Lions Eye Institute

Research Highlights

The Lions Eye Institute is founded on philanthropy. Our sight-saving work is only made possible thanks to the generosity of our supporters.

German philosopher
Arthur Schopenhauer
1851

At the Lions Eye Institute, research drives everything we do.

Since our establishment in 1983 we've had many successes and breakthroughs, including several world firsts.

As well as our ongoing eye health research, and with philanthropic support, we have recently committed to invest in new research areas such as optometry and ophthalmic big data.

Our history of research success is rich and the future is bright thanks to our many supporters.

I hope you enjoy reading about a selection of our research.

Best wishes,
Professor Bill Morgan Managing Director, Lions Eye Institute

Our translational research framework

Discovery research

Discovery research is scientific research conducted in universities and in the laboratory. Our discovery research is published, which translates to outcomes by us and other research institutes.

Proof of concept

The proof of concept phase of research covers both technical devices and new treatments for eye disease.

Population studies

Population-based studies can identify the causes and impact of eye health and diseases in the community, which can drive future discovery research.

Putting into practice

Adoption of research into clinical practice is led by our clinicians and clinician researchers.

Clinical trials

Clinical trials aim to test medicines and new therapies, and confirm their safety and efficacy. We conduct both pharmaceutical-sponsored and investigator-led clinical trials.

Your vision means everything to us

Our work involves six key areas of translational research.

Glaucoma

Disease: Glaucoma refers to a group of eye diseases where vision is lost due to damage to the optic nerve, causing irreversible vision loss.

Research goal: Our research aims to identify the underlying physiology of glaucoma, work towards better understanding of the eye and develop novel therapies to save sight.

Indigenous and community eye research

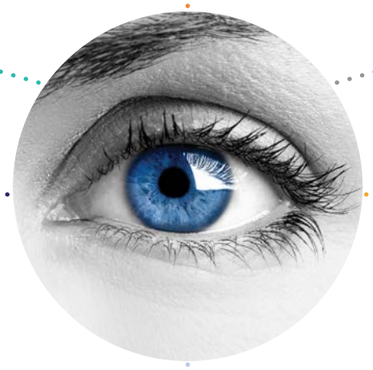
Disease: There is a substantial gap in eye health between rural and remote Western Australians and their urban counterparts. 94% of vision loss is preventable or treatable, yet people living in these areas needlessly experience higher rates of blinding eye disease.

Research goal: We work with Indigenous, remote and rural communities to detect and treat common and insidious, non-reversible diseases such as diabetic retinopathy. Our work extends overseas to places such as Indonesia.

Myopia

Disease: Myopia or short-sightedness causes refractive error and blurred distance vision. It is predicted to affect half the world's population by 2050. High myopia increases the risk of developing cataract, retinal detachment, macular disease and glaucoma.

Research goal: Our myopia research aims to study how environmental factors and genetics interact and contribute to the development of childhood myopia. We are conducting clinical trials to test treatments to slow myopia progression.



Diabetic and vascular retinopathies

Disease: Retinopathies are diseases that damage the retina (the part of the eye that senses light). There are several types of retinopathy, including diabetic retinopathy, a complication of diabetes, and vascular retinopathy, caused by high blood pressure.

Research goal: We are developing new detection and monitoring techniques of early-to-late changes in diabetic and retinal vascular disorders and treatments to improve the quality of life for patients with these conditions.

Genetic eye disease, gene therapies and macular degeneration

Disease: More than 350 eye diseases are attributed to hereditary factors, including retinitis pigmentosa and 15-20% of people with age-related macular degeneration. Inherited retinal diseases are a broad group of genetic eye conditions that cause vision loss and sometimes complete blindness.

Research goal: We aim to reduce blindness caused by conditions of singular genetic eye diseases. To achieve this, we are developing a greater understanding of genetic causes of eye disease, and creating novel treatments and therapies.

