Spring 2023

visionary

Hope in sight®

Daniel defines his future

Transforming clinical trials

Magnify the impact of research

CENTRE FOR
Eye Research
Australia

HOPE IN SIGHT
GIVING DAY
12 October 2023

New therapies in reach

It takes thousands of people, all pulling towards the same goal, to create new treatments for eye diseases.

This includes our scientists, who every day in the lab and the clinic are searching for new ways to diagnose disease, learning how conditions progress and creating innovative ways to deliver treatments.

There are also people like Daniel, appearing on the cover of this *Visionary* with his father Vince, who generously give their time to take part in research.

Daniel lives with Stargardt's disease – an inherited retinal disease that results in a gradual loss of central vision.

His curiosity and passion for science are helping us get closer to a treatment.

And there is also our community of supporters who power our work.

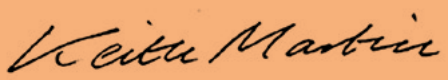
People like sisters Kerry, Leesa and Sharon, who this year raised more than $30,000 in the Lions Ride for Sight in support of their parents.

This community makes all the research you read about in *Visionary* possible, and has been instrumental in supporting our vision for a new, world-leading clinical trials centre. You can read more about this on page 12.

I'm excited to see what we will achieve together next.

This year, we're celebrating World Sight Day by magnifying the impact of our community. On Thursday 12 October, our fourth annual **Hope in Sight Giving Day** will see donations tripled up to our $150,000 goal thanks to matched donations.

Join us to find out how your gift to CERA can have the greatest impact to bring hope in sight.



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THE UNIVERSITY OF MELBOURNE

the royal victorian eye and ear hospital

Photo: Anna Carlile

A deeper bond

When he was a kid, Daniel's vision didn't bother him too much.

"At first, my teachers thought I was just avoiding work when I couldn't see the whiteboard," Daniel recounts.

"When I was nine or 10, I was given prescription glasses, but they were horribly inappropriate and only really worked for reading."

Daniel, now 15, has a condition called Stargardt's disease, which creates a blur over his central field of vision.

Sometimes known as juvenile macular degeneration, Stargardt's is a condition of the eye that leads to low vision.

The cause is locked within Daniel's DNA.

As the instruction manual for the body, deoxyribonucleic acid, more commonly known as DNA, is responsible for all kinds of tasks within the eye.

From producing new cells to clearing the waste left behind by sight, DNA guides the delicate processes that allow us to see.

For Daniel and other people with Stargardt's disease, a specific gene mutation acts like a typo in those instructions.

Instead of sweeping away the by-products of sight, proteins in the eye allow small flecks of material to build up across the macula that interferes with central vision.

(Continued Page 4)

Photo: Anna Carlile

"If 'normal' vision is a clear and developed image, mine is like you've just loaded up the webpage: it's blurry," says Daniel.

Inherited retinal diseases (IRDs) – of which Stargardt's is just one – are the most common cause of legal blindness among working-age adults.

About 16,000 Australians experience IRDs in some form but understanding the full scope and impact of them is a huge project.

"We look at the individual and their vision, especially as it changes over time; that gives us a starting point," says Bhaj Grewal, Clinical Trial Coordinator in CERA's Retinal Gene Therapy Unit.

"We can compare what we see in their genetic results, and place that side-by-side with genetic information from their parents, siblings and other family members.

"By zooming in to that level of detail we can build a much richer picture of inherited retinal disease more broadly."

Research has made enormous leaps in mapping the hundreds of thousands of genes that make up DNA.

That instruction manual, however, still contains mysteries – which is why CERA research tackles IRDs from multiple perspectives, including an extensive natural history study with global reach.

"By collecting as much information as possible, we begin to build a picture of what happens within the eye leading to these conditions," Bhaj explains.

"If we can identify the gene mutations responsible for vision loss, we can focus on understanding that series of events – which brings us closer to being able to treat, cure or even prevent IRDs."

Through his eyes

Like many people with an IRD, Daniel's vision has changed over the years.

← *Looking closer: Optometrist Bhaj Grewal with Daniel.*

"I've become more aware, as my sight has gotten worse, that it has a significant impact on how I engage with the world," he says.

For Daniel, the main consequence of Stargardt's is the absence of detail in his central field of vision - although, notably, his peripheral vision is more than sharp enough for after-school boxing twice a week.

The bigger challenge is a social one.

"When I'm walking past someone, it takes until the last minute to recognise them – when I'm close enough to actually distinguish their face," he says.

"I worry that I've insulted them, or come across as rude.

