Autumn 2022

visionary

Hope in sight®

Share our vision to beat glaucoma

CENTRE FOR
Eye Research
Australia

World Glaucoma Week
6-12 March 2022

Share our vision to beat glaucoma

Each year for World Glaucoma Week, CERA joins the international effort to raise awareness of the risk factors for glaucoma and the importance of regular eye checks.

That's important because when glaucoma is detected early – we have a great chance of saving sight.

Thanks to research, glaucoma treatment has really improved in recent years. But there's still much more we need to do – particularly for the 15 per cent of people with glaucoma who don't respond to current treatments.

At CERA, our commitment to beating glaucoma extends beyond World Glaucoma Week. It's a challenge that occupies our team every single day of the year.

As a glaucoma researcher and specialist, one of the things that attracted me to move to CERA from Cambridge was the breadth of research happening here.

At CERA, glaucoma research isn't just done by one team or a small group – but across the many specialist teams with extensive national and international collaborations.

In this edition of *Visionary*, I'm thrilled to introduce you to just some of our team who are doing critical glaucoma research – including two of our newest principal investigators Associate Professor Rick Liu and Dr Luis Alarcon-Martinez.

Research is never done in isolation – and your support has been critical in enabling CERA to continue expanding and advancing glaucoma research.

I encourage you to support our 2022 Glaucoma Appeal so we can transform the research that is happening in the lab and put hope in sight for people with glaucoma.

Professor Keith Martin
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**All of the photography in this publication complies with COVID-19 restrictions that were in place at the time they were taken. The images in this report were taken at different times from 2020-2022.*

Photo: Anna Carlile

Meet the team tackling glaucoma

Team effort: Researchers (from left) Associate Professor Ian Trounce, Dr Xavier Hadoux, Dr Flora Hui, Associate Professor Rick Liu, Professor Mingguang He and Dr Manisha Shah.

CERA researchers are spreading the word about how eye research can combat the world's leading cause of irreversible blindness.

During World Glaucoma Week, CERA researchers are standing up as part of a global campaign to raise awareness of the world's leading cause of irreversible blindness.

"It's estimated that in Australia about 300,000 people have glaucoma but around 150,000 don't know they have it," says CERA Managing Director **Professor Keith Martin**, a glaucoma specialist and vision scientist.

"Sadly, once vision is lost there is no way of restoring sight. Also, current therapies don't work for everyone, with about 15 per cent of patients continuing to lose their sight despite treatment.

"That's why our team is passionate about the critical role of research in finding better ways to detect and treat the disease."

Starting with pre-clinical research in the lab all the way through to patient trials, CERA researchers are looking at ways to better understand the disease, improve diagnosis, and develop new treatments to save people's sight.

Starting in the lab

CERA's basic scientists are examining key elements of the complex transport system that sends signals between the eye and

(Continued Page 4)

Photo: Anna Carlile

brain that enables us to see, as well as how glaucoma stops this from working.

Principal Investigator Neurodegeneration Research **Associate Professor Ian Trounce** is investigating how changes in the DNA of the mitochondria, the tiny batteries which power our cells, could cause optic nerve damage.

Professor Martin's research group, a collaboration between the universities of Melbourne and Cambridge, is investigating potential gene therapies to strengthen the optic nerve and protect it from damage.

Meanwhile, CERA's newest research team, Vascular Neuroscience, led by **Dr Luis Alarcon-Martinez**, is examining the intricate, never-before-seen processes that regulate blood supply to the cells of the retina (pages 6-7).

Early Detection

As research tells us more about what causes glaucoma there is also an opportunity to get better at identifying early signs of disease.

CERA's Clinical Genetics team, led by **Professor Alex Hewitt**, has been part of a research collaboration to identify the genes that put someone at risk of glaucoma.

Professor Hewitt and his team worked with colleagues from QIMR Berghofer Medical Research Institute, Flinders University and others to pinpoint genes which could eventually be used in screening to more accurately predict glaucoma risk.