Cornea, ocular surface and ocular immunology

Disease: Many eye diseases, including uveitis, keratitis, age-related macular degeneration and diabetic retinopathy, have an immune or inflammatory component. Inflammation can also induce retinal degeneration, impair vision and contribute to the development of autoimmune eye diseases, including Sjogren's syndrome.

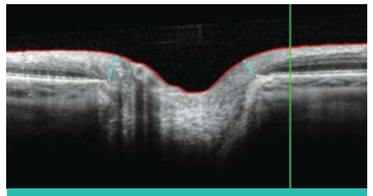
Research goal: We aim to understand how immune responses are regulated in the eye, and the impact of inflammation as a cause of eye disease. These studies will guide the design of new strategies to safeguard vision. Further, we aim to improve corneal transplant outcomes by defining the factors that affect transplant success.

Led by our research teams

Physiology & Pharmacology
Genetics & Epidemiology
Ocular Tissue Engineering
Retinal Genomics & Therapy
Experimental Immunology
Functional Molecular Vision

Discovery research

Discovery research is often where the research journey begins. Without sufficient funding and philanthropic support, discovery research may never commence. At the Lions Eye Institute, we have a wide range of discovery research projects across our different scientific groups. The examples below are a few of our selected highlights.



Glaucoma

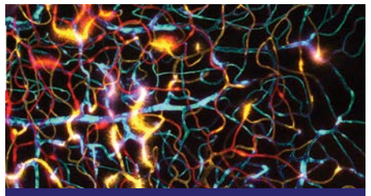
Professor David Mackey AO is leading the **International Glaucoma Genetics Consortium**, which has published the largest ever study on the genes causing glaucoma.

Using information from almost 35,000 glaucoma patients, the work has combined data from research studies around the world to **identify 127 genes associated with the disease**. Of the genes identified, **44 were new discoveries**.

The work allows the development of polygenic risk scores to predict those individuals at higher risk of developing glaucoma.

This opens pathways for developing new treatments for glaucoma as well as improving family screening for early identification of individuals at high risk.

In separate research led by **Professor Dao-Yi Yu AM** and **Dr Geoffrey Chan**, OCT lymphangiography is being used to visualise the normally invisible, clear vessels on the surface of the eye that drain fluid. This work is vital to improving success rates following glaucoma surgery.



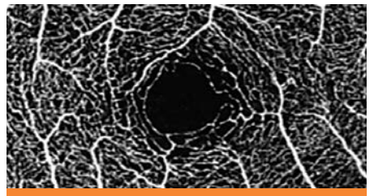
Diabetic and vascular retinopathies

With funding from the Stan Perron Charitable Foundation, the Perth Eye Foundation and the Channel 7 Telethon Trust, **Associate Professor Chandra Balaratnasingam, Professor Dao-Yi Yu AM** and their team are studying the use of **optical coherence tomography angiography (OCTA).**

This non-invasive technique could detect very early-stage retinal microvascular dysfunction in children with type 1 (T1) and type 2 (T2) diabetes.

The study will follow children with T1 and T2 diabetes and a healthy cohort of children, collecting annual data over a period of five years. We are collaborating with researchers at The University of Western Australia and Perth Children's Hospital.

By developing a new way to potentially detect retinal vascular dysfunction prior to the occurrence of sight threatening complications, there is the possibility to address a major gap in the clinical management of diabetic retinopathy.



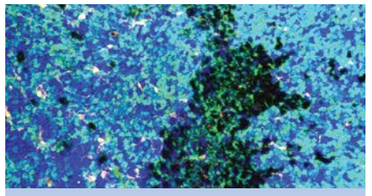
Indigenous and community eye research

From our Broome clinic, **Associate Professor Angus Turner** in partnership with University College of London is conducting an optical coherence tomography angiography (OCTA) study of Indigenous people's eyes. The study uses Lions Outback Vision's existing database of de-identified eye images to study diabetic retinopathy.

The aim of the study is to use **novel imaging techniques to determine whether diabetic retinopathy can be picked up earlier than current standards allow** using traditional colour fundus photography.