"It does make me feel more alienated and disconnected from others."

Expectations and reality

In adjusting to his vision and diagnosis, Daniel has come to expect a lack of awareness from the people around him.

"Even when I've explained what I require, like a digital exam paper or a larger print out, I'm still counting on others to meet those needs – some people are just uninformed, or don't get it."

Since joining CERA's investigations of IRDs, Daniel's knowledge of his condition has grown, and alongside it he's learned to advocate for his own needs.

"I used to be pretty incurious – since beginning the clinical trial, I've gained so much knowledge relating to my condition and how it affects me," he says.

"My vision hasn't taken over my life, which is honestly my ideal state.

"It's an immutable part of me, but it doesn't define me."

Focus on the future

With the strength and support of his family, especially parents Vince and Sara, Daniel is prepared to tackle the future challenges of his condition.

"So much of my experience is fundamentally forged through social relations, rather than putting emphasis on my vision," Daniel explains.

"I know that I can reach my fullest potential with the empowerment of the people closest to me."

Navigating his changing vision is just one aspect of Daniel's life, and he approaches it with the same curiosity as he does his STEM (Science Technology Engineering and Mathematics) school subjects.

"It's exciting to me, following instincts to understand and relate concepts to each other," Daniel says.

"Engineering is like a symphony of my interests in mathematics, physics, and chemistry."

The drive to understand action and consequence is part of Daniel's motivation to participate in research and contribute a piece to the IRD puzzle.

"Yes, my vision is declining, and we have to really bear out the effects of the treatment, but I hope it stagnates – that the rate of deterioration slows."

Thanks to people like Daniel, a growing library of genetic data is unravelling the mechanics of these conditions – putting new treatments within reach.

Photo: Anna Carlile

International effort

CERA has joined a worldwide collaboration to ensure rare genetic diseases receive the same attention as more common conditions.

A new international partnership will provide a major boost for CERA's inherited retinal disease (IRD) research and help bring more clinical trials for rare eye diseases to Australia.

CERA has joined the Foundation Fighting Blindness Consortium alongside more than 40 other research centres from around the world.

It will be the first Australian research site contributing to Uni-Rare – a global registry of people with extra-rare genes to improve understanding of IRDs and boost the development of potential therapies.

Associate Professor Lauren Ayton and Dr Tom Edwards from CERA's Retinal Gene Therapy Unit are leading the Australian research.

"Most of the global research is currently focusing on the more common IRDs, such as X-linked retinitis pigmentosa, choroideremia and Stargardt's disease – as it should be," says Associate Professor Ayton.

"However, there are still many more people with rarer forms of these diseases that also need treatments.

"We want to make sure these other IRDs are still being researched."

IRDs are a group of eye conditions caused by a mistake in one or more genes, which leads to damage in the light-sensitive retina at the back of the eye.

Over 300 genes are known to cause IRDs, and while all lead to some level of vision loss each individual disease affects the retina quite differently.

← *VENTURE Team: (from left) Dr Ceecee Britten-Jones, Parker Truong, Dr Tom Edwards, Associate Professor Lauren Ayton, Sachinee Jayasuriya, Associate Professor Heather Mack and Fleur O'Hare.*

Studying such a large group of conditions is a challenge, especially particularly rare IRDs that may affect less than a few hundred people worldwide.

Associate Professor Ayton is co-leader of the Victorian Evolution of Inherited Retinal Diseases Natural History Registry (VENTURE study) - a collaboration between the CERA and the University of Melbourne.

VENTURE collects data from Australians with IRDs to perform research and identify those who may be eligible for upcoming clinical trials for new treatments.

Now they will also be contributing to a global project.

Greater access

"We're currently the only Australian research institute in the Foundation Fighting Blindness Consortium and are very excited to work with our international counterparts on learning more about these rarer IRDs," says Associate Professor Ayton.

Local VENTURE participants will be given the option to anonymously take part in the Uni-Rare global registry if they have an IRD that relates to the study.

"The idea is that all consortium research centres will use the same research methods and pool our data, so we can reach better conclusions," says Associate Professor Ayton.

As one of the consortium's 40 Research Centres of Excellence, CERA can also become a site for their future clinical trials.

"That means we have an excellent chance of bringing new treatments for IRD to Australia in a timely manner," says Associate Professor Ayton.

"The Foundation Fighting Blindness are one of the largest international IRD advocacy and funding groups in the world and have been highly involved in the development of several treatments.

"By sharing information about the different IRDs Australians have, and how common they are, we can help the Foundation decide what IRDs they will target next."

