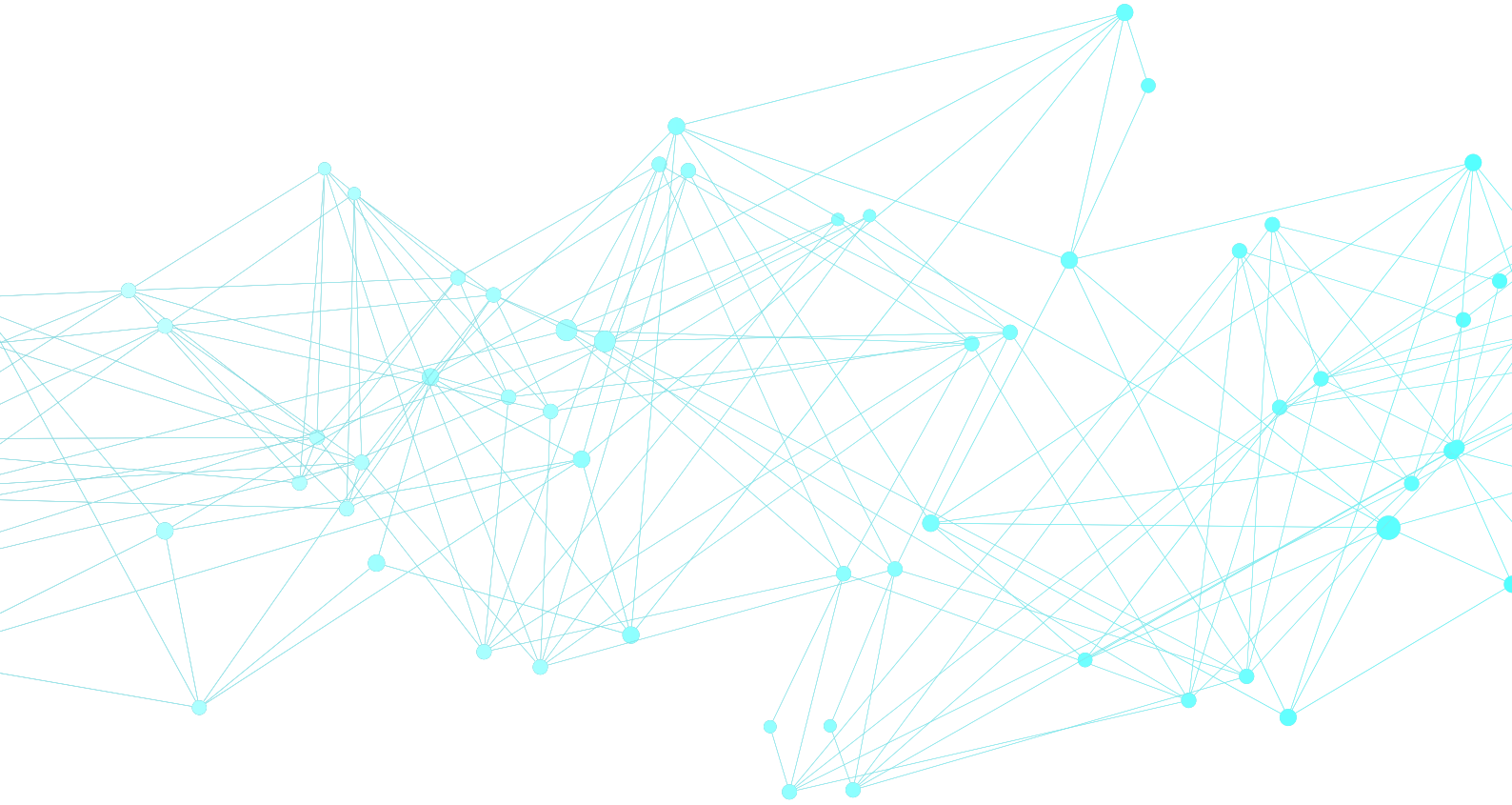
The Ophthalmic Research Institute of Australia **Annual Report 2019-2020**

ORIA

Contents



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ABN: 37008393146

ORIA

ADVANCING EYE RESEARCH

Chair's Report

In 2020, a year like no other due to the COVID pandemic, I am pleased to update you on the achievements of the Ophthalmic Research Institute of Australia (ORIA). The ORIA has continued to support eye research and people with eye disease. We have funded valuable research and promoted eye research within our field and to the larger medical community and wider public.

Australian research supported by the ORIA has placed RANZCO members on the international map. The *ORIA Research Funding and Impact 2019* report highlighted the increase in Australian ophthalmology peer-reviewed research publications with ORIA funding. In 2019, the ORIA had a funding leverage of 36 times, with successful projects resulting in citations in high-ranked publications and the media, and, importantly, enabling improvements in patient care.

In 2020, a total of $596,825 funded 12 ophthalmic research projects with most able to continue their work despite COVID. In 2019, the ORIA grants supported a wide range of research including artificial intelligence, dengue virus infection, endothelial dystrophy, switchable gene therapy, and UV damage to the corneal epithelium. I was impressed with the outcomes of these projects, detailed in this report, with translation already occurring into clinical trials, publications, collaborative care with GPs and data to develop novel therapies.

Donations from the RANZCO NSW branch, Perth Eye Foundation and the Australian and New Zealand Eye Foundation were gratefully received this year. The RANZCO NSW Branch grants supported ophthalmic research in NSW that would otherwise not have been able to be supported—a great initiative from the NSW branch. The Eileen Hansen Trust, the Richard and Ina Humbley Foundation, the Anselmi estate, Ivy May Stephenson, the estate of the late Gladys Clare Renesson and the estate of the late Mary H Tilden have also provided support, and the generosity and support of such donors is critical to ophthalmic research. The standard of ophthalmic research in Australia is high and each year there are many more grant applicants than we can fund. In 2020, COVID-19 has impacted ORIA's finances.

Please contact the ORIA if you would like your practice, surgery or society to benefit from supporting the ORIA by emailing **oria@oria.org.au.**

In May we employed a new CEO, Diane Harapin, who was formally the CEO of the breast surgeons' society, BreastSurgANZ. Diane comes to us highly experienced, skilled and very passionate about the health sector and improving patient outcomes. One of Diane's key focuses has been to improve ORIA's communication to members. A Twitter, Instagram, Facebook, and LinkedIn presence has been established using @oria_au and @oria.au. to promote the work of our members and those working in our sector.

We have also been undertaking a governance and compliance review and update. We are thrilled to report that ORIA is recognised under the Australian Charities and Not-for-profits Commission (ACNC) as a Health Promotion Charity (HPC). This charity subtype befits our work, as we are an 'institution whose principal activity is to promote the prevention or control of diseases in human beings'. As a compliant HPC we have tax deductibility (DGR) for all donations and publish all our reports online; they can be accessed on the ACNC's website.

ORIA provided feedback to the development of RANZCO's 2021-2023 strategic plan. ORIA highlighted that research is highly valued by patients, the profession, and the public. Patients treated in research-active healthcare settings have better outcomes and receive better care. Research provides evidence so that better decisions on how to treat patients, how to educate the profession, and how to develop policy to influence stakeholders can be made. In Australia, research has key benefits for patients, the ophthalmic profession and the public. For example, in the recent MBS Reviews for Ophthalmology and Optometry, findings presented by ORIA members from Australian research informed policy makers. It is widely acknowledged that research-informed policy assists decision-making that can have a direct effect on a nation's health and economic prosperity.

Our association with Sydney Long, a great Australian artist, has raised our public profile, The Art Gallery of New South Wales acknowledged the ORIA for the use of *Midday* (1896, oil on canvas) in its *Fieldwork* touring exhibition.

The ORIA could not continue our work without you—our membership—and we are grateful for your support. I, personally, would like to thank all of our past and present donors, without whom none of ORIA's important work would be possible. Thank you also to the Research Committee Chair Prof Alex Hewitt, Secretary A/Prof Samantha Fraser Bell, Treasurer Clin. A/ Prof Paul Healey, the ORIA Board, the ORIA Research Advisory Committee, our volunteer reviewers, the RANZCO staff and all ORIA members for their hard work and continued support over this past year. In addition, thank you to Diane, our new CEO.

Stephanie Watson
Chair, ORIA

Thank You!

ORIA would like to thank the external referees who kindly gave advice that helped with the allocation of the 2019/20 grants. Their work is invaluable.

Ang, Marcus
Bedggood, Phillip
Brandli, Alice
Broadhead, Geoff
Brown, Karl
Bui, Bang
Bykhovskaya, Yelena
Caffery, Liam
Chan, Elsie
Chen, Fred
Chidlow, Glyn
Chilov, Michael
Chinnery, Holly
Chu, Colin
Clark, Antony
Comyn, Oliver
Coote, Michael
Cornish, Elisa
Dawes, Lucy
De Baere, Elfride
Dean, Simon
Deva, Narme
Downie, Laura
Eamegdool, Steven
Elder, James
Essex, Rohan
Fagan, Xavier
Fan Gaskin, Jennifer
Fletcher, Erica
Fox, Todd
Gatzioufas, Zisis
Gillies, Mark
Gonzalez, Anai
Gore, Daniel
Green, Matthew
Grigg, John
Guest, Stephen
Guggenheim, Jeremy
Hadoux, Xavier
Hardcastle, Alison
Harkin, Damien
Harvey, Alan
Hassall, Mark
Holekamp, Nancy M.
Huckfeldt, Rachel
Hui, Alex
Jamieson, Robyn
Kerr, Nathan
Khong, Jwu Jin
Kong, George
Lee, Ming
Li, Jingming
Lidgerwood, Grace
Liew, Gerald
Liskova, Petra
Liu, Guei-sheung (Rick)
Ljubimov, Alexander
Mack, Heather
Mackarenkov, Elena
Madigan, Michele
Magno, Aaron
Mandal, Nawajes
McGuinness, Myra
McLenachan, Samuel
Mehta, Hemal
Mohr, Susanne
Mora, Justin
Niederer, Rachel
O'Connor, Michael
O'Day, Justin
Oliver, Verity
Osborne, Neville
Paul, Joseph
Peet, Daniel
Rahman, Anmar
Rutar, Matthew
Samalia, Priya
Sharma, Shiwani
Sheck, Leo
Shen, Weiyong
Sheng, Hong
Shu, Daisy
Siggs, Owen
Simunovic, Matthew
Stevenson, Clark
Symes, Richard
Tan, Zachary
Teo, Kelvin
Turner, Angus
Vavvas, Demetrios
Verhoeven, Virginie
Vincent, Ajoy
White, Andrew
Wickremasinghe, Sanjewa
Williams, Peter
Willoughby, Colin
Wong, Raymond
Wood, John
You, Yuyi
Young, Jennifer
Zaytsev, Kirrill
Zhang, Jie

ORIA would like to offer a special thank you to our generous donors, without whose support we would not have been able to fund such amazing research projects over the year.