OCTA is essentially a high resolution image of the eye that allows important measurements such as blood vessel density to be taken.

If successful, earlier diagnoses could assist Indigenous people to better manage their diabetes at an earlier stage.



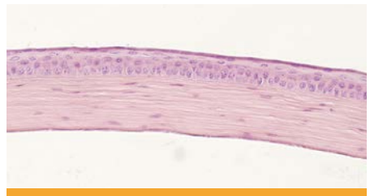
Genetic eye disease, gene therapies and macular degeneration

Dr Livia Carvalho and our Retinal Genomics and Therapy Group is investigating potential **gene-independent therapies for inherited retinal diseases (IRDs)** such as retinitis pigmentosa and achromatopsia (people who see only in black and white).

A recent study in collaboration with researchers from Tübingen University in Germany, has shown for the first time that diseased cone photoreceptors lose epigenetic markers.

Using advanced techniques such as single-cell RNA sequencing, we showed that continuous delivery of a drug (called GSK-J4) into an achromatopsia diseased eye model increases cone cell survival.

This study is the first to suggest that IRD affected cones respond positively to epigenetic drugs. This approach shows the **potential of developing a broad class of novel therapies to slow cone degeneration in IRDs**.



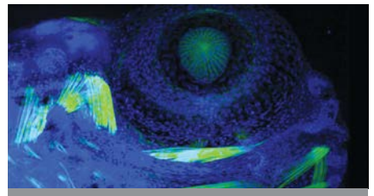
Cornea, ocular surface and ocular immunology

Professor Mariapia Degli-Esposti and our **Experimental Immunology Group** are researching how immune responses are regulated in the eye, and the impact of misguided immune responses and inflammation on eye diseases.

Inflammation is an important response to infection and injury. **When inflammation is sustained over time it can cause damage to tissues and organs, including the eyes**.

Our research team has shown that viral infection can contribute to the development of a common autoimmune disease – **Sjogren's syndrome**. In this disease the immune system attacks the glands that produce secretions including tears and saliva. Patients can suffer overwhelming discomfort, and the syndrome can result in severe damage to the cornea, thus compromising vision.

We have established a **preclinical model that accurately represents human Sjogren's syndrome**. In ongoing studies, we are **examining the cellular mechanisms involved** in the disease with the aim of **identifying pathways that can be targeted therapeutically**.



Myopia

Dr Jessica Mountford is using zebrafish **to study how environmental factors and genetics interact and contribute to the development of childhood myopia**.

Our research combines genome-wide association studies, cutting edge gene editing techniques and a zebrafish model of ocular disease to specifically target the mechanisms behind early-onset myopia.

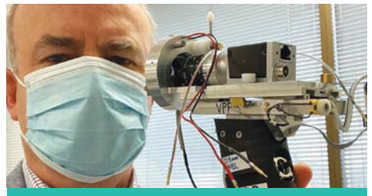
Zebrafish are an important model of ocular disease as they breed prolifically, producing transparent embryos and larvae that encompass large eyes that are comparable in both structure and function to the human eye.

This enables us to observe their development under the microscope from single cell fertilised embryos through to larvae with fully developed eyes, in a matter of days.

The power of philanthropy is accelerating scientific discoveries.

Proof of concept

The proof of concept phase of research is especially exciting, as we begin to see the results of our work. It can take many years to get to this stage, which is why ongoing support is so critical. The proof of concept phase can lead to further translational research such as clinical trials.



Glaucoma

Professor Bill Morgan, Professor Dao-Yi Yu AM and their team are further developing a prototype handheld device called OcuLinx™, which will **change the way cerebrospinal fluid pressure is measured**. The hope is to reduce the need for invasive and risky procedures used currently, such as drilling a hole in the head or inserting a large needle into a person's back (lumbar puncture).