Improving trials

Through the consortium, Associate Professor Ayton is also helping shape the future of how new treatments will be brought to patients.

"We're working with the American Food and Drug Administration towards developing better ways of measuring the effectiveness of treatments," she says.

This includes looking for improved ways of imaging the eye and measuring vision to better show how well new treatments works.

The goal is to help future therapies move smoothly through trials as they are tested to make sure they are safe and effective.

"I'm hopeful we can improve clinical trials and get more treatments underway for patients in Australia living with IRD", says Associate Professor Ayton.

"That's something I'm really excited about."

AMD or IRD?

Spotting the differences between macular diseases isn't always easy – finding new ways to do so will have a big impact.

For many visitors to the zoo, the differences between a lizard and a salamander might be very hard to spot: both have long bodies, stretched tails and crawl among plants on their four legs.

However, a trained eye would notice that lizards have scales while salamanders have smooth skin and stumpy toes.

Doctors go through a similar process when diagnosing disease.

For some eye diseases the signs are easy to spot, but for others the signs are so subtle that getting the correct diagnosis can be hard.

Dr Ceecee Britten-Jones, CERA Honorary Research Fellow and Postdoctoral Research Fellow at the University of Melbourne, is working on improving the diagnosis between atrophic age-related macular degeneration (AMD), also known as dry AMD, and inherited macular dystrophies.

With new treatments on the horizon, faster and more accurate diagnosis is more important than ever.

"It's important that all patients with macular diseases first get the correct diagnosis, so they don't miss opportunities for clinical trials and can also receive the right treatment for their condition," she says.

Spot the difference

It can be easy to misdiagnose macular dystrophies as AMD because they both affect the macula and eventually lead to loss of central vision – but that's where the similarities end.

"On examination, these two diseases can appear very similar, but genetically they are very different," says Dr Britten-Jones.

While the underlying causes of AMD are not yet known, both genetic and lifestyle factors seem to play a role.

In contrast, macular dystrophies are a group of inherited retinal diseases (IRDs), which includes Stargardt's disease, and are caused by changes or 'mistakes' in a single gene.

Genetic testing is the only way to get an absolute confirmed diagnosis of a macular dystrophy.

As genetic testing is not easily accessible and interpreting the results can be challenging, it's important the testing is only done on people who don't have a clear-cut diagnosis.

By looking more closely at the differences between macular diseases, Dr Britten-Jones and her team aim to help clinicians better understand which patients should be referred for targeted genetic testing.

Joining forces

Before Dr Britten-Jones and her team can help clinicians diagnose these similar yet genetically different diseases, they need to find people in the community who may have been misdiagnosed.

Study participants have already been referred through the Macular Research Unit, led by Professor Robyn Guymer AM.

"Some participants may have first been referred to macular research with AMD," says Dr Britten-Jones.

"After examination, if Professor Guymer believes they may instead have a macular dystrophy, these participants will then be referred to the study."

Dr Britten-Jones is also collaborating with CERA Honorary Researcher Associate Professor Heather Mack AM, who is reviewing patients diagnosed with AMD from private ophthalmology clinics.

Better diagnosis: Dr Ceecee Britten-Jones

"By looking at both research and real-world settings, this study will help us obtain a broader and more accurate representation of potential misdiagnosis," says Associate Professor Mack.

Improving treatment access

Once they have identified potentially eligible participants, Dr Britten-Jones and her team will investigate the genetic changes that are known to be associated with both types of macular diseases.

After the genetic diagnosis is made, they will then look for distinguishing features that can set the macular diseases apart.

"We want to help other clinicians to better diagnose macular diseases, so that the right patients can be referred for targeted genetic testing," says Dr Britten-Jones.

"Our goal is for every patient with macular diseases to eventually get the right treatment for their condition."

Photo: Anna Carlile

Next stop: the retina

CERA is searching for better ways to get new treatments for inherited retinal diseases to their destination.

Only a few years ago, people living with an inherited retinal disease (IRD) were expected to experience gradual vision loss, but new gene therapy technology has the potential to stop these conditions in their tracks.

These therapies need to be taken to the right part of the eye by a delivery vehicle – usually a safe, modified virus called a viral vector.

The adeno-associated virus is a commonly used viral vector, but its limited size means it cannot fit the larger genes associated with many of the 300 other known IRDs.

Treatments for many IRDs will need a different vehicle.

The problem is a little like a large group of passengers needing to get directly to their destination together.

"Some delivery vehicles are a bit like a taxi – they can transport you directly to your destination but will only fit a limited number of passengers," says Dr Sandy Hung, Research Fellow in CERA's Clinical Genetics Unit.