CERA's new Clinical Biomarkers team, led by **Dr Zhichao Wu**, is using artificial intelligence and state-of-the art imaging techniques to identify new clinical

Improving treatment: Dr Nathan Kerr, Dr Elsa Chan, Dr Luis Alarcon-Martinez, Peter Larsen and Dr Jennifer Fan Gaskin.

Gene therapy: Professor Keith Martin (right) is investigating potential gene therapies to repair the optic nerve.

biomarkers for glaucoma (see pages 12-13). These biomarkers could be used to detect the disease earlier as well as provide personalised treatments to help prevent vision loss.

Imaging and AI are at the heart of several CERA projects. Innovative research by **Dr Xavier Hadoux** and **Associate Professor Peter van Wijngaarden** is investigating biomarkers of Alzheimer's disease, diabetic retinopathy and other eye conditions.

And pioneering research by **Professor Mingguang He** is using artificial intelligence to develop technology that will increase access to eye screenings in remote and regional areas where there is a shortage of eye care professionals.

CERA's Health Services Research Unit, led by **Peter Larsen**, is continuing its research to improve early glaucoma detection rates and eliminate undetected glaucoma in our community.

New and better treatments

For patients who need surgery to control their glaucoma, it's important to ensure that the techniques we use and the drugs that aid recovery are as effective as they can be.

CERA's Principal Investigator Ocular Fibrosis **Dr Jennifer Fan Gaskin**, along with **Dr Elsa Chan** and **Dr Manisha Shah** are investigating several possible drugs to reduce the scarring that can sometimes occur after surgery and cause operations to fail.

Principal Investigator Glaucoma Surgical Trials **Dr Nathan Kerr** is also continuing his research into the surgical management of glaucoma, comparing new minimally invasive surgical techniques and implants to traditional therapies like eye drops.

Principal Investigator Genetic Engineering **Associate Professor Rick Liu** is investigating ways to improve how glaucoma treatments are delivered. His research uses nanoparticles to develop new therapies that need to be administered less often and eliminate the need for more invasive procedures like injections or surgery (see pages 8-9).

Also **Dr Flora Hui** is investigating another potential way of improving the effectiveness of glaucoma treatments by combining existing therapies with a high daily dose of vitamin B3. Her upcoming study provides hope for a potential new treatment that could not only protect against ongoing vision loss, but also improve the function of cells that have already been damaged (see pages 10-11).

Between all these efforts, CERA researchers are working towards better outcomes for every aspect of glaucoma treatment from diagnosis to management.

Photo: Mathew Lynn

Seeing the retina in a new light

A new CERA research team is using groundbreaking experimental methods to uncover previously unseen structures in the retina, with the hope of improving treatments for glaucoma.

Dr Luis Alarcon-Martinez, who leads CERA's new Visual Neurovascular Research Unit, is investigating the mechanisms which control blood flow to the retina, a complex layer of cells at the back of the eye.

When our vision works correctly, light is picked up in the retina and turned into electrical signals which are transmitted to the brain by millions of retinal ganglion cells.

These cells transmit visual information to the brain via long nerve fibres, known as axons, which make up the optic nerve.

Inadequate blood supply can damage the retinal ganglion cells and lead to vision loss.

Dr Alarcon-Martinez's research aims to gain a better understanding of how exactly blood is distributed in the retina in order to prevent damage and preserve sight.

"We know that interruption of blood supply is found in diseases such as glaucoma, diabetic retinopathy, retinopathy of prematurity, and age-related macular degeneration," says Dr Alarcon-Martinez.

"But we currently have only limited understanding of the exact mechanisms that control the distribution of blood in the retina.

"The neurons are saying 'I need more energy', and the vessels supply the elements to produce it. But we don't know exactly how that happens."

A new experimental set-up

This lack of understanding about such basic functions might come as a surprise, but Dr Alarcon-Martinez says there are two very good reasons for it.

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New insights: Dr Luis Alarcon-Martinez's research is using powerful microscopic techniques to observe the distribution of blood in the retina.