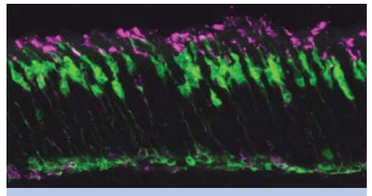
The team's invention will **measure intracranial pressure (ICP) via the eye in a non-invasive way**. The device could be taken into space to measure ICP in astronauts, and there are benefits to a wide range of patients in neurology, neurosurgery and hospital accident and emergency departments.

Indigenous and community eye research

In an exciting research collaboration, Lions Outback Vision in partnership with Google, has **validated deep learning algorithms for detecting diabetic retinopathy in Indigenous people**.

Using Lions Outback Vision's database of de-identified colour fundus photographs of Indigenous peoples' eyes, we tested whether Google's mathematical algorithms and artificial intelligence could detect and determine the severity of diabetic retinopathy in Indigenous people.

We demonstrated the Google algorithm worked better in Aboriginal people than other published artificial intelligence algorithms.



Genetic eye disease, gene therapies and macular degeneration

As part of a four-year long effort, **Dr Livia Carvalho's** team is in the final stages of completing a proof of concept study on the efficacy and safety of a **novel gene replacement therapy for a type of inherited cone-rod dystrophy**.

The results from this study are currently being prepared for publication and show that the gene therapy treatment is capable of restoring expression of the faulty gene and improving visual function in the short and long term.

The next step for this study is to prepare and complete the preclinical safety evaluations. This will enable us to obtain approvals from the appropriate regulatory agencies to start a clinical trial soon.

Cornea, ocular surface and ocular immunology

In collaborative studies, **Professor Mariapia Degli-Esposti** and our Experimental Immunology team have **developed a model of sicca syndrome following bone marrow transplantation**. Sicca syndrome affects many bone marrow transplant patients and significantly reduces their quality of life. The **original preclinical models and innovative organoid systems** we developed have provided a proof of concept about new pathways involved in the disease and have **enabled us to identify novel therapeutic targets**.

Population studies

Population studies can identify the causes and impact in the community of eye health and diseases, which can drive future research. At the Lions Eye Institute, we have a long history of leading the eye health studies of many wider population health studies.

The TARRGET study

We are collaborating with several other health organisations to conduct the Australia-wide TARRGET study (Targeting At-Risk Relatives of Glaucoma cases for Early Treatment), which is **identifying people at high risk of developing glaucoma blindness and facilitating early monitoring and intervention**.

First degree relatives (brothers, sisters, sons and daughters) are at much higher risk of developing glaucoma than the general population.

In Western Australia, we aimed to see if a family screening strategy would help to improve early diagnosis in glaucoma, particularly in regional areas where access to eye services is not as good as in the cities.

Kimberley Aboriginal eye health study

Lions Outback Vision and **Associate Professor Angus Turner** are hoping to set up a **population-based eye study of people in the Kimberley region**, based out of our new Kimberley Eye Hub in Broome, Western Australia.

The study is still in the ethics and planning phase and the hope is to recruit a cohort of patients in the Kimberley region, who will be monitored over time for their eye health. If funding can be secured, we will undertake the largest research project into Aboriginal eye health in the country.

This is an important area of research, as we recently published a systematic review showing that diabetes affects Aboriginal people more than non-Aboriginal people when it comes to eye health.

Major population health studies

Professor David Mackey AO and his research team manage the eye health component of major population studies such as the **Raine Study and the Busselton Healthy Ageing Study**. The Raine Study began in 1989 by recruiting almost 3,000 women at around 18 weeks of pregnancy.

It then followed these children from birth and is one of the world's largest and most successful studies of the **influences of genetics, pregnancy, childhood and adolescence on subsequent health and developmental outcomes**.

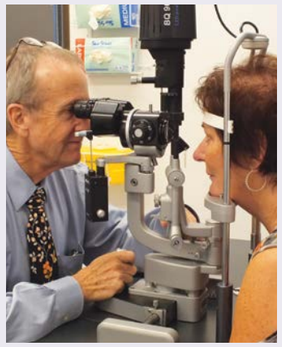
The Busselton Healthy Ageing Study began in the 1960s and explores why some people can remain healthy and active throughout their senior years, while others suffer ongoing illness.