Eileen Hansen Trust	$128,020.01
Perth Eye Hospital Foundation	$50,000.00
ANZEF	$50,000.00
RANZCO NSW Branch	$100,000.00
Humbley Foundation	$39,177.29
Total	**$367,197.30**

Grants Awarded 2019 for 2020

Name of Investigator	Title of Grant	Title of Project	Amount
Dr Elsa Chan	ORIA Grant	A new drug to control scarring after glaucoma surgery	$49,377.00
Dr Fred Chen	Australian and New Zealand Society of Retinal Specialists (ANZSRS) Grant	Optimizing a pipeline for developing treatment for CRB1-related inherited retinal diseases	$50,000.00
Dr Glyn Chidlow	R and L Lowe Bequest Grant	A novel calpain antagonist for ischemic retinal vein occlusion	$49,446.00
Dr Nitin Chitranshi	ORIA Grant	Developing a gene therapy for glaucoma	$49,440.00
Prof Jamie Craig	Perth Eye Foundation Grant	Machine learning approaches to predicting glaucoma conversion and progression using OCT retinal imaging in the PROGRESSA study	$49,061.00
Dr Thomas Edwards	Hardie-Anselmi Grant	Pre-clinical validation of gene therapy for Bietti crystalline dystrophy	$49,679.00
Prof Mark Gillies	Richard and Ina Humbley Grant	Target the Notch signalling pathway to prevent retinal fibrosis	$50,000.00
Dr Sandy Hung	ORIA Grant	Engineering molecular tools to correct Leber's Hereditary Optic Neuropathy mutations in the mitochondria	$50,000.00
Prof Robyn Jamieson	RANZCO NSW Branch Grant	Steps to therapy in early-onset retinal dystrophies	$50,000.00
Mr Mohd Khairul Nizam Mohd Khalid	Ivy May Stephenson Grant	Engineering a synthetic microbial treatment for gyrate atrophy	$50,000.00
Prof Chris Layton	ORIA Grant	Development and characterisation of a novel adeno-associated viral vector for targeted therapy of metastatic Uveal Melanoma	$49,997.00
A/Prof Michele Madigan	ORIA Grant	Choroidal Melanocytes and Melanocortins: Much More than Melanin	$49,825.00
Total for 2019-2020			**$596,825.00**

Progress Reports on 2018/19 Grants

Hardie-Anselmi Grant

Title: Cone Rescue in Retinitis Pigmentosa by Photobiomodulation

Investigator: Prof Robert J. Casson

Co-investigator: Dr Glyn Chidlow

Aim: We used a novel slit lamp-delivered retinal laser to treat rd1 mice with 670 nm light. Cones were counted using immunohistochemical methods.

Key Results: We demonstrated a remarkable protective effect on cone survival.

Conclusion: PBM laser was safe and rescued cones from degeneration in a mouse model of RP.

Clinical Translation: These results enabled our team to rapidly translate this ORIA-funded research to a Phase I clinical trial at the Royal Adelaide Hospital Ophthalmology Department. We showed that treatment with PBM in patients with RP was safe and produced an average recovery of 5 letters of visual acuity. A manuscript reporting these findings is in preparation and the findings strongly motivate further clinical research of the PBM laser as a novel therapy in RP.

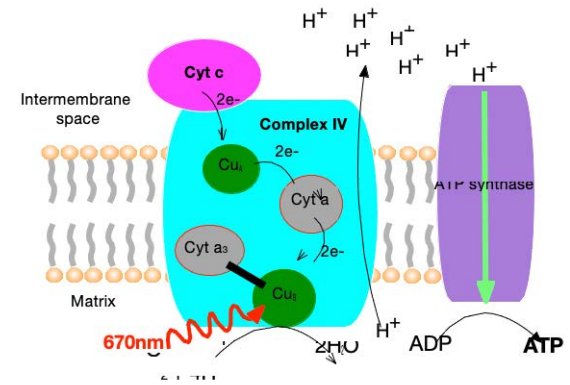


Fig. 1. PBM at 670 nm photoexcites the CuB component of Complex IV, enhancing the reduction of O_2 and increasing ATP.

Esme Anderson Grant

Title: Antisense oligomer mediated modulation of CNOT3 for the treatment of retinitis pigmentosa 11

Investigator: Dr Fred K. Chen

Co-investigator: Prof Sue Fletcher

Aim: This project aimed to develop antisense oligonucleotide (AON) drugs for the treatment of an inherited retinal disease known as retinitis pigmentosa 11 (RP11) and to screen these drugs in laboratory grown retinal cells generated from patients' skin cells.

Methods: RP11 is caused by mutations in the PRPF31 gene that ultimately lead to reduced levels of PRPF31 protein production. AONs were designed to reduce a natural repressor of the PRPF31 gene called CNOT3. Skin cells derived from RP11 patients were cultured in the laboratory and reprogrammed to produce retinal cells for drug screening.

Key Results: AON sequences suitable for inducing knockdown of CNOT3 expression were identified. Retinal cells derived from RP11 patients displayed reduced expression of PRPF31.

Retinal pigment epithelial cells derived from an RP11 patient displayed reduced microvilli density. Treatment of RP11 patient retinal cells with AONs reduced CNOT3 and increased PRPF31 protein level in the treated cells.

Conclusion: We successfully identified the AON drug capable of decreasing CNOT3 in retinal cells derived from RP11 patients. The preliminary results from our pre-clinical drug screening trial indicate this drug can increase PRPF31 gene expression and protein production and it may represent a novel treatment for RP11.

Implications for Clinical Practice/Science and Future Research: Our preclinical studies now include 26 patients from 8 families with RP11 caused by mutations in the PRPF31 gene. This project has attracted support from our commercial partner, PYC Therapeutics, allowing the continuation of our AON screening program in patient-derived retinal cells and animal models with a view to obtaining approval for future progression into clinical trials. A patent for the AONs generated in this project has been filed.

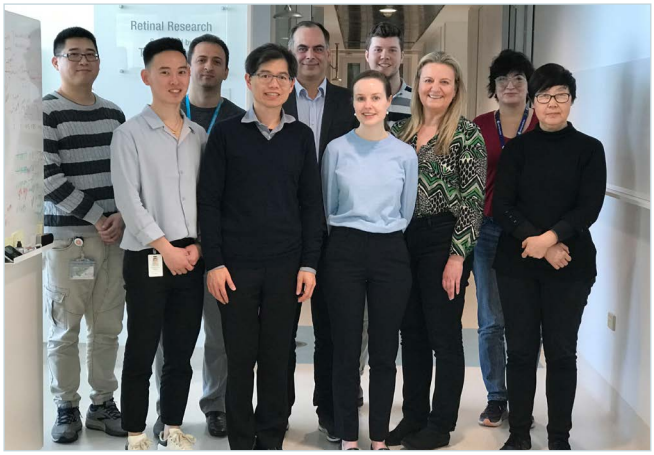
Publications or conference abstracts arising from this work:

Published Articles:

1. Generation of two induced pluripotent stem cell lines from a patient with dominant PRPF31 mutation and a related non-penetrant carrier. McLenachan S, Zhang D, Zhang X, Chen SC, Lamey T, Thompson JA, McLaren T, De Roach JN, Fletcher S, Chen FK. Stem Cell Research 2019 10;34:101357.
2. Roshandel D, Thompson JA, Charng J, Zhang D, Chelva E, Arunachalam S, Attia MS, Lamey TM, McLaren TL, De Roach JN, Mackey DA, Wilton SD, Fletcher S, McLenachan S, Chen FK. Exploring microperimetry and autofluorescence endpoints for monitoring disease progression in PRPF31-associated retinopathy. Ophthalmic Genetics. 2020 Sep 27:1-14.

Poster Presentations:

1. Characterization of the c.1205C>A PRPF31 variant in patient derived fibroblasts and retinal organoids. Dan Zhang, Samuel McLenachan, Xiao Zhang, Shang-Chih Chen, Jen Thompson, Terri McLaren, Tina Lamey, John De Roach, Fred K Chen. Science on the Swan Conference, Perth, Western Australia, Jun 2019
2. Functional Disruption of a Disease Modifier Gene Using Antisense Oligomers: A Potential Molecular Therapy for PRPF31-associated Retinitis Pigmentosa 11. Janya Grainok, Ianthe L Pitout, Steve D Wilton, May T. Aung-Htut, Chalermchai Mitrpant, Kim Rice, Fred K Chen, Sam McLenachan, Dan Zhang, Laura Florez and Sue Fletcher. Oligonucleotide Therapeutics Society Conference, Munich, Oct 2019.



(Left to right) Shang-Chih Chen, Sang Yoon Moon, Danial Roshandel, Fred Chen, Sam McLenachan, Rachael Heath Jeffery, Luke Jennings, Janice Amaranti, Amanda Scurry, Dana Zhang

ORIA Grant

Title: Descemetorhexis for guttata predominant Fuchs' Endothelial Dystrophy: A prospective, interventional case series. Project code: 18/1378H

Investigator: A/Prof Elaine Chong

Co-investigators: Dr Elsie Chan, Dr Gregory Moloney

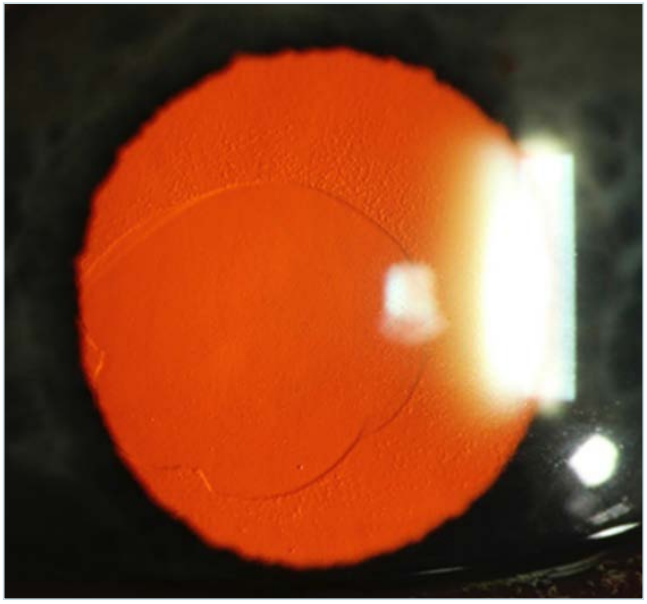
Aim: We investigate a new treatment for treating Fuchs' Endothelial Dystrophy (FED) where unhealthy endothelial cells are removed and the patient's cornea is encouraged to heal on its own, without corneal transplantation.