The first is that the processes are happening at a very small scale: that of single nerve cells and capillaries.

The second is that they need to be observed in living organisms.

"Until recently, we simply didn't have the technology to be able to look at such small environments in the retinas of living organisms," says Dr Alarcon-Martinez.

Dr Alarcon-Martinez was part of a team at the University of Montreal which developed a new experimental set-up to do just that.

Nanotube discovery

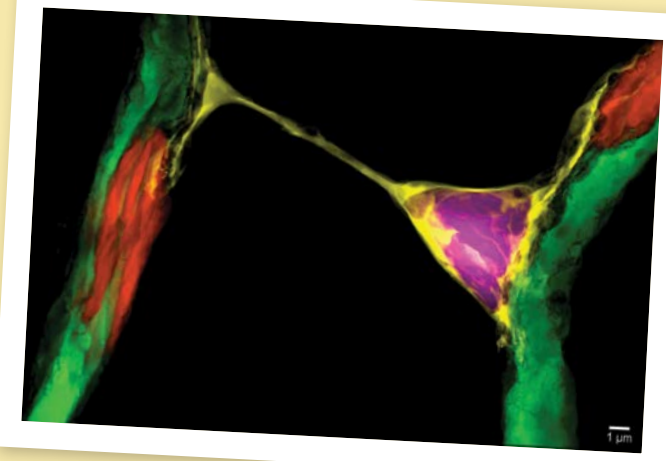
Using cutting-edge two-photon microscopy, Dr Alarcon-Martinez and colleagues were the first to observe these processes in living organisms at such high levels of resolution.

They discovered a previously unknown mechanism by which cells in the retina communicate to regulate blood supply.

Embedded within the capillaries are pericytes, cells that can control the amount of blood passing through the capillaries.

Looking at vascular changes in the retinas of mice, Dr Alarcon-Martinez and colleagues showed that pericytes project very thin tubes – known as nanotubes – to communicate with one another and supply blood where it is most needed.

Their study, published in *Nature* in 2020, also showed that capillaries lose their ability to regulate blood supply when these nanotubes are damaged.



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Communication system: Research has uncovered tiny nanotubes that allow cells in the retina to communicate with each other. Alarcon-Martinez et al., 2020. Nature. 2020. 585(7823):91-95.

These findings suggest that the interruption of blood supply found in retinal neurodegenerative diseases might be a result of these nanotubes breaking down.

Where to next

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

Its potential applications are not limited to vision, but also include diseases such as Alzheimer's disease and strokes.

Dr Alarcon-Martinez says he's excited to join the CERA research team, which combines basic science with clinical research.

"We do the work we do to help people, and I can't think of a greater reward than seeing the impact our research can have."

Read the research

Alarcon-Martinez, L., et. al. (2020). Interpericyte tunnelling nanotubes regulate neurovascular coupling. *Nature*, doi: 10.1038/s41586-020-2589

Photo: Mathew Lynn

Engineering better glaucoma treatments

CERA's new Genetic Engineering research team is investigating how nanotechnology could improve glaucoma treatment.

Treatments to reduce eye pressure – like multiple daily eye drops, or surgery – are part of life for many people living with glaucoma.

Although these treatments can successfully halt damage to retinal and optic nerve cells caused by glaucoma, they can be invasive, difficult to use and have side effects. Also, they can't repair any damage that has already occurred or strengthen cells to prevent further injury.

CERA's Genetic Engineering Research Unit, led by Associate Professor Rick Liu, hopes to change that and create new treatments that are more accurate, longer-lasting and have fewer side effects for people with glaucoma.

The team's research is investigating how nanoparticles – particles so tiny that you'd need to combine 80,000 to 100,000 to equal the thickness of a strand of human hair – can be used to improve the way current therapies are delivered.

Strong focus: Associate Professor Rick Liu's research aims to develop more effective and less invasive treatments for eye disease.