Myopia

Excessive near activity (e.g. screens and education), lack of outdoor activity and reduced exposure to sunlight are potentially associated with myopia. **Professor David Mackey AO's** and **Dr Samantha Lee's** research is investigating how factors such as **sun exposure interacts with genetic markers to predict myopia** in the Kidskin, Raine, Busselton, WA Twins and Eye Protection studies.

Dr Jessica Mountford and **Dr Antony Clark** are also working towards screening Western Australian children to help determine which genes are associated with the development of early-onset myopia using Genome Wide Association Studies (GWAS). This work will aid our understanding of which genes contribute to the progression of myopia in childhood.

Diabetic and vascular retinopathies



Professor Ian McAllister has developed **a laser treatment that creates an alternative channel for blood to drain** when the main vein draining blood from the back of the eye has become blocked (**central retinal vein occlusion**). His research team's **central retinal bypass study** has shown that patients who receive a **combination of his laser treatment and eye injections of anti-VEGF agents have better vision that is maintained with time** compared to the placebo group. They also required fewer injections than patients who received injections only.

The research has been extended to include a larger cohort, including patients who have not done so well on the injection treatment only. **This extension study** is ongoing.

Glaucoma

As one of four sites in Australia, we are participating in a **glaucoma and ocular hypertension study** that aims to test a **new oral tablet treatment that may reduce intraocular pressure**.

Myopia studies

We are conducting extensive research into childhood myopia (short-sightedness), which includes a clinical trial to test whether **low dose atropine drops can slow myopia progression**.

The Western Australian **ATOM Study (Atropine for the Treatment of Myopia)** being run by **Dr Samantha Lee**, is the first study of its kind in Australia, and has recently published the first paper on low concentration atropine drops to prevent myopia in children of European ancestry.

Clinical trials

You play a significant role in helping us bring research to the clinical trial stage.

Our Clinical Trials Centre is one of the largest ophthalmological clinical trial research centres in the world, managing over 30 trials per year.

Most of our clinical trials are sponsored by the pharmaceutical industry. We also conduct trials that are developed and led by our ophthalmologists. This provides benefits for our patients, who receive access to the newest and most advanced treatments available, often before they are available to the public.

In addition to the trials we manage, we also collaborate with other research teams on non-ophthalmic clinical trials. This work includes investigations for diseases such as cancer, cystic fibrosis and other chronic illnesses, which require monitoring and treatment for potential ophthalmic side effects.

Genetic eye disease, gene therapies and macular degeneration

With a rich history in participating in landmark clinical trials for **age-related macular degeneration (AMD) and diabetic macular oedema (DMO)**, we have supported the translation of experimental therapies into clinical practice. In particular, we have managed clinical trials for the current gold-standard anti-VEGF treatments such as lucentis, bevacizumab, aflibercept and soon to be available vabysmo. This most recent medication has the potential to extend out treatment times for wet AMD beyond the traditional four-weekly injections, which could be a major step forward in improving the quality of life of our patients.

We also completed recruitment and follow-up visits for the Exonate Trial, which investigated a new eye drop solution for the treatment of DMO. The study will now undergo analysis and publication of results.

Genetic eye disease, gene therapies and macular degeneration

The **Belite study** is a clinical trial being led by **Associate Professor Fred Chen**, which researches the safety and effectiveness of a medication to **assist adolescents who have Stargardt disease**.

Stargardt disease is an inherited retinal disease that causes progressive central vision loss in early childhood and young adults. There is currently no cure for Stargardt disease and until recently no treatments have been tested in Australia.