Methods: We remove a small 4mm area of Descemet's membrane along with its diseased endothelial cells, without implanting a corneal transplant. This procedure is known as 'Descemetorhexis Without Endothelial Keratoplasty (DWEK)' or 'Descemet's stripping only (DSO)'. Rho-kinase inhibitor eye drops are used as rescue therapy in certain cases.

Key results: We have recruited 6 cases, with 5 DWEK procedures performed. Surgery was deferred due to the lockdown for 1 patient and all patients referred for screening appointments were put on hold due to prolonged Victorian COVID-19 lockdown since March 2020. Our study started mid 2019, the delay was due to recruitment of a research assistant and we will recommence the study once COVID-19 restrictions are lifted. Of the 5 patients who had DWEK, 4 patients had improved vision without requiring a cornea transplant, and 1 patient required a transplant, with good outcome.

Conclusion: DWEK had an 80% success rate with an improvement in visual acuity in all patients.

Implications for Clinical Practice/Science and Future Research: DWEK is a potential intermediary step in the treatment of FED, before offering corneal transplantation. Refinement in its technique and further prospective studies are required to establish a clear role in the management of FED, with and without concurrent use of rho-kinase inhibitors.



A/Prof Elaine Chong

New Investigator Grant

Title: Examining the therapeutic potential of microRNAs to regulate inflammasome activation in retinal degenerations

Investigator: Dr Nilisha Fernando

Co-investigators: Prof Si Ming Man, A/Prof Rohan Essex, Prof Jan Provis

Supervisor: Dr Riccardo Natoli

Aim: We investigated the role that microRNA-223 (miR-223) plays in maintaining homeostasis and regulating inflammation in the normal and degenerating retina.

Methods: miR-223-null mice were investigated in normal and photo-oxidative damage conditions. Encapsulated miR-223 mimics were locally and systemically injected into wild type mice, following which functional and molecular analyses were performed.

Key results: In normal conditions, miR-223-null mice had a lower retinal function compared to wild type controls, associated with a loss of photoreceptors. Both local and systemic delivery of miR-223 mimics improved retinal function in mice undergoing retinal degeneration. In retinal damage, miR-223 was elevated in the retina, circulating serum and in retinal extracellular vesicles. Conversely, retinal immune cells (microglia and macrophages) displayed a downregulation of miR-223. Further, in miR-223-null mice, the immune profile of circulating immune cells was altered to a pro-inflammatory state.

Conclusion: miR-223 is required for maintaining normal retinal function, as well as regulating inflammation in degenerative conditions. Further investigations are required to determine the targets of miR-223 and their key biological pathways and interactions that are relevant to retinal diseases.

Dr Nilisha Fernando

Implications for Clinical Practice/Science and Future Research: MicroRNAs are small non-coding RNA regulatory molecules with a high abundance in the central nervous system and a promising therapeutic potential for neuroinflammatory diseases. In this study, we identified that local and systemic delivery of miR-223 improved retinal function in degeneration. Future studies should further assess the therapeutic potential of miR-223 mimics and investigate whether sustained delivery of miR-223 into the retina (both locally and systemically) is sufficient to protect the photoreceptors from progressive degeneration.

Publications:

1. Fernando, N, Wong, JHC, Das, S, Dietrich, C, Aggio-Bruce, R, Cioanca, AV, Wooff, Y, Chu-Tan, J., Schumann, U, Ngo, C, Essex, RW, Dorian, C, Robertson, SA, Man, SM, Provis, J, Natoli, R. MicroRNA-223 regulates retinal function and inflammation in the healthy and degenerating retina. Front. Cell Dev. Biol. 8, 516, doi:10.3389/fcell.2020.00516 (2020)
2. Wooff, Y, Fernando, N, Wong, JHC, Dietrich, C, Aggio-Bruce, R, Chu-Tan, JA, Robertson, AAB, Doyle, SL, Man, SM, Natoli, R Caspase-1-dependent inflammasomes mediate photoreceptor cell death in photo-oxidative damage-induced retinal degeneration. Sci. Rep. 10, 2263, doi:10.1038/s41598-020-58849-z (2020)

Ivy May Stephenson Grant

Title: Endogenous Rexinoid and Retinoid X receptors as Neuroprotective molecules in Glaucoma

Investigator: Dr Vivek Gupta

Co-investigators: Prof Stuart Graham, Dr Mehdi Mirzaei

Aim: The aim of this study is to determine the role of Retinoid X receptors (RXR) in the retina in normal healthy conditions and in glaucoma.

Methods: Adeno associated virus (AAV) constructs encoding RXR genes were administered intravitreally into the mice. Mice were subjected to experimental glaucoma conditions using microbead injections to understand the effects of RXR modulation in both healthy and glaucoma conditions.

Key Results: Immunostaining of retinal sections and immunoblotting analysis revealed that RXR α, β and γ isotypes are well expressed in the retina. RXR expression was assessed in human glaucoma tissues as well as in two different models of experimental glaucoma. RXR agonist treatment is neuroprotective for the retina in experimental glaucoma conditions.

Conclusion: RXRs are well expressed in the retina and RXR biochemical network is negatively affected in glaucoma, in both human retina as well as in mouse models of glaucoma. Our results utilising two different mouse models of glaucoma highlight that pharmacological modulation of RXRs using specific agonists is protective for the retinal ganglion cells (RGCs) and the optic nerve. These animals show remarkable protection against retinal functional, structural and biochemical deficits induced by experimental glaucoma.

Dr Vivek Gupta

Implications for Clinical Practice/Science and Future Research: The initial results are very promising. The experiments will need to be carried out using a larger sample size. Future studies will identify whether pharmacological targeting of RXR is protective only if the treatment is started before the injury or if it also protects the retinal cells once the glaucoma injury has initiated. Future studies will also identify any potential side effects associated with modulating RXRs.

New Investigator Grant

Title: AAV gene therapy for ganglion cell neuroprotection in glaucoma

Investigator: Dr Mark Hassall

Co-supervisors: Dr Glyn Chidlow, Dr Jaime Craig

Aim: Demonstrate that *Neuroglobin* gene therapy protects retinal nerve cells in a rat model of glaucoma eye disease.

Methods: Rat eyes were injected with a modified, safe, virus that delivered the *Neuroglobin* gene to the retinal nerve cells normally damaged in glaucoma. Laser was applied to the rat eyes to create a model of high-pressure glaucoma and then the number of surviving retinal cells was counted after 10 days.

Key results: In rats with laser-induced glaucoma, the eyes treated with *Neuroglobin* gene therapy had more surviving retinal ganglion cells (1813±158 cells/field) than untreated eyes (1417±202 cells/field; P=0.046; N=19 rats).

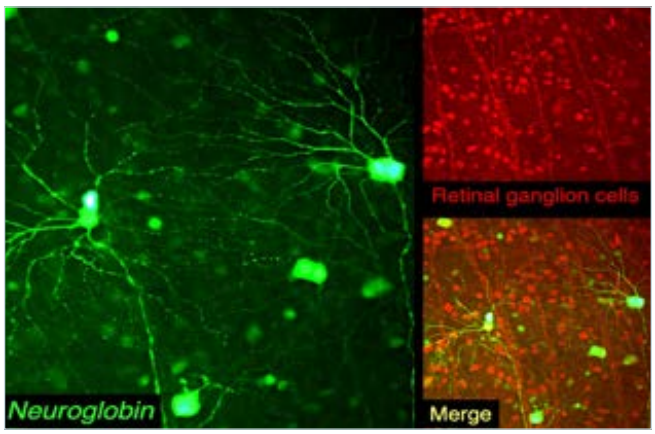
Conclusion: *Neuroglobin* gene therapy is a promising method of nerve cell protection in glaucoma.

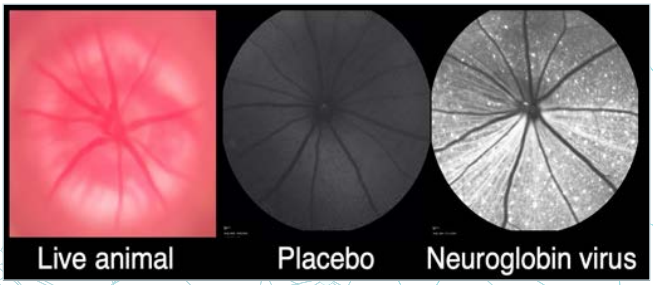
Implications: Some glaucoma patients continue to lose vision despite medication drops, laser and successful surgery to lower the pressure in their eye. Our gene therapy results show that retinal cells can also be protected by the *Neuroglobin* gene. The next step is to repeat our positive results in a different small animal model of glaucoma, then undertake a primate study.

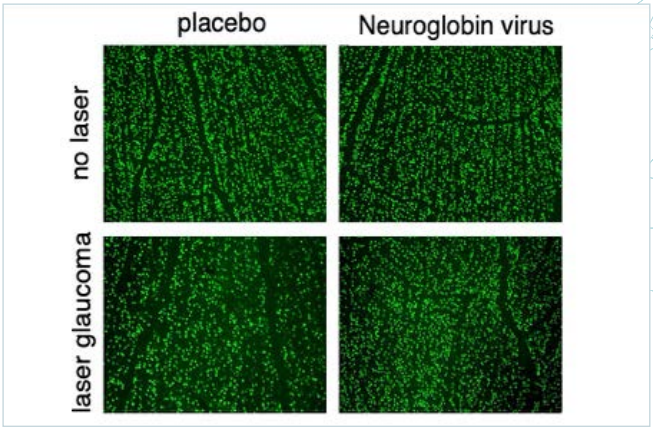
Dr Mark Hassall

Publications and presentations arising from this work:

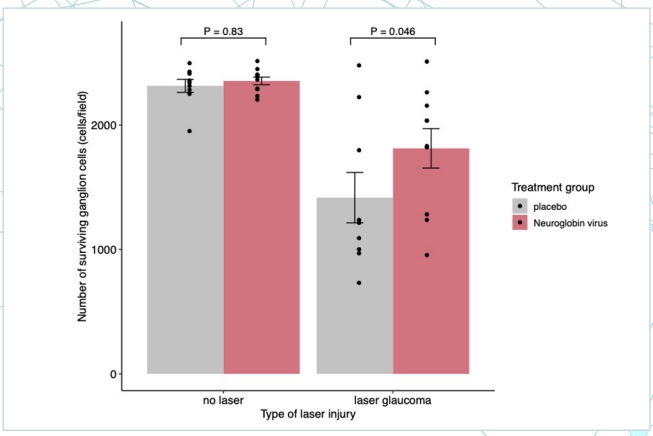
1. [*Invited presentation*]. Gene Therapy for glaucoma. Asia-Pacific Academy of Ophthalmologists annual congress, Bangkok, 2019.
2. Hassall MM, Liu R, Mammone T, Wood J, Casson R, Hewitt A, Craig J, Chidlow G. Pronase E improves rAAV transduction of retinal ganglion cells. In: Supplement of the 51st Annual Scientific Conference of the Royal Australian and New Zealand College of Ophthalmologists, 2019 Nov 8-12; Sydney, Australia. Abstract nr 101.
3. Hassall MM, Chidlow G, Liu G-S, Wood J, Hewitt AW, Casson R, Craig JE. Neuroglobin gene therapy for retinal ganglion cell neuroprotection in a rodent model of glaucoma. Australian and New Zealand Glaucoma Society annual meeting 2020, Adelaide, SA
4. Neuroglobin gene therapy for retinal ganglion cell neuroprotection in a rodent model of glaucoma. Ophthalmology grand round, Central Adelaide Local Health Network, SA