They are also working with this technology to deliver new, targeted treatments straight to cells that can repair damage and protect cells from further injury.

Nanomedicine potential

Nanoparticles can transport drugs to places they wouldn't be able to reach on their own, such as injured cells.

They can also enable the slow release of drugs over a long period, reducing the need for repeated doses.

"Nanotechnology is an exciting and expanding research area, especially in medicine application," says Associate Professor Liu.

"Nanoparticles can help deliver a drug more efficiently, or to a specific location, enabling eye disease to be managed more effectively."

It is hoped the new therapies will improve the lives of patients by requiring treatments that need to be administered less often and eliminate the need for more invasive procedures like injections or surgery.

Research findings

In 2021, Associate Professor Liu collaborated with researchers from Monash University and the University of Melbourne to develop a potential method of using nanoparticles to deliver treatment to retinal cells damaged by elevated eye pressure.

The research, completed while Associate Professor Liu was at the University of Tasmania, was published in *Acta Biomaterialia*.

"We developed a nanoparticle that allowed us to pack the drug and then target the damaged cells," says Associate Professor Liu.

"This system can also help to reduce the drug dose because you don't need to target all the retinal cells, you can just target the cells that are injured."

It involved injections, but Associate Professor Liu says its benefits could last between a few weeks and up to a month.

In the longer term, the team hope to further develop this technology so it can be delivered via eye drops.

The way forward

Ultimately, Associate Professor Liu and his team aim to replace invasive procedures such as eye injections – not only for glaucoma but also many other eye conditions.

In another research project, his team have used nanoparticle technology to enable eye drops to uniformly coat and penetrate the eye surface, improving absorption at the front.

These 'nanoformulation' eye drops could also reduce side effects and the frequency of administration of eye drops from several times a day to once.

"Ultimately, we want to use nanoparticles in an eye drop to deliver the drug into the injured retinal cells and protect them," Associate Professor Liu says.

"It would be a major step forward in treating glaucoma and offers the promise of effective, long-term treatment."

Vision and vitamin B3

Photo: Anna Carlile

Research to determine if vitamin B3 can treat optic nerve damage caused by glaucoma is set to move into a new phase.

Most therapies for glaucoma aim to reduce eye pressure to prevent nerve cell damage and vision loss.

CERA researchers are investigating a form of vitamin B3 that could help existing treatments prevent the disease's progression.

If demonstrated to be effective, the simple daily tablet would be the first treatment that specifically targets nerve cells in glaucoma.

CERA Glaucoma Research Fellow Dr Flora Hui led a world-first clinical trial on high-dose nicotinamide (vitamin B3) that found it could lead to improvement in visual function.

Published in *Clinical & Experimental Ophthalmology* in 2020, the study showed improvement in the visual function of glaucoma patients who took a high dose of nicotinamide daily for 12 weeks on top of their regular treatment to reduce eye pressure.

Investigating impact

Dr Hui is now co-principal investigator of a larger trial set to start in 2022 after securing a $200,000 Glaucoma Australia Quinlivan Research Grant.

Participants with three common types of glaucoma will take vitamin B3 daily for two years and have the progression of their glaucoma monitored every four months.

At the same time, Assistant Professor Pete Williams from Sweden's Karolinska Institutet will conduct a similar trial there.

Other collaborators include CERA Managing Director Professor Keith Martin, Professor Jonathan Crowston, from Duke NUS-Medical School, Singapore, and Professor Robert Casson, from the University of Adelaide.

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New treatments: Dr Flora Hui is investigating if vitamin B3 can be used to reduce vision loss from glaucoma.

Supplementing treatments

If the new trial is successful, vitamin B3 could become part of a holistic glaucoma treatment plan.

The idea grew from previous research into mitochondria, which give cells the energy they need to function. If this supply is interrupted the nerve cells, in this case at the back of the eye, can lose function.

Vitamin B3 had been shown to improve function in other cells and is now showing promise in the eye. The dose is higher than that found in food sources but is easily sourced in a tablet.