"Whereas others are more like a bus – they can carry more passengers but may take

← *Urgent delivery: Dr Sandy Hung working in the lab.*

"Developments have advanced so fast there are now many new tools that can potentially allow us to correct the genetic 'mistakes' that occur in different IRDs."

– Dr Sandy Hung

an indirect route and not arrive directly at your destination."

Dr Hung is working to develop ways to ensure larger delivery vehicles can better target specific cells in the light-sensing retina.

"This will help us deliver more treatments to the cells affected in IRDs," she says.

Correcting genes

There are many different types of IRD – each caused by a change or mistake in one or more different genes.

Once the specific genetic mistake is found, researchers like Dr Hung use gene editing tools to try and find a way to correct the mistakes.

"Developments have advanced so fast there are now many new tools that can potentially allow us to correct the genetic 'mistakes' that occur in different IRDs," says Dr Hung.

"However, a current major bottleneck for researchers is the ability to deliver these gene editing tools to the cells that are affected in the retina.

"Now we are going to try and make virus delivery systems with the retinal cell specificity that can also carry larger gene editing systems or large genes."

Different IRDs or genetic mistakes cause different cell types of the retina to not function properly, which can lead to vision loss.

"The first cell type that we're targeting is the photoreceptor cells," says Dr Hung.

Photoreceptors are tiny light-sensing cells that line our retina at the back of the eye, sending messages to our brain which enable us to see.

If successful, the research could potentially benefit people with IRDs such as retinitis pigmentosa.

"While we currently aim to target photoreceptor cells, there is a potential to target other retinal cell types and have an impact on more people with other IRDs," says Dr Hung.

Keeping patients in mind is what motivates Dr Hung to push her research forward.

"From a young age, I wanted to become a scientist as a close family member became ill, and I wanted to help find a treatment," she says.

"Being able to work on projects where the ultimate aim is helping patients is still what motivates me to continue science."

Transforming clinical trials

Work is underway on a new state-of-the-art clinical trial centre that will give more people the chance to take part in research.

CERA Managing Director Professor Keith Martin says the new centre will become a go-to location for global clinical trials of new treatments to prevent blindness, restore sight and transform the lives of people living with incurable conditions.

"The new clinical trial centre will enable us to offer more cutting-edge treatments to patients with diseases that until very recently have been considered incurable, like inherited retinal diseases – which are the leading cause of blindness in working age Australians," he says.

"It will also enable us to expand trials available to people with age-related macular degeneration, glaucoma and diabetic eye diseases."

The new eye clinical trials centre will be embedded in CERA, which is co-located with the University of Melbourne Department of Surgery (Ophthalmology) at the Royal Victorian Eye and Ear Hospital.

It is expected to be fully operational by the end of 2024.

"Together, CERA, the University of Melbourne and the Eye and Ear Hospital form one of the world's leading partnerships in eye health and research," says Professor Martin.

"The new eye clinical trial centre will enable us to make an even greater impact and move us closer to our goal of a world free from vision loss and blindness."

The new centre is supported by $10 million in backing from Breakthrough Victoria – an independent agency which manages an investment fund set up by the Victorian Government designed to make the state a global leader in innovation.

← *Clinical trial: An artist's impression of the new centre.*

Plans for the new centre were announced in June by Victoria's Minister for Industry and Innovation Ben Carroll and Minister for Health Mary-Anne Thomas.

Building on success

The new centre will cater for the global growth in new treatments for eye disease.

In 2022, CERA conducted 60 clinical research projects involving more than 2300 people.

Forty of these involved an intervention or investigational treatment – and there is strong future demand from industry partners who want CERA researchers to run their clinical trials.

Professor Martin says the international standing of CERA's clinician-researchers – like Head of Macular Research Professor Robyn Guymer AM, Head of Clinical Trials Research Associate Professor Lyndell Lim, and Dr Tom Edwards, an expert in the delivery of retinal gene therapies – has been central to bringing many of these trials to Australia.

"Our new centre will provide clinical trial facilities that match the high calibre of the research done by CERA researchers and our industry, hospital and university partners," he says.

Patient experience

The new trial centre will be located on Level 7 of the Royal Victorian Eye and Ear Hospital.

It will include a modern, relaxing patient lounge area – complete with assistance dog station – for trial participants and their carers.

It will also include state-of-the-art new imaging suites, vision lanes, laser and dark rooms, complemented by an eye care telehealth service and a referral network which will enable more people living in rural and regional areas to take part in trials.