Brn3a-stained RGC cell counts on retinal flat mounts



Neuroglobin virus shows RGC neuroprotection

R and L Lowe Bequest Grant

Title: Investigating the role of a novel locus associated with the development of Giant Cell Arteritis

Investigator: Prof Alex Hewitt

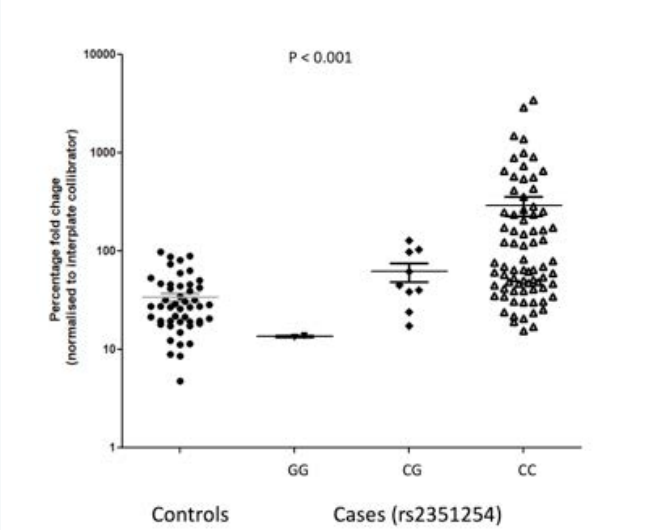
Co-investigators: Dr Elisabeth De Smit, Dr Sandy Hung, Dr Kristof Wing

Aim: The aim of this research was to directly interrogate a novel locus on chromosome 15, which was found to be associated with Giant Cell Arteritis.

Methods: We performed a CRISPR/Cas activation screen tiling across the chromosome 15q26 locus, to identify cis-acting variants that influence expression of neighbouring genes in large vessel smooth muscle cells, as well as CD4+ T cells and macrophages in an in vitro co-culture model.

Key Results: A tiling CRISPR/Cas activation library across chromosome 15q26 identified key sites of increased *MFGE8* and *HAPLN3* expression in immortalised aortic smooth muscle cells. CRISPR/Cas-mediated activation for *MFGE8* peaked close to the transcriptional start site; however, for *HAPLN3* a clear signal near position 89,580,049 on chromosome 15 was uncovered. Quantitative PCR in temporal artery samples from people with or without histological features of GCA revealed increased expression of *HAPLN3* ($p<0.001$) but not *MFGE8*, and a clear stepwise variation in expression for each allele was observed for SNP rs2351254. No firm evidence of increased expression in T cells or macrophages was found.

Conclusion: Our results implicate HAPLN3 as the likely causative gene at this novel locus association with Giant Cell Arteritis.



Implications for Clinical Practice/Science and Future Research: This work has provided substantial functional information, implicating variation in expression of a novel gene as being associated with increased risk for developing Giant Cell Arteritis. Therapeutic options for this blinding disease are currently limited, and this research has helped uncover a new therapeutic target for this blinding disease. Ongoing work investigating compounds which specifically target HAPLN3, and directly modulate expression in target inflammatory or arterial wall cells is required.

Publications and presentations arising from this work: Results were presented in part at the 2019 RANZCO Annual Scientific Meeting.

New Investigator Grant Report

Title: Development of intelligent portable fundus camera as a unique solution for opportunistic screening of eye diseases at general practice settings.

Investigator: Dr Stuart Keel

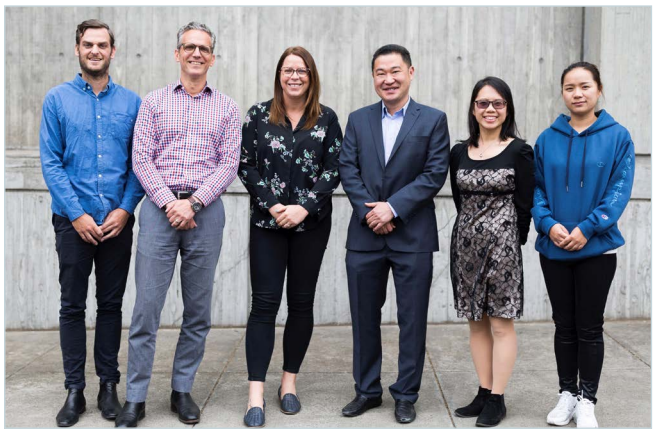
Supervisor: Prof Mingguang He

Aim: To integrate the AI system with a portable fundus camera to build an opportunistic screening service for primary care settings.

Methods: Clinical accuracy, end-user acceptability, and feasibility of the portable, AI-based automated screening system were assessed at general practice and indigenous health care clinics.

Key Results: Remidio non-mydratic Fundus On Phone was chosen as the handheld camera. Data were collected in 30 indigenous patients and 508 patients for the clinical assessment on DR and glaucoma classification. Qualitative research on patient acceptability and satisfaction, clinician satisfaction and technical feasibility in the field target clinics was completed. Clinical accuracy analysis is on-going. Qualitative research suggests that this handheld fundus camera +AI system is easy-to-use for the clinicians, but lack of dedicated staff in the clinic is the major barrier for implementing such a model in a primary care setting.

Conclusion: Integration of the AI system and a portable fundus camera is simple to operate, reliable, and efficient in primary care settings.



(Left to right) Dr Stuart Keel, Dr Andreas Mueller, Dr Jane Scheetz, Prof Mingguang He, Dr Liying Li, Dr Guobei Xiao

Implications for Clinical Practice/Science and Future Research: The intelligent portable fundus camera allows GPs to perform opportunistic screening for diabetic retinopathy and other eye diseases that would significantly improve accessibility to eye care. A fully-automated self-testing and operator-free system would further improve the feasibility and impact of this solution.

Australia New Zealand Society of Retinal Specialists (ANZSRS) Grant

Title: Switchable Gene Therapy for Controlled Intervention in Neovascular Blindness

Investigator:
A/Prof Guei-Sheung Liu

Co-investigators:
A/Prof Bang V. Bui,
Dr Vickie HY Wong

Chief Investigator A/Prof Guei-Sheung Liu

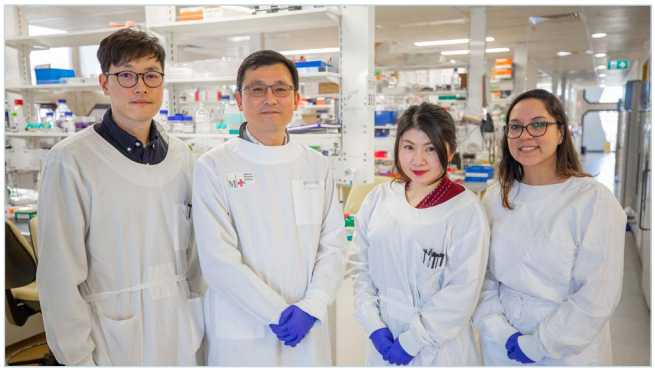
Aim: Excessive growth of leaky blood vessels in the eye causes loss of vision. Our project aims to validate a new strategy for blocking VEGF (a protein which stimulates new leaky vessel growth in the eye), with the advantage that it is long-lasting and can be switched on only when needed.

Methods: We have developed a new approach of gene therapy that blocks VEGF by a fusion gene, consisting of a VEGF-targeting decoy receptor and a protein-switchable system. A clinically-proven viral vector was used to deliver the VEGF-targeting gene to the back of the eye through a single injection, and the amount of the expressed therapeutic protein was controlled by the administration of a simple antibiotic drug.

Key Results: Our study demonstrated that gene delivery of drug-tunable VEGF-targeting decoy receptor and subsequent administration of antibiotic drug allows controlled disruption of VEGF signalling. We also showed that this approach resulted in a tailored suppression of new leaky vessel growth in the eye in a rat model of retinopathy.

Conclusion: Our proof-of-principle study has provided evidence that drug-tunable strategy enables anti-VEGF gene therapy with the capacity for sustained, temporal flexibility while minimising potential adverse side effects associated with constitutive VEGF inhibition and frequent eye injections.

Implications for Clinical Practice/Science and Future Research: Our comprehensive strategy can avoid the need for multiple injections and has the potential for greater and more sustained efficacy without the potential risks associated with long-term systemic suppression of VEGF or angiogenesis.

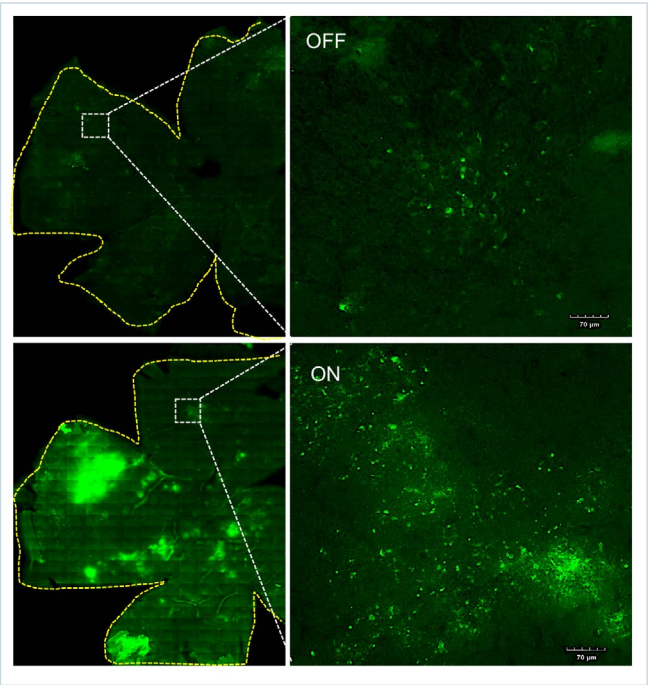


Liu Lab scientists (left to right) Dr Fan-Li Lin, A/Prof Guei-Sheung Liu, Dr Yu-Fan Chuang, and Ms Jessika H Garcia at the Menzies Institute for Medical Research

Publications or conference abstracts arising from this work:

1. Chen J et al. A drug-tunable Flt23k gene therapy for controlled intervention in retinal neovascularization. Angiogenesis. 2020 Sep 15. doi: 10.1007/s10456-020-09745-7.
2. Lin FL et al. Gene therapy intervention in neovascular eye disease: a recent update. Mol Ther. 2020, S1525-0016(20)30341-5.
3. Wang JH et al. Updates on gene therapy for diabetic retinopathy. Curr Diab Rep. 2020, 20(7):22.