"All the current glaucoma therapies target eye pressure and reducing eye pressure," Dr Hui says.

"We do know that despite current treatments, some people continue to progress and lose vision.

"The idea with vitamin B3 is to try and supplement the nerve cells at the back of the eye and help them to function better. This can help reduce further vision loss."

If successful, the trial could translate into a new treatment relatively quickly as nicotinamide is already available.

"If we find that it's useful in glaucoma … once we get the news out doctors can start giving it to their patients almost immediately," Dr Hui says.

"It's really exciting because it's what you want to do in research – you want to make a difference."

Participant Q&A

How do I qualify for the trial?

You must be aged 18 and over and have primary open angle, normal tension or pseudoexfoliative glaucoma.

How do I join?

The best way is to join the CERA trial registry, which notifies you of trials that may be suitable. Join here: **cera.org.au**

How long will it take?

Participants will take vitamin B3 and have their health monitored every four months over two years. Check ups will take place in Melbourne and Adelaide.

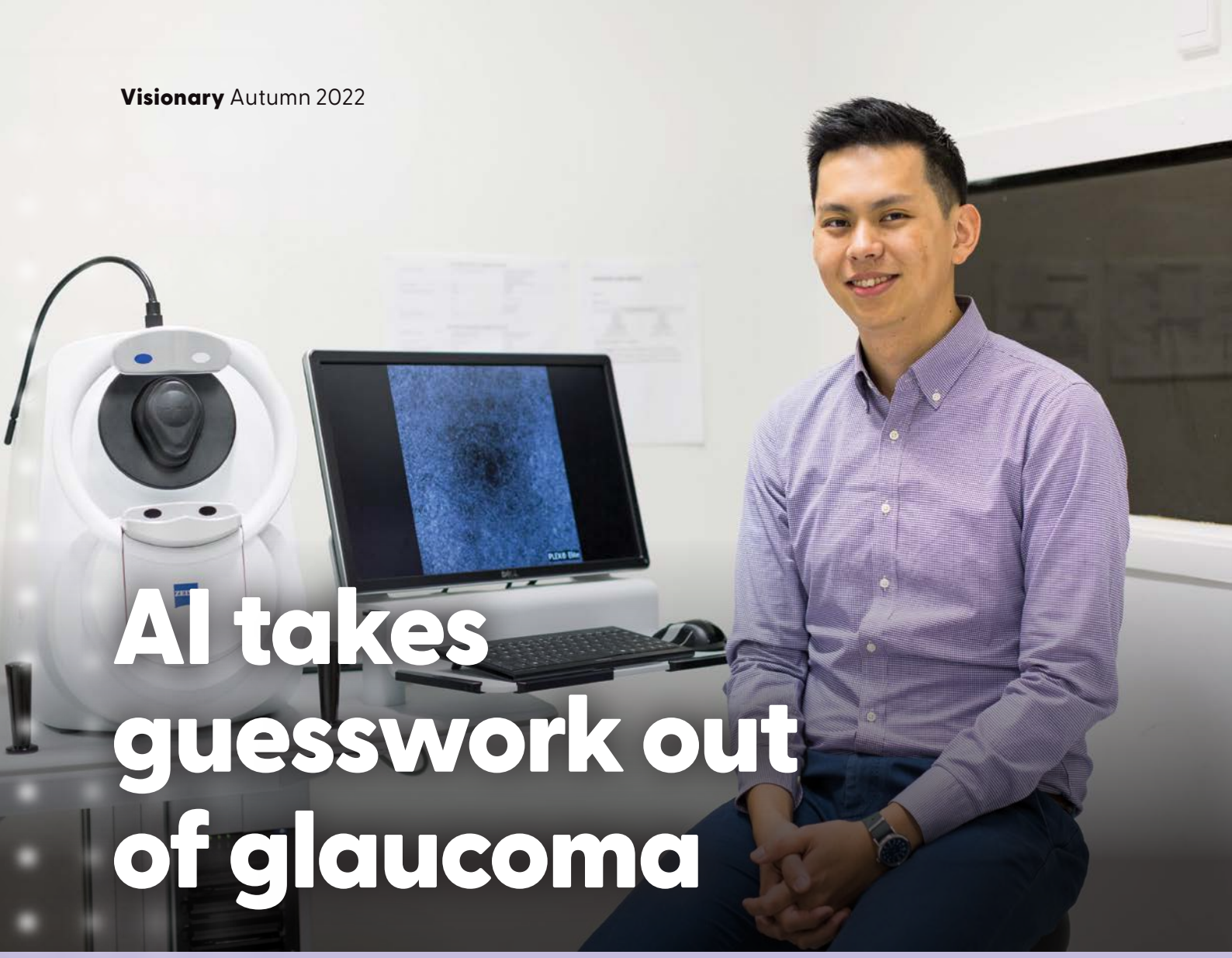
How will my progress be monitored?

