSOLIDATED STATEMENT OF FINANCIAL POSITION
as at 31 December 2021

	2021 $'000	2020 $'000
ASSETS		
Current assets		
Cash and cash equivalents	865	1410
Trade and other receivables	1498	1678
Other assets	253	244
Total current assets	**2 616**	**3 332**
Non-current assets		
Financial assets	33 306	26 337
Property, plant and equipment	744	667
Trade and other receivables	417	80
Right-of-use assets	218	532
Total non-current assets	**34 685**	**27 616**
Total assets	**37 301**	**30 948**
LIABILITIES		
Current liabilities		
Trade and other payables	2 590	3 455
Employee Benefits	1949	1560
Lease Liabilities	230	330
Total current liabilities	**4 769**	**5 345**
Non-current liabilities		
Employee Benefits	178	179
Lease Liabilities	25	255
Total non-current liabilities	**203**	**434**
Total liabilities	**4 972**	**5 779**
Net assets	**32 329**	**25 169**
EQUITY		
Reserves	16 694	13 316
Retained earnings	15 635	11 853
Total equity	**32 329**	**25 169**

CONSOLIDATED STATEMENT OF PROFIT OR LOSS AND OTHER COMPREHENSIVE INCOME

for the year ended 31 December 2021

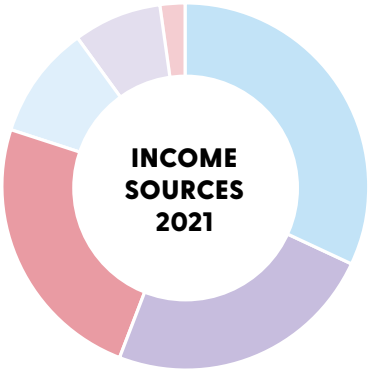
	2021 $'000	2020 $'000
REVENUE		
Federal and State Government grants	5 932	4 549
Clinical trials and contract research	5 976	4 681
Donations and bequests	2 357	2 332
Philanthropic and other grants	1957	867
Government subsidies*	445	2 504
Investment and other income**	7 932	558
Total revenue	**24 599**	**15 491**
EXPENSES		
Research expenses	11 698	9 257
Research support expenses	4 824	4 481
Occupancy expenses	299	253
Depreciation and amortisation	429	434
Finance expenses	189	182
Total expenses	**17 439**	**14 607**
Net surplus	**7 160**	**884**

These abridged audited Financial Statements have been extracted from the full audited Financial Statements for CERA and its controlled entity. The full audited Financial Statements can be extracted from the ACNC (Australian Charities and Not-for-profits Commission) website.

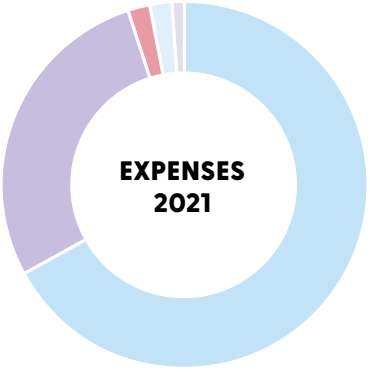
Centre for Eye Research Australia – ABN: 72 076 481 984

**Commonwealth Government JobKeeper and Cash Flow boost payments.*

***CERA operates as a not-for-profit organisation. Accordingly, accumulated surpluses are held as reserves to support future research projects and operations. In 2021 this included proceeds from the sale of Oculo, which will be reinvested into CERA's Innovation Fund.*



32% Investment and other income**
24% Federal and State Government grants
24% Clinical trials and contract research
10% Donations and bequests
8% Philanthropic and other grants
2% Government subsidies*



67% **Research expenses**
28% **Research support expenses**
2% **Depreciation**
2% **Occupancy expenses**
1% **Finance expenses**

2021 Supporters and acknowledgements

Thank you to the many individuals and organisations whose support in 2021 enabled us to keep advancing our work towards a world free from vision loss and blindness. We are grateful for the generous contributions to our research from individual donors, along with the support of philanthropic trusts and foundations, industry, government and other member organisations.

Major gifts ($10 000+)

Rita Andre

Ainslie M Cummins

Professor Andrew Cuthbertson AO

Renate Daniell

Connie Kimberley and Craig Kimberley OAM

Peter Lemon

Andrew G Michelmore AO and Janet Hailes Michelmore AO

The late Baillieu Myer AC and Samantha Baillieu AM and a network of generous donors through their support of the Yulgilbar Alzheimer's Research Program (YARP)

Loris Peggie

Margaret S Ross AM

Elizabeth Xipell

We would also like to acknowledge the support of other donors who wish to remain anonymous.

CERA would like to acknowledge the generous donation of the Macquarie Group Foundation of $10 000 under its staff non-profit support policy in recognition of the Board service provided by employee Suwanee Dharmalingam.

Trusts and foundations ($10 000+)

Alzheimer's Drug Discovery Foundation

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Estate of William Ernest McConnell

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Royal Victorian Eye & Ear Hospital

We gratefully acknowledge the Royal Victorian Eye & Ear Hospital for facilitating support from the following donors for our research:

H&L Hecht Trust

Endowments

We gratefully acknowledge the support of the University of Melbourne in the ongoing management and direction of the following endowed funds to support our research:

Dorothy Adele Edols Research Fund (managed by Perpetual Ltd)

Hazel Jean Eastham Bequest

Kathleen Rankin Bequest

Louisa Jean de Bretteville Bequest

Maurice Cantlon Memorial Fund

The Annemarie Mankiewicz - Zelkin Fellowship Fund

The Floris J & H Dallas Weiseman Charitable Trust

The Mavis and Ivan Rowe Prize for Retinal Diseases Research

The Noel Curphey Fund

The Ringland Anderson Chair of Ophthalmology Fund

Winifred Hallam Monds Bequest

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Melbourne Academic Centre for Health

International Agency for the Prevention of Blindness

Vision 2020 Australia

The MedTech Actuator

St Vincent's Hospital Melbourne

World Health Organisation

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In memoriam

CERA extends its deepest sympathies to the families of the late Baillieu Myer AC and Joan Clemenger AO. We sincerely appreciate their support of CERA over many years. Their generosity and commitment to medical research has made an enormous impact which will benefit future generations.

About the photography in this report.

The images in this report were taken at different stages of the COVID-19 pandemic. All followed the restrictions that were in place at the time.

CERA's research and clinical trials continued operating under strict COVID-safe guidelines.

In some instances, this report also includes file images taken in previous years.

↗ Team work: (from left) Optometrist Sandy Rezk, Dr Zhichao Wu, orthoptist Nora El Sayed from the Clinical Biomarkers Unit with Associate Professor Peter van Wijngaarden and Dr Xavier Hadoux from the Ophthalmic Neuroscience team.

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With your support we can continue our world-leading research and accomplish scientific breakthroughs previously deemed unattainable.

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Partnership and funding opportunities

As true innovators, our scientists are on the brink of new discoveries every day. For a confidential discussion about how you can partner with our researchers to help them discover new ways to prevent vision loss contact Ryan McCarthy, Senior Manager Philanthropy on rmccarthy@cera.org.au or +61 9929 8796.

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