Funding made possible due to this ORIA grant:
2020 NHMRC Idea Grant (GNT1185600)



Representative images of retinal flat-mounts showing drug-tunable strategy enabled to tailor protein expression (green) in the rat eye

Richard and Ina Humbley Grant

Title: Dengue Virus Infection of Human Retinal Pigment Epithelial Cells

Investigator: Prof Justine R. Smith

Co-investigator: Dr Genevieve Oliver

Dengue virus infection is a tropical disease that has a broad clinical spectrum and may be life-threatening. The disease—commonly termed 'dengue'—is increasing in incidence worldwide, and in Australia. Recent clinical reports have highlighted the potential for inflammatory eye disease in individuals infected with dengue virus (DENV). The most serious threat to vision is dengue retinopathy, which commonly presents as maculopathy, including macular oedema and foveolitis. Clinical observations implicate the retinal pigment epithelium in the maculopathy.

Methods: Our team initiated the first laboratory research of the mechanisms of dengue retinopathy. In this project, we explored the interactions between human retinal pigment epithelial cells and DENV. For real-world relevance, we used a special collection of viruses isolated in Singapore from patients with dengue. The collection included DENV strains that were circulating during an outbreak which was associated with dengue retinopathy, and DENV strains that were circulating during an outbreak in which dengue retinopathy was not reported.

We have successfully propagated 6 different DENV strains from Singapore outbreaks in our laboratory. To be able to directly compare the activity of different strains in retinal pigment epithelial cells, we developed a PCR-based assay using primers for the DENV envelope protein that had base mismatches across all 6 strains and were consistently efficient for detecting any strain.

We conducted comprehensive testing of the ability of the 6 DENV strains to infect human retinal pigment epithelial cells, working with both the ARPE-19 retinal pigment epithelial cell line, and multiple primary retinal pigment epithelial cell isolates cultured from human eyes. We performed infectivity assays, with quantification of viral load in infected cells by real-time PCR, and by fluorescent immunolabelling. We also evaluated the retinal pigment epithelial cell molecular response to infection, focusing on the anti- viral type 1 interferon response. In addition, we made comparisons with human retinal endothelial cells, which also may play a role in dengue retinopathy.

Results: Our experiments showed that the different DENV strains from Singapore outbreaks replicated much more readily in human retinal pigment epithelial cells in comparison to human retinal endothelial cells. We observed a marked difference in infectivity of DENV strains isolated during the dengue outbreak that resulted in retinopathy versus strains isolated during the outbreak that did not result in eye disease, with the former producing considerably higher viral loads in cells. This higher infectivity

Mr Liam Ashander and Dr Yuefang Ma

Prof Justine Smith and Dr Amanda Lumsden

Prof Justine Smith and Dr Genevieve Oliver (grantees) with A/Prof Jillian Carr (collaborating virologist)

was associated with a stronger molecular response when cells were infected with strains isolated during the outbreak associated with retinopathy, including induction of interferon- stimulated genes. Comparison of infections in retinal pigment epithelial cell isolates cultured from different human eye donors showed some variation between donors, although infections and responses were consistent overall.

Conclusion: Our research has yielded important resources and interesting results that address the mechanisms of dengue retinopathy. The team is presently preparing a manuscript for peer-review that presents the results of the investigation. Related work with the DENV strains from Singapore has become part of Dr Oliver's PhD studies on neglected retinal infections. Future studies will focus on molecular differences between DENV strains that may account for the differential infectivity of human retinal cells.

ORIA Grant

Title: Ultraviolet light and the cornea: Understanding what can go wrong

Investigator: Prof Stephanie Watson

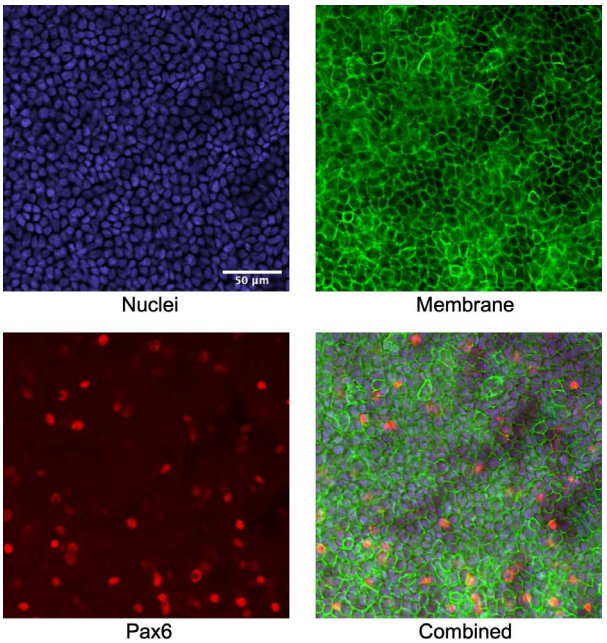
Co-investigator: A/Prof Guy Lyons

This study investigated the cellular mechanisms of ultraviolet radiation (UVR) damage to the cornea. UVR from sunlight causes common eye disorders, such as pterygium, and serious conditions including ocular surface squamous neoplasia and stem cell damage, but how this happens on a cellular level is poorly understood. Our team of multidisciplinary experts used world-first tools and techniques with the aim of finding answers to prevent and repair UV damage to the eye, saving sight.

Aim: To understand how ultraviolet radiation (UVR) damages cells in the cornea.

Methods: We exposed mouse eyes to a single low dose of UVR, similar to what a person's eyes would receive when outside for 20 minutes on a sunny summer day in Sydney. We analysed the effects of the UVR on the outermost cells of the cornea, by culturing them in flasks to determine how many times they can undergo cell division, and using a microscope to determine how quickly the cells are shed from the cornea.

Key Results: The corneal cells grew poorly in culture, which we overcame by analysing cell divisions in whole tissues by microscopy. This showed that UVR causes an increase in cell division that lasts at least 2 weeks. This is compensated for by an increase in the amount of cells being shed, so that the total number of cells is kept constant, at least in the short term.



Prof Stephanie Watson

Conclusion: Exposure to UVR increases the turnover of cells in the cornea by increasing the number gained through cell division and increasing the number lost through cell shedding.

Implications for Clinical Practice/Science and Future Research: If the increase in turnover of corneal cells occurs for a sustained time, due to chronic exposure to UVR from sunlight, the stem cells that supply the cells of the cornea might age prematurely, becoming 'exhausted' and unable to maintain the cornea properly. This could result in conditions such as keratoconus, which is known to be more prevalent where sunlight is strongest.

Publications or conference abstracts arising from this work:

1. NC Delic, S Watson, N Di Girolamo, GM Halliday, JG Lyons, 'Ultraviolet radiation as an initiator of keratoconus', European Society for Photobiology and International Union for Photobiology World Congress, Barcelona, 25-30 August 2019
2. JG Lyons, 'Acute epithelial cell dynamic response to low dose UV radiation', European Society for Photobiology and International Union for Photobiology World Congress, Barcelona, 25-30 August 2019
3. NC Delic, GM Halliday, S Watson, N Di Girolamo, JG Lyons, 'Grace under pressure: maintaining the balance between proliferation and delamination in a stratified epithelium', Gordon Research Conference on Epithelial Differentiation and Keratinization, Newry, ME, USA, 7-12 July 2019.
4. JG Lyons, NC Delic, N Di Girolamo, S Watson, GM Halliday, 'Chronic exposure to ambient levels of UV radiation causes keratoconus-like symptoms in mice', Gordon Conference on Cornea and Ocular Surface Biology and Pathology, Il Ciocco, Italy, 14-25 February 2020

RANZCO NSW Branch Grant

Title: Optic nerve damage in neuromyolitis optica spectrum disorder (NMOSD) and multiple sclerosis (MS)

Investigator: Dr Yuyi You

Co-investigators: A/Prof Alexander Klistorner, Prof Con Yiannikas

Aim: This study aims to investigate different mechanisms of optic nerve damage in neuromyolitis optica spectrum disorder (NMOSD) and multiple sclerosis (MS).

Methods: We performed OCT scans, MRI and visual electrophysiological recordings in NMOSD and MS patients. We also collected blood samples from patients for biochemical analysis.

Key results: In this study, we found Müller cell dysfunction in the retina in NMOSD patients which indicated the disease to be an astrocytopathy (You et al. Ophthalmology 2019). We also performed blood sample analysis and found that brain-derived neurotrophic factor (BDNF) polymorphisms were associated with more severe optic nerve damage in NMOSD (Shen et al. Front Neurosci 2019) and MS (unpublished data), suggesting a new role of BDNF in neuroinflammatory pathways.

Conclusion: While optic neuritis is frequently seen in both NMOSD and MS patients, the two diseases represent distinct pathological mechanisms.

Implications for Clinical Practice/Science and Future Research: Understanding the mechanisms of the two diseases is important for clinical differential diagnosis of optic neuritis and for development of new treatments.

Dr Yuyi You

Publications or conference abstracts arising from this work:

1. You et al. (2019). Evidence of Müller glial dysfunction in patients with AQP4-IgG-positive neuromyelitis optica spectrum disorder. Ophthalmology; 126:801-810
2. Shen T, Gupta VK, Yiannikas C, Klistorner A, Graham SL, You Y. (2019) Association between BDNF Val66Met polymorphism and optic neuritis damage in neuromyelitis optica spectrum disorder. Front Neurosci; 13:1236

ORIA People

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Prof Stephanie Watson and Prof David Mackey

* RANZCO appointee

Financial Statements

In accordance with a resolution of the directors, the directors submit herewith the financial statements of The Ophthalmic Research Institute of Australia for the year ended on 30 June 2020 and report as follows:

1. Meetings of Directors

During the financial year three meetings of directors were held. Attendances were:

Board Members	Number Eligible to Attend	Number Attended
Prof Stephanie Watson, NSW – Chair	3	3
Prof Mark Gillies, NSW – Vice Chair	3	1
Prof Richard Mills, SA – Honorary Secretary	3	3
A/Prof Paul Healey, NSW – Honorary Treasurer	3	3
Dr Jennifer Fan Gaskin, VIC	3	3
A/Prof Clare Fraser, NSW	3	3
A/Prof Sam Fraser Bell, NSW	3	3
Prof Stuart Graham, NSW	3	3
A/Prof Alex Hewitt, TAS	3	3
Dr George Kong, VIC	3	2
Prof David Mackey, WA	3	3
Prof Peter J McCluskey, NSW	3	2
Dr John Males, NSW	3	2
Dr Chameen Samarawickrama, NSW	3	2
A/Prof Andrea Vincent, New Zealand	3	3
A/Prof Peter van Wijngaarden, VIC	3	3

2. Indemnifying Officer or Auditor

The company has not during or since the financial year in respect of any person who is or has been an officer or auditor of the company or a related body corporate indemnified or made any relevant agreement for indemnifying against a liability incurred as an officer including costs and expenses in successfully defending legal proceedings or paid or agreed to pay a premium in respect of a contract of insurance against a liability incurred as an officer for the costs or expenses to defend legal proceedings.