Every four months participants will visit a clinic in Melbourne or Adelaide for an eye check-up. It is similar to a regular glaucoma check, with a few extra aspects and an optional blood test for genetics analysis.

What happens when it's over?

Researchers will collate the results to see if vitamin B3 used in conjunction with conventional therapies has helped to stem the progress of glaucoma-related vision loss. If so, doctors may start recommending it as part of an overall treatment plan.

Earlier stages of this research were supported by the Jean Miller Foundation, Connie and Craig Kimberley Foundation, Ophthalmic Research Institute of Australia, Jack Brockhoff Foundation, Marian and EH Flack Trust, Fund and Board of Research Faculty Karolinska Institutet.



AI takes guesswork out of glaucoma

Combining the latest imaging techniques with artificial intelligence, CERA researchers are developing new ways to identify glaucoma and other eye diseases.

Glaucoma affects as many as 1 in 50 Australians, with half of those unaware they are living with the condition. It is usually caused by high intraocular pressure, due to fluid in the eye not properly draining, which gradually damages the optic nerve resulting in a permanent loss of vision.

The condition is painless and typically progresses slowly but identifying those who are likely to lose vision quickly is a difficult task.

Specialists use visual field tests to track the progress of a patient's vision loss.

The test, which requires a patient to respond to brief flashes of dim lights shown throughout their field of vision, can produce inaccurate results due to its subjectively challenging nature.

"It's a bit like playing the board game Guess Who?" says Dr Zhichao Wu, Head of Clinical Biomarkers Research at CERA.

"Every time a person with glaucoma comes in to see the specialist they do a visual field test, but you have got to do that every six months for up to six years before you can be certain that there is real change happening to a patient's sight.

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Faster diagnosis: Dr Zhichao Wu's research is aiming to diagnose those at risk of losing their sight from glaucoma sooner.

"If someone is truly losing vision at a rate that will significantly affect their functional vision and it takes that many years to find out, you're going to find out when it's far too late."

Looking for signs

Dr Wu's new Clinical Biomarkers Research team is working to identify new biomarkers of glaucoma using artificial intelligence that will reduce the reliance on visual field tests and find those patients who are in urgent need of care.

Biomarkers are measures of processes in the body that can be used to identify a disease and monitor its progression. The more that can be found, the more ways a practitioner can track the progress of a particular disease.

Using state-of-the-art imaging of the eye and artificial intelligence, Wu's new team will find new biomarkers that will help precisely determine an individual's 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 AI for pattern recognition to pick up characteristic patterns that indicate very early signs of progressive glaucoma damage," says Dr Wu.

This new research will enable patients to receive the highly individualised treatment needed to prevent irreversible vision loss.

"We're aiming to go from six years to six months in terms of our timeframe for detecting glaucoma progression," says Dr Wu.

AI revolution

Using artificial intelligence to find new ways of identifying and monitoring disease is at the heart of several projects currently underway at CERA.

Professor Mingguang He, Head of Ophthalmic Epidemiology at CERA, is developing an integrated AI screening system to find patients who are at risk of losing their sight from diabetic eye disease, glaucoma or age-related macular degeneration.