This disease causes loss of sight due to the build-up of a substance called lipofuscin in the eye. **A new drug called tinlarebant is designed to prevent the build-up of lipofuscin** in order to slow down disease progression. **The trial is at phase 1-2 stage and is evaluating safety, tolerability and dosage.**

Indigenous and community eye research

In a world first all-Indigenous clinical trial, **Associate Professor Hessom Razavi** and his research team recently published results from **the OASIS study into diabetic macular oedema (DMO)**. DMO is caused by swelling (oedema) of the central part of the retina (the macula) and causes blurring of central vision.

DMO is managed with medications known as anti-VEGF agents, which are injected into the eye. However, these are relatively short-acting, requiring appointments with an ophthalmologist as often as every month. Longer acting medications do exist, such as a dexamethasone implant (a steroid) also injected into the eye, which only need to be dosed every three months.

Our OASIS study tested the longer acting dexamethasone implant compared with shorter acting injections of an anti-VEGF agent. The **results showed a 15% visual advantage** for patients who received the dexamethasone implant. **In the participants who lived in remote locations**, the benefits of the implant were even more pronounced, with a **37% advantage** over the anti-VEGF agent.

It is often impractical for Indigenous people to have frequent eye injections due to geographical, cultural and other barriers. **Dexamethasone's success in the trial can be attributed to its less frequent, hence more practical dosing regimen.**

Diabetic and vascular retinopathies

Macular telangiectasia (MacTel) is an uncommon disease that affects the macula, causing gradual deterioration of central vision. To further understand this disease, a worldwide registry was established in 2005 to collect data from people with this eye disorder. With **Professor Ian Constable AO's** leadership, we have enrolled 131 participants onto the registry.

We have spent seven years trialling an **experimental implant** with 20 participants from the Lions Eye Institute.

Results of the trials are positive so far and may soon lead to the first ever treatment becoming available for this rare condition.

Putting into practice

Adoption of research into clinical practice is led by our clinicians and clinician researchers. Since 1983, there have been many inventions, discoveries and innovative achievements that have made their way into clinical practice.

Glaucoma

The Lions Eye Institute's Physiology and Pharmacology Group has been responsible for one of the most significant translational research programs in the history of the Institute. The group, led by **Professor Dao-Yi Yu AM**, spent 20 years researching and developing a new surgical device to treat glaucoma.

The **XEN® Gel Stent** is a **biocompatible microfistula implant that reduces intraocular pressure** in the eye, which is the biggest risk factor for glaucoma. The XEN® Gel Stent has been **implanted in about 100,000 patients around the world** and is a far less invasive treatment for glaucoma compared with traditional surgery.

Indigenous and community eye research

Lions Outback Vision is currently collaborating with the Centre for Eye Research Australia in Melbourne (CERA) and Eyetelligence to see how well an **automatic retinal camera works in Indigenous people**. The aim is to test the camera in the real world and with Indigenous patients before putting it into clinical practice.

The new camera is approximately the size of a shoebox and has inbuilt artificial intelligence to detect diabetic retinopathy. The camera is **more portable, more affordable and easier to operate** (no operator training is required) than existing equipment options. This makes it potentially very useful to deploy to remote settings where there is little access to diabetic retinopathy screening or trained operators.

Lions Outback Vision **is trialling the prototype camera at Derbarl Yerrigan in Maddington**, with the aim of improving the camera before it gets deployed remotely. Separate trials in non-Indigenous communities are being conducted by Eyetelligence in Victoria.

Greatest inventions and innovative achievements

Made possible by philanthropic support.

Glaucoma

Invented the **XEN® Gel Stent** which has been successfully implanted in more than **100,000** patients globally.

Prototype development for non-invasive **intracranial pressure** measurement, which will provide a benefit to hospital accident and emergency departments, and to astronauts in space.

Houses the facility for a national **DNA bank** – Australia's only biobank that stores DNA from patients and their family members with a genetic eye disease.

Home to one of the largest **glaucoma biobanks** in the world, with over 5,000 DNA samples and clinical material from familial and sporadic cases of glaucoma, supporting research into the genetics of glaucoma.