3. Principal Activities

The principal activity of the company in the course of the financial period was to provide funds for ophthalmic research. There has been no significant change in the nature of this activity during that period.

4. Operating Results

(1) Operating Revenue

Revenue is mainly derived from investing in shares and interest bearing securities.

	2019/20	2018/19
	$	$
Net dividend, interest and trust distribution income	547,929	709,988
Less Expenses	76,030	75,185
	471,899	**634,083**

(2) Operating Surplus

The surplus of the company before other comprehensive income for the year ended 30 June 2020 was $806,896 (2019: $788,679). This amount is comprised of the following:

	2019/20	2018/19
	$	$
Trust Fund	739,096	790,719
Administration	67,800	(2,040)
	806,896	**788,679**

Other comprehensive income before grants and Director of Research allocation amounted to a loss of $1,099,402 (2019: loss of $24,921) and included a loss on rearrangement of investments of $131,137 (2019: gain of $48,447) and valuation loss on available-for-sale financial assets of $968,265 (2019: loss of $73,368).

5. Review of Operations

The surplus for the year was $806,896 compared to $788,679 in 2019. The administrative operations of the institute for the year resulted in a profit of $67,800 compared with a deficit of $2,040 in 2019.

6. Dividends

The company's Articles of Association preclude the payment of dividends to any of its members.

7. State of Affairs

There has been no significant change in the state of affairs of the company occurring during the year.

8. Impact of COVID-19

The pandemic has resulted in a reduction in investment income and the carrying value of investments assets this year.

9. Events Subsequent to the end of the Reporting Period

Other than the ongoing, currently unknown effect of COVID-19, there have been no matters or circumstances arisen since the end of the financial year which significantly affected or may significantly affect the operations of the company, the results of those operations, or the state of affairs of the company in future financial years.

10. Likely Developments

At the date of this report, there are no known unusual developments that will affect the results of the company's operations in subsequent financial years.

11. Share Options

No share options were issued during the year.

12. Directors' Benefits

With the exception of the grant made or allocated to Professor Mark Gillies, no director of the company has since the end of the previous financial year received or become entitled to receive a benefit not disclosed in the accounts as directors' emoluments by reason of a contract made by the company or a related corporation with the directors, or with a firm in which he or she has a substantial financial interest.

Statement of Financial Position

For The Year Ended 30 June 2020

	Note	2019/20	2018/19
		$	$
Current Assets			
Cash and Cash Equivalents	3	2,482,450	1,425,028
Receivables	4	196,460	402,723
Investments	5	9,900,007	11,631,587
		12,578,917	**13,459,339**
Non-Current Assets			
Plant & Equipment	6	835	1,312
Total Assets		**12,579,752**	**13,460,651**
Current Liabilities			
Payables	7	893,956	679,151
Provisions	8	-	-
Total Liabilities		893,956	679,151
Net Assets		11,685,796	12,781,500
Equity			
General Fund	13 (a)	-	-
Capital Funds			
Research Fund	9	2,588,305	2,546,181
Settled Funds	10	472,556	472,556
Financial Assets Reserve	11	67,694	1,035,960
Capitalised Profit on Re-arrangement of Investments, Capital Distributions & Transfers	12	7,313,599	7,444,740
		10,442,154	11,499,437
Retained Income- Available for grants	13 (b)	1,243,642	1,282,062
Total Equity		**11,685,796**	**12,781,500**

The accompanying Notes form part of these financial statements.

Trust Fund Statement of Comprehensive Income

For The Year Ended 30 June 2020

	Note	2019/20	2018/19
		$	$
Income			
Dividends received from:			
Other Corporations		454,062	555,966
Adjustment for imputation credits		-	-
Total Dividends		**454,062**	**555,966**
Interest received from:			
Other Entities		17,390	47,272
Trust distributions received from:			
Other Entities		76,477	106,750
The Richard and Ina Humbley Foundation		39,177	30,190
Donations		228,020	50,000
Other Income from Escala		-	71,492
		815,126	861,670
Legacies - Anselmi Estate		-	-
Ivy May Stephenson			
Renensson Bequest			
The Estate of The Late Mary H Tilden			
Sundry Income			4,235
Total Income for the Year		**815,126**	**865,904**
Expenses			
Commission Paid		76,030	75,185
		76,030	75,185
Surplus For The Year		**739,096**	**790,719**
Other Comprehensive Income			
Valuation Gains/(Losses) on available-for-sale financial assets		(968,265)	(73,368)
Profit/(Loss) on Re-arrangement of Investments		(131,137)	48,446
Total other comprehensive income		(1,099,402)	(24,921)
Surplus for the year before allocation		(360,306)	765,798
Grants Allocated/made during the year	14	591,930	553,839
Allocation to Director of Research - Victoria	15	126,000	189,000
		717,930	742,839
Total Comprehensive Income/(Loss)		**(1,078,238)**	**22,958**
Profit/(Loss) Attributable to Members of the Entity		21,164	47,880
Total Other Comprehensive Income/(Loss) Attributable to Members of the Entity		(1,099,402)	(24,921)

The accompanying Notes form part of these financial statements.

Statement of Changes in Equity

For The Year Ended 30 June 2020

	GENERAL FUND			CAPITAL FUNDS			TOTAL
	Accumulated Surplus/Deficit	Research Fund	Settled Funds	Realised Profits on Re-arrangement of Investments & Capital Distributions & Transfers	Financial Assets Reserve	Retained Income	
	$	$	$	$	$	$	$
Balance at 1 July 2018	**-**	**2,503,890**	**472,556**	**7,396,293**	**1,109,328**	**832,522**	**12,314,589**
Profit / (Loss) for Year	(2,040)	-	-	-	-	47,880	45,840
Total Other Comprehensive Income	-	-	-	48,447	(73,368)	-	(24,921)
Capitalised Bequests	-	-	-	-	-	-	-
Transfer from Capital	-	-	-	-	-	-	-
Transfers to/(from) Reserves	2,040	42,429	-	-	-	401,522	445,991
Balance at 30 June 2019	**-**	**2,546,180**	**472,556**	**7,444,740**	**1,035,960**	**1,281,924**	**12,781,499**
Balance at 1 July 2019	**-**	**2,546,180**	**472,556**	**7,444,740**	**1,035,960**	**1,281,924**	**12,781,499**
Profit / (Loss) for Year	67,800	-	-	-	-	21,164	88,964
Total Other Comprehensive Income	-	-	-	(131,137)	(968,265)	-	(1,099,402)
Capitalised Bequests	-	-	-	-	-	-	-
Transfer from Capital	-	-	-	-	-	-	-
Transfers to/(from) Reserves	(67,800)	41,984	-	-	-	(59,449)	(85,265)
Balance at 30 June 2020	**-**	**2,588,303**	**472,556**	**7,313,603**	**67,694**	**1,243,639**	**11,685,796**

The accompanying Notes form part of these financial statements.

Administration Statement of Comprehensive Income

For The Year Ended 30 June 2020

	Note	2019/20	2018/19
		$	$
Income			
Membership Subscriptions		187,980	154,206
Interest		540	
Total Income		**188,521**	**154,206**
Expenses			
Accountancy Fees		7,900	-
Sundry Expenses		10,902	9,074
Auditors' Remuneration	16	8,000	6,000
Admin Expenses		81,639	120,000
Bank Charges		120	120
Consulting Fees		-	-
Depreciation		477	845
General Expenses		-	99
IT & Webpage Expenses		-	3,150
Insurance		1,855	1,770
Printing & Stationery		-	-
Staff Salaries		-	-
Legal Fees		-	-
Admin expenses – reimbursement to RANZCO		-	-
Superannuation Contribution		1,014	-
Salary and Wages		8,814	-
Provision Employee Benefits		-	-
Meeting and Travelling Expenses		-	15,189
Total Expenses		**120,721**	**156,579**
Surplus/(Deficit) For The Year	13(a)	**67,800**	**(2,040)**
Other Comprehensive Income		**-**	**-**
Total Comprehensive Income		**67,800**	**(2,040)**

The accompanying Notes form part of these financial statements.

Statement of Cash Flows

For The Year Ended 30 June 2020

	Note	2019/20	2018/19
		$	$
Cash Flows From Operating Activities			
Receipts			
Dividends Received		334,431	397,320
Interest Received		17,931	47,272
Trust Distributions		76,477	93,858
Legacies		-	-
Other Revenue		631,322	75,727
RANZCO - Reimbursement of membership fees		187,980	321,296
Payments			
Commissions		(76,030)	(75,185)
Research Grants Paid		(551,185)	(612,869)
Payments to Director of Research - Victoria		-	-
Other		(110,416)	(158,366)
Net Cash (Used in)/Provided by Operating Activities	17	**510,510**	**89,053**
Cash Flows From Investing Activities			
Proceeds from Re-arrangement of Investments		7,055,139	1,173,364
Payments for Property, Plant & Equipment		-	-
Payments for Investments		(6,508,227)	(1,055,370)
Net Cash Used in Investing Activities		546,912	117,996
Net(Decrease)/Increase in Cash and Cash Equivalents		1,057,422	207,049
Cash and Cash Equivalents at 1 July 2019		1,425,028	1,217,979
Cash and cash equivalents at 30 June 2020	3	**2,482,450**	**1,425,028**

The accompanying Notes form part of these financial statements.

Notes to the Financial Statements

1. Statement Of Accounting Policies

The financial statements are for the Ophthalmic Research Institute of Australia, incorporated and domiciled in Australia. The Ophthalmic Research Institute of Australia is a company limited by guarantee.

(A) BASIS OF PREPARATION

The financial statements are general purpose financial statements that have been prepared in accordance with Australian Accounting Standards (including Australian Accounting Interpretations) and the Australian Charities and Not-for-profits Commission Act 2012.