In other studies underway at CERA, led by Associate Professor Peter van Wijngaarden and Dr Xavier Hadoux, novel imaging methods are being combined with artificial intelligence to investigate biomarkers for Alzheimer's disease, diabetic retinopathy and a range of other conditions.

Overall, this work aims to provide practical benefits for patients who otherwise might have not had their disease identified soon enough to start treatment to avoid vision loss.

"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 or glasses update," says Dr Wu.

"In glaucoma people sometimes turn up with half their vision gone. We should have picked that up years and years ago.

"Our hope is that with new imaging methods and AI tools we can be better equipped to detect eye disease and save sight."

High-flyers' lasting legacy

CERA pays tribute to John and Joan Garden whose generous bequest to eye research will benefit future generations.

Joan Garden knew what it was like to experience vision problems, although that didn't prevent her from living a full life.

The popular flight attendant, who later trained staff at Myer's CBD store, 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 research to help others. After she died in August 2018, aged, 79, her brother John ensured her wishes were carried out.

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

When John, who also worked for an airline (TAA) died in September 2020, aged 88, he left a significant donation to CERA on behalf of Joan. It was a generous gesture from siblings who lived full and rich lives during the heyday of air travel.

Both were born and grew up in Kew, in Melbourne's leafy east. Their older sister, Mary, was the only sibling who married. Sadly, Mary and her husband, Gordon Morris, both died relatively young.

Instilling good values

As a QANTAS flight attendant, Joan saw the world and chaperoned children who travelled alone. She loved it and her penchant for manners and etiquette made her ideal for a later training role with the airline.

After being diagnosed with a benign brain tumour, Joan had the first of two operations – its position made it impossible to fully remove.

Siblings John and Joan Garden are remembered fondly by their friend Phillip Russell.
Right: Joan, Phillip's godmother, holding him when he was a baby.

She continued to work part-time as a staff trainer at Myer in Melbourne's CBD, and enjoyed instilling her values and knowledge in the next generation.

Eventually Joan's sight deteriorated, and she suffered from double vision. This sparked an interest in CERA's development of treatments for a range of eye conditions.

Two lives well lived

When their parents died about 40 years ago, Joan and John moved to Deepdene. Neither drove a car, so they walked or relied on taxis or lifts with close friends Phillip and Michele Russell.

Phillip's older sister, Josie Gayther, was close friends with Joan and another primary school classmate, Bev Speed. Their lifelong friendship included Joan being Phillip's godmother, as both families were Catholic.

Phillip remembers that Joan was always immaculately presented and wore nice jewellery. "She got on well with people and everyone liked her," he says.

Despite having access to discount air fares with TAA, John liked nothing more than travelling on cargo ships, which allow a small number of paying passengers.

He'd have his own room and the run of the ship as it headed to Asia, Africa, or the Americas.

The siblings were also known for their elaborate Christmas Day spreads. Joan would cook a five-course meal and prepare a written menu for the guests, which she kept in an album with a photo from the day.

John didn't cook much but when Joan went into care, he soon began whipping up gourmet meals for himself and cakes for Joan and others. "He used to make these cakes and they were delicious," Phillip says.

A lasting legacy

While Joan's health declined in later years, she and John stayed active in their community and enjoyed gardening at their unit.

John was known to walk five kilometres to Bunnings in Hawthorn if he needed something. "John walked everywhere." Phillip says. "And I mean everywhere and, at a great pace!"

Despite living with prostate cancer and his own eye problems for many years, John continued to care for Joan. When Joan said she wanted to provide for CERA and other charities in her will, John carried her wishes out in his.

Both will be remembered for their generosity and community spirit.

If you're considering leaving a gift in your will to advance CERA's research, please call our Donor Relations Advisor, Elaine Levine, on **03 9929 8360** for a confidential discussion. Learn more at **cera.org.au/gifts-in-wills/**

Glaucoma Appeal 2022

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