Professor Martin says Breakthrough Victoria's support for the new clinical trial centre is an investment in the future of eye health and research.

"It will strengthen Victoria's reputation as an international leader in medical research and fighting blindness."

Professor Martin says the new clinical trial centre will also provide a boost for CERA's lab-based scientists.

"The new centre will provide a direct pathway from the pre-clinical research to clinical trial, making it easier for our discovery scientists to translate their research into treatments that will benefit patients," he says.

"In the past, many Australian inventors and scientists have had to take their work offshore.

"The new centre will ensure that new eye treatments and devices developed here in Australia are trialled here to benefit local patients."

Donor support

Professor Martin says the continued support of donors has been instrumental in CERA's vision for a new clinical trials centre.

"Without donor support of both our discovery and clinical research programs, CERA would not have been able to attract this important investment," he says.

"We look forward to sharing updates, and we are excited by the opportunities to give more people access to innovative, sight-saving treatments."

‘Team Sisters’ success

Three siblings from South Gippsland have achieved their goal of completing the Lions Ride for Sight, while raising over $30,000 for vision research.

The thought of doing a multi-day, 240-kilometre endurance bike ride is unimaginable to many people.

But for sisters Leesa Willmott, Kerry Fitzgerald and Sharon Oates, signing up for the 2023 Lions Ride for Sight was an opportunity to challenge themselves physically and raise funds for a cause close to their heart – saving sight.

Their parents, Pam and Colin Willmott, have advanced age-related macular degeneration (AMD) – an eye disease that causes progressive vision loss.

There is no approved treatment for the ‘dry’ form of AMD that Colin has, which has led to him becoming legally blind. Pam has ‘wet’ AMD and must get regular eye injections to stabilise her vision. Their four daughters are also showing the early signs of AMD.

“It’s great if we can raise some money and they can find a cure for AMD. Not only for us but for our kids too. Feeling a bit of discomfort on a bike and begging lots of people for money is the least we can do,” says Kerry.

In it together

Kerry and Leesa are avid cyclists, but road riding was completely new to Sharon, who hadn’t picked up a bike since childhood. With less than two-and-a-half months to train, she had to quickly learn the ropes.

“For me, it was a crash course in everything to do with riding a bike. And then I had to put in the miles to get the strength to be able to keep going,” says Sharon.

To prepare for the event, the trio would travel to different parts of Gippsland for training rides. They recall a particularly challenging day, where they had to cycle off-road in the pouring rain.

“There were a few ‘Why the hell are we doing this?’ moments. But at the end of

← *Ride for Sight: (from left) Lions' District Governor Dave Culpitt, Ride for Sight Chair Ian de Bruyne, Sharon Oates, Kerry Fitzgerald, CERA Head of Communication and Fundraising Janine Sim-Jones at the cheque handover.*

↓ *Riding together: Sisters Kerry, Leesa and Sharon.*

the day, we're doing it for mum and dad," says Leesa.

She concedes the "killer" training rides did have one surprising upside.

"I think we've spent more time together in the last two months than we have in the last 20 years!"

The 2023 Lions Ride for Sight

This year's event was held April 14-16 and involved 25 cyclists pedalling over 150 kilometres through South Gippsland's picturesque, but notoriously hilly, terrain. Another seven riders completed the Ride for Sight Challenge, cycling a distance of their choice over four weeks.

For Team Sisters, it was a challenging but rewarding experience.

"I was a bit nervous as I had no idea what to expect, but the team that put it on are a great group of people. All the Lions Clubs helped out and it was really well organised," says Leesa.

"At times you questioned yourself and your sanity, but we stuck together and totally enjoyed it."

When the last day of the event was unexpectedly cancelled due to inclement weather, the sisters decided to complete the final leg the following week. They were also joined by seven other event riders.

"We had to do it for the people who had donated – as well as for ourselves," says Sharon.

Riding for research

Team Sisters initially aimed to raise $10,000, but surpassed all expectations, reaching a total of $30,800.

Pam and Colin are long-standing members of the Lions Club, and the whole family lives and works in the South Gippsland area.

"When you've been involved in the community, the community supports you," he says.

This year's Lions Ride for Sight raised a record-breaking $75,000.

Managing Director Professor Keith Martin said the support will have a significant impact on CERA's research.

"A massive thanks to all the riders, donors, organisers who help make the event a success," he says.

"And congratulations to Ride for Sight Chair Ian de Bruyne for receiving the Ian M Stockdale Humanitarian Award – well deserved for his many years of service leading the event."


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Donate on 12 October to see your gift TRIPLED
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