The accounting policies set out below have been consistently applied to all years presented, unless otherwise stated. The financial report has been prepared on an accruals basis and is based on historical costs and does not take into account changing money values or, except where stated, current valuations of non-current assets. Cost is based on the fair values of the consideration given in exchange for assets.

The following is a summary of the significant accounting policies adopted by the company in the preparation of the financial report.

(B) INCOME TAX

The company is an approved research institute and is exempt from income tax.

(C) TRANSFERS TO CAPITAL FUNDS

(i) Capital profits and losses on disposal of investments & capital distributions.

Realised capital profits and losses on disposal of investments are brought to account in the trust fund as profit/ (loss) on rearrangement of investments, however, these amounts are transferred to capital funds and do not form part of retained income available for grants.

Capital Distributions and special dividends together with associated imputation credits recognised in the statement of comprehensive income are also transferred to the capital fund and do not form part of retained income available for grants.

(ii) General Research Capital Fund

Ten percent of the net surplus of the General Fund including imputation credits are transferred to the General Research Capital Fund this financial year.

(iii) Allocation of Income to Each Fund

During the year ended 30 June 1993, the investments of the company were separated into the D.W. Research Fund and the General Fund in the ratio of 72% and 28% respectively. As the flow of investment and donation income to and from the two funds does not occur in the same proportion, the ratio of the D.W. Research Fund and the General Fund is no longer at 72% and 28%.

Income from the General Fund which comprises of all funds except the D.W. Research Fund, is allocated as follows:

Research Fund	10.0%
Esme Anderson	51.4%
G.J.Williams	8.9%
B. Mitchell	8.9%
Dame Ida Mann	12.5%
R. & L. Lowe Research	8.3%

If and when further donations are received by specific fund(s) the allocation of future income will be distributed to each fund in accordance with its revised proportion to the General Fund.

Fifty percent of the income derived from the D.W. Research Fund and its investments is allocated to the Director of Research Victoria.

(D) CASH AND CASH EQUIVALENTS

For the purpose of the statement of cash flows, cash and cash equivalents include cash on hand and at call deposits with banks.

(E) INVESTMENTS

Investments are carried at fair value. Changes in fair value will be held in an equity reserve until the asset is disposed, at which time the changes in fair value will be brought to account through the statement of comprehensive income.

(F) REVENUE

Interest and dividends are recognised when received.

Grants, donations and distributions income are recognised when received.

(G) GOODS AND SERVICES TAX (GST)

All revenue, expenses and assets are recognised net of the amount of goods and services tax (GST), except where the amount of GST incurred is not recoverable from the Australian Tax Office. In these circumstances the GST is recognised as part of the cost of acquisition of the asset or as part of an item of the expense.

Receivables and payables in the statement of financial position are shown inclusive of GST.

(H) FINANCIAL INSTRUMENTS

Recognition and Initial Measurement

Investments and other financial assets are initially measured at fair value. Transaction costs are included as part of the initial measurement, except for financial assets at fair value through profit or loss. Such assets are subsequently measured at either amortised cost or fair value depending on their classification. Classification is determined based on both the business model within which such assets are held and the contractual cash flow characteristics of the financial asset unless an accounting mismatch is being avoided.

Financial assets are derecognised when the rights to receive cash flows have expired or have been transferred and the consolidated entity has transferred substantially all the risks and rewards of ownership. When there is no reasonable expectation of recovering part or all of a financial asset, its carrying value is written off.

Financial assets at fair value through other comprehensive income include equity investments which the Company intends to hold for the foreseeable future and has irrevocably elected to classify them as such upon initial recognition.

(I) IMPAIRMENT OF ASSETS

The company recognises a loss allowance for expected credit losses on financial assets which are either measured at amortised cost or fair value through other comprehensive income.

The measurement of the loss allowance depends upon the company's assessment at the end of each reporting period as to whether the financial instrument's credit risk has increased significantly since initial recognition, based on reasonable and supportable information that is available, without undue cost or effort to obtain.

Where there has not been a significant increase in exposure to credit risk since initial recognition, a 12-month expected credit loss allowance is estimated. This represents a portion of the asset's lifetime expected credit losses that is attributable to a default event that is possible within the next 12 months. Where a financial asset has become credit impaired or where it is determined that credit risk has increased significantly, the loss allowance is based on the asset's lifetime expected credit losses. The amount of expected credit loss recognised is measured on the basis of the probability weighted present value of anticipated cash shortfalls over the life of the instrument discounted at the original effective interest rate.

For financial assets measured at fair value through other comprehensive income, the loss allowance is recognised within other comprehensive income. In all other cases, the loss allowance is recognised in profit or loss.

2. Members' Guarantee

If the company is wound up the Memorandum of Association states that each member is required to contribute a maximum of $10.00 each towards meeting any outstanding obligations of the company.

	2019/20	2018/19
	$	$

3. Cash and Cash Equivalents

General Account	1,457,007	702,026
D.W. Research Fund Account	1,025,443	723,002
	2,482,450	**1,425,028**

4. Receivables

Sundry Debtors	196,460	402,723
	196,460	**402,723**

5. Investments

Shares in Listed Corporations & Other Securities	9,900,007	11,631,587
Total Available-for-sale Financial Assets	9,900,007	11,631,587
Total Investments	**9,900,007**	**11,631,587**

6. Plant and Equipment

Office Equipment - at cost	13,151	13,151
Less: Accumulated Depreciation	(12,315)	(11,838)
	835	**1,312**

Reconciliation

Reconciliation of the carrying amount of plant and equipment at the beginning and end of the current & previous financial year:

Carrying amount at beginning of year	1312	2,157
Additions	-	-
Disposal of Equipment	-	-
Less: Depreciation expense	(477)	(845)
Carrying amount at end of year	**835**	**1,312**

7. Payables

Creditors and Accruals	43,340	(4,719)
Grants Payable	360,616	319,870
Director of Research - Victoria (refer note 15)	490,000	364,000
	893,956	**679,151**

8. Provisions

Employee Benefits	-	-

	2019/20	2018/19
	$	$
9. Research Capital Fund		
General		
Balance 1 July 2019	2,224,964	2,182,535
Allocation to Capital:		
- 10% Surplus & Imputation Credits & Other Legacies	41,984	42,429
- Capitalised Bequests	-	-
Transfer from Capital:		
- Amount transferred to Income	-	-
Balance 30 June 2020	**2,266,948**	**2,224,964**
Anselmi Estate		
Balance 1 July 2019	290,979	290,979
Allocation during year	-	-
Transfer during year	-	-
Balance 30 June 2020	**290,979**	**290,979**
Ivy May Stephenson Estate		
Balance 1 July 2019	30,376	30,376
Allocation during year	-	-
Transfer during year	-	-
Balance 30 June 2020	**30,376**	**30,376**
TOTAL	**2,588,303**	**2,546,319**

10. Settled Funds

D.W. Research Funds	200,000	200,000
Esme Anderson	124,326	124,326
G.J. Williams	25,500	25,500
B. Mitchell	26,023	26,023
Dame Ida Mann (Est. 31/03/84)	56,707	56,707
Ronald & Lois Lowe	40,000	40,000
	472,556	**472,556**

11. Financial Assets Reserve

Balance 1 July 2019	1,035,960	1,109,328
Revaluation increment/(decrement)	(968,265)	(73,368)
Balance 30 June 2020	**67,694**	**1,035,960**

Financial assets reserve records unrealised gains on revaluation of financial assets to fair value.

12. Capitalised Profit on Re-Arrangement of Investments, Capital Distributions & Transfers

	Balance 30/06/19	Allocation of Realised Profit/ (Loss) on Rearrangement of Investments & Capital Distributions & Transfer	Balance 30/06/20
	$	$	$
Research Fund			
General	156,957	(3,528)	153,429
Anselmi Estate	56,220	(1,264)	54,955
Ivy May Stephenson	145	(3)	140
D.W. Research Funds	5,315,192	(83,184)	5,232,009
Esme Anderson	1,104,463	(24,648)	1,079,815
G.J. Williams	189,950	(4,268)	185,684
B. Mitchell	188,014	(4,268)	183,747
Dame Ida Mann	265,309	(5,994)	259,316
Ronald & Lois Lowe	168,490	(3,980)	164,509
	7,444,740	**(131,137)**	**7,313,599**

13. Accumulated Funds

	Note	2019/20	2018/19
		$	$
(a) Administration			
Accumulated Deficits			-
Total Comprehensive Income		67,800	(2,040)
Total available for appropriation		67,800	(2,040)
Aggregate of amounts transferred from Administration	13 (a)	(67,800)	2,040
Accumulated Deficits - 30 June 2020		-	-
Capital Funds			
(b) Trust Fund			
Retained income		1,281,924	832,522
Total Comprehensive Income		21,166	47,880
Total available for appropriation		**1,303,090**	**880,402**
Aggregate of amounts transferred to General/Capital Funds			
Adjustment on investment value		(85,265)	445,853
Administration	13 (b)	67,800	(2,040)
Research Trust		(41,984)	(42,290)
Retained income - 30 June 2020		**1,243,642**	**1,281,924**

14. Grants Allocated / Made During the Year

	2019/20	2018/19
	$	$
Prof Alex Hewitt*		49,846
Dr Guei-Sheung Liu		49,920
Dr Mark Hassell		49,879
Prof Justine Smith		49,954
Dr Yuyi You		45,380
Dr Stuart Keel		49,617
Dr Nilisha Fernando		49,977
A/Prof Elaine Chong		48,899
Prof Stephanie Watson*		50,000
Dr Vivek Gupta		49,967
Prof Robert Casson		49,800
Dr Weng Onn Chan		47,500
Dr Fred Chen	50,000	50,000
Dr Elsa Ching Chan	49,377	
Dr Glyn Chidlow	49,446	
Dr Nitin Chitranshi	49,440	
Prof Jamie Craig	49,061	
Dr Thomas Edwards	49,679	
Prof Mark Gillies*	50,000	
Dr Sandy Hung	50,000	
Prof Robyn Jamieson	50,000	
Dr Mohd Khairui Nizam Khalid	50,000	
A/Prof Chris Layton	49,997	
Dr Michele Madigan	49,825	
Adjustments	(4,895)	
Sub total	**591,930**	**640,739**
Deduct contributions from:		
Other Grants Received	-	11,900
Eye Hospital Foundation	50,000	-
ANZSRS	50,000	
ANZEF	50,000	
RANZCO NSW Branch	-	50,000
Grant from RANZCO	-	25,000
Sub total	150,000	86,900
Net	**441,930**	**553,839**

* Grant received by director

15. Funds Allocated to Director of Ophthalmic Research - Victoria

	2019/20	2018/19
	$	$
Balance as at 1 July 2019	364,000	175,000
Interest for the year	-	-
Allocation for year	126,000	189,000
	490,000	364,000
Payment made to Director of Research	-	
Balance as at 30 June 2020	**490,000**	**364,000**

16. Auditors Remuneration

Financial Statements - Audit Service Other services	8,000	6,000
	8,000	**6,000**

17. Reconciliation of Net Cash Provided by Operating Activities to Results for Year

Net Surplus/(Deficit)		
- Trust Fund	(1,078,236)	22,958
- Administration	67,800	(2,040)
	(1,010,436)	**20,918**
Depreciation	477	845
Disposal of Equipment	-	-
Provision for Employee Benefits	-	-
Transfer from Capital to Contribute Towards Grants	-	-
(Increase)/Decrease in Receivables	206,262	(170,305)
Increase/(Decrease) in Creditors and Accrued Expenses	48,060	(4,196)
Increase/(Decrease) in Grants Payable	40,745	27,869
Increase/(Decrease) in allocation to Director of Research - Victoria	126,000	189,000
Valuation (Gains)/Losses on available-for-sale financial assets	968,265	73,368
(Profit)/Loss on Rearrangement of Investments	131,137	(48,446)
Net Cash Provided by /(used in) Operating Activities	**510,510**	**89,053**

18. Disclosures on Directors and Other Key Management Personnel

DIRECTORS

Prof Mark Gillies was the only director who received a grant this year.