Age-related macular degeneration

Developed **Adenoviral vector 101** gene therapy with Adverum Biotechnologies for the treatment of wet age-related macular degeneration. Listed on the New York Stock Exchange and currently in trials.

Developed the **central retinal vein occlusion bypass laser surgery** procedure. A treatment improving vision for sufferers of nonischemic central retinal vein occlusion.

Invented the **Barrett Universal II Formula**, considered to be one of the most accurate intraocular lens power calculation formulas. It is globally recognised and used to improve the refractive accuracy outcomes of cataract surgery.

Cornea

The Lions Eye Bank is the only facility in Western Australia that coordinates the collection, processing and distribution of **donor eye tissue** for transplantation. More than 5,500 corneal transplants have been completed since the Lions Eye Bank started in 1986.

Developed **immune therapy** to manage treatment of cytomegalovirus (CMV) in transplant patients. This breakthrough provides a new strategy to control CMV reactivation and has the potential to reduce rates of sickness and death among organ and bone marrow transplant recipients.

Excimer laser surgical system to correct refractive errors of the eye such as myopia, with successful international sales of machines up to 2010.

Cornea

Developed the **first artificial cornea**, the AlphaCor, and successfully implanted it into patients in the US, Australia and India.

Glaucoma

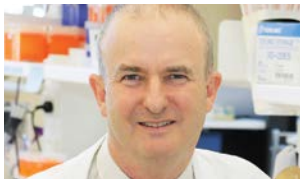
Invented the **Virna Glaucoma Drainage Device**, a low cost device now being manufactured and used in Indonesia with over 1,000 implanted. This device is the only one approved by the Indonesian Ministry of Health and is sold at cost price (AUD$100, one tenth the common commercial charge) for affordable, effective treatment of glaucoma.

You can help accelerate scientific discoveries

With your support, our world-leading researchers can continue their work to advance treatments for blinding eye disease.

Professor Ian Constable AO

Founder of the Lions Eye Institute and leader in ophthalmic care in Western Australia. Led clinical trials to discover gene therapy to treat wet age-related macular degeneration and the artificial cornea.



Professor William Morgan

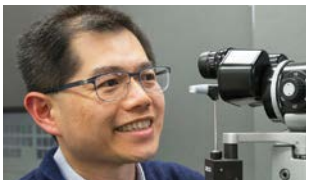
Co-invented the original XEN® Gel Stent and Virna Glaucoma Drainage Device, ICP prototype and space agency work.

Professor Dao-Yi Yu AM

Co-invented the XEN® Gel Stent that revolutionised the treatment of glaucoma, CRVO bypass, ICP prototype and tonometer.

Professor David Mackey AO

Received the largest National Health and Medical Research Council government grant for eye research in Australia.



Associate Professor Fred Chen

Leading development of cures for genetic eye disease, in particular retinitis pigmentosa, and significant clinical trials.

Professor Ian McAllister

Pioneered the central retinal vein occlusion bypass laser surgery procedure.

Professor Mariapia Degli-Esposti

Received the Eureka Prize in Scientific Research 2019 for discoveries in the field of immune therapy.

Associate Professor Chandra Balaratnasingam

Specialises in retinal vascular research, with a focus on diabetic retinopathy.

Professor Graham Barrett AM

Leading cataract surgeon and intraocular lens design, calculation and assessment pioneer.

Associate Professor Angus Turner

Expert in Indigenous eye health delivery using a variety of medical access models.

Dr Livia Carvalho

Head of the Lions Eye Institute's Retinal Genomics and Therapy Group.

Dr Jessica Mountford

Specialises in world-leading research into myopia in children.

Our other leading researchers include:
Dr Geoffrey Chan, **Dr Antony Clark**, **Associate Professor Hessom Razavi** and **Dr Evan Wong**.

Front cover image shows a cornea infected with the herpes virus. Diagnosis is based on the characteristics of the dendritic ulcer or sometimes through a culture. Treatment involves topical applications or systemic antiviral drugs. (Image by Chris Barry)

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