The names of the directors who have held office during the financial year are:

Prof Stephanie Watson, NSW – Chair
Prof Mark Gillies, NSW – Vice Chair
Prof Richard Mills, SA – Honorary Secretary
A/Prof Paul Healey, NSW – Honorary Treasurer
Dr Jennifer Fan Gaskin, VIC
A/Prof Clare Fraser, NSW
A/Prof Sam Fraser Bell, NSW
Prof Stuart Graham, NSW
A/Prof Alex Hewitt, TAS
Dr George Kong, VIC
Prof David Mackey, WA
Prof Peter J McCluskey, NSW
Dr John Males, NSW
Dr Chameen Samarawickrama, NSW
A/Prof Andrea Vincent, New Zealand
A/Prof Peter van Wijngaarden, VIC

KEY MANAGEMENT PERSONNEL

Key management personnel are those persons having authority and responsibility for planning, directing and controlling the activities of the entity, directly or indirectly, including any director (whether executive or otherwise) of that entity. Control is the power to govern the financial and operating policies of an entity so as to obtain benefits from its activities.

KEY MANAGEMENT PERSONNEL COMPENSATION

Key Management Personnel has been taken to comprise the directors and one member of the executive management responsible for the day to day financial and operational management of the entity.

	2019/20	2018/19
	$	$
(a) Short-term employee benefits	8,814	-
(b) Post-employment benefits	1,014	-
(c) Other long-term benefits	-	-
(d) Termination benefits	-	-
(e) Share-based payment	-	-

19. FINANCIAL INSTRUMENTS

(A) FINANCIAL RISK MANAGEMENT POLICIES

The entity's financial instruments consist mainly of deposits with banks, local money market instruments, short- term investments, accounts receivable and payable.

The entity does not have any derivative instruments at 30 June 2020.

(i) Treasury Risk Management

An investment committee consisting of Board members of the entity meet on a regular basis to analyse financial risk exposure and to evaluate treasury management strategies in the context of the most recent economic conditions and forecasts.

The committee's overall risk management strategy seeks to assist the entity in meeting its financial targets, whilst minimizing potential adverse effects on financial performance.

Risk management policies are approved and reviewed by the Board on a regular basis. These include credit risk policies and future cash flow requirements.

(ii) Financial Exposures and Management Risk

The main risks the entity is exposed to through its financial instruments are interest rate risk, liquidity risk and credit risk.

Interest rate risk
Interest rate risk is managed with a mixture of fixed and floating rates on investments.

Foreign currency risk
The entity is not exposed to fluctuations in foreign currencies.

Liquidity risk
The entity manages liquidity risk by monitoring forecast cash flows.

Credit risk
The maximum exposure to credit risk, excluding the value of any collateral or other security, at balance date to recognised financial assets, is the carrying amount, net of any provisions for impairment of those assets, as disclosed in the statement of financial position and notes to the financial statements.

The entity does not have any material credit risk exposure to any single receivable or group of receivables under financial instruments entered into by the entity.

Price risk
The group is not exposed to any material commodity price risk.

(B) FINANCIAL INSTRUMENT COMPOSITION AND MATURITY ANALYSIS

The entity's exposure to interest rate risk, which is the risk that a financial instrument's value will fluctuate as a result of changes in market interest rates and the effective weighted average interest rates on those financial assets and financial liabilities, is as follows:

	Weighted Average Effective Interest Rate		Floating Interest		Fixed Interest Rate Maturing				Non Interest Bearing		Total Carrying Amount Per Statement of Financial Position	
	2020	2019	2020	2019	2020	2019	2018	2017	2020	2019	2020	2019
	%	%	$	$	%	%	%	%	$	$	$	$
Financial Assets												
Cash and Cash Equivalents	0.40	1 .40	2,482,450	1,425,028	-	-	-	-	-	-	2,482,450	1,425,028
Listed Investments												
Shares	N/A	N/A	-	-	-	-	-	-	9,900,007	11,631,587	9,900,007	11,631,587
Bank Bills	N/A	N/A	-	-	-	-	-	-	-	-	-	-
Receivables			-	-	-	-	-	-	196,460	402,723	196,460	402,723
Total Financial Assets			**2,482,450**	**1,425,028**	**-**	**-**	**-**	**-**	**10,096,467**	**12,034,310**	**12,578,917**	**13,459,338**
Financial Liabilities												
Payables			-	-	-	-	-	-	893,956	679,151	893,956	679,151
Total Financial Liabilities			-	-	-	-	-	-	893,956	679,151	893,956	679,151
Net Financial Assets			**2,482,450**	**1,425,028**					**9,202,511**	**11,355,159**	**11,684,961**	**12,780,187**

(C) NET FAIR VALUES

The net fair values of listed investments have been valued at the quoted market bid price at balance date. For other assets and other liabilities the net fair value approximates their carrying value. No financial assets and financial liabilities are readily traded on organised markets in standardised form other than listed investments.

The aggregate net fair values and carrying amounts of financial assets and financial liabilities are disclosed in the statement of financial position and in the notes to and forming part of the financial statements.

(D) SENSITIVITY ANALYSIS

Interest Rate Risk

The entity has performed a sensitivity analysis relating to its exposure to interest rate risk at balance date. This sensitivity analysis demonstrates the effect on the current year results and equity which could result from a change in this risk.

Interest Rate Sensitivity Analysis:

At 30 June 2020, the effect on profit and equity as a result of changes in the interest rate, with all other variables remaining constant, would be as follows:

	Carrying Amount	Interest Rate Risk			
	$	-1% Profit	+1% Profit	-1% Equity	+1% Equity
2019/20					
Financial Assets					
Cash and Cash Equivalents	2,482,450	(24,825)	24,825	(24,825)	24,825
2018/19					
Financial Assets					
Cash and Cash Equivalents	1,425,028	(14,250)	14,250	(14,250)	14,250

20. FAIR VALUE MEASUREMENTS

Financial assets and financial liabilities measured at fair value in the statement of financial position are grouped into three Levels of a fair value hierarchy. The three Levels are defined based on the observability of significant inputs to the measurement, as follows:

Level 1: quoted prices (unadjusted) in active markets for identical assets or liabilities;

Level 2: inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly;

Level 3: unobservable inputs for the asset or liability.

The following table shows the Levels within the hierarchy of financial assets and liabilities measured at fair value on a recurring basis at 30 June 2020 and 30 June 2019:

	Note	Level 1	Level 2	Level 3	Total
		$	$	$	$
30 June 2020					
Assets					
Listed securities	5	9,900,007	-	-	9,900,007
Net fair value		**9,900,007**	**-**	**-**	**9,900,007**
30 June 2019					
Assets					
Listed securities	5	11,631,587	-	-	11,631,587
Net fair value		**11,631,587**	**-**	**-**	**11,631,587**

There were no transfers between Level 1 and Level 2 for assets measured at fair value during 2020 or 2019.

Listed Securities

Fair values have been determined by reference to their quoted bid prices at the reporting date.

21. BENEFICIARY ENTITLEMENT

The company is a beneficiary of The Richard & Ina Humbley Foundation and has an entitlement to income from the foundation to be used for grants in support of research conducted into macular degeneration.

The company accounts for this income on a cash basis.

The income received for the year ended 30 June 2020 from the foundation was **$39,177**.

22. IMPACT OF COVID-19

The spread of novel coronavirus (COVID-19) was declared a public health emergency by the World Health Organisation on 31 January 2020 and upgraded to a global pandemic on 11 March 2020. The rapid spread of the virus has seen an unprecedented global response by governments, regulators and numerous industry sectors. The Australian Federal Government enacted its emergency plan on 29 February 2020.

ORIA's assets are principally represented by investments in public listed entities. The COVID-19 pandemic resulted in a major correction in the Australian Stock Market and this has affected the assets base of ORIA. Additionally, companies have reduced the amount of dividends declared and the attached franking credits which have impacted the financial result.

Timing of the lifting of remaining restrictions remain uncertain at the date of this report, and overall financial impact cannot yet be reliably estimated. At the date of this report the company has sufficient cash reserves to continue operations, at a minimum, for the next 12 months.

23. SUBSEQUENT EVENTS

Other than as noted at note 22 Impact of COVID-19, there have been no significant events occurring after balance date, which may affect either the company's operations, or results of those operations, or the company's state of affairs.

Directors' Declaration

1. The financial statements and notes as set out on pages 20-36:

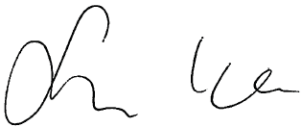
   (a) comply with Accounting Standards and Australian Charities and Not-for-profits Commission Act 2012; and

   (b) give a true and fair view of the financial position as at 30 June 2020 and performance for the year ended on that date of the company.

2. In the director's opinion there are reasonable grounds to believe that the company will be able to pay its debts as and when they become due and payable.

The declaration is made in accordance with a resolution of the Board of Directors.

On behalf of the Board.



Professor Stephanie Watson
Director

Associate Professor Paul Healey
Director

Sydney, this 3rd day of Dec 2020

Auditor's Report

Orr, Martin & Waters
CHARTERED ACCOUNTANTS

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INDEPENDENT AUDITOR'S REPORT TO THE MEMBERS OF THE OPHTHALMIC RESEARCH INSTITUTE OF AUSTRALIA

Report on the Audit of the Financial Report

Opinion

We have audited the financial report of The Ophthalmic Research Institute of Australia (the registered entity), which comprises the statement of financial position as at 30 June 2020, the statement of profit or loss and other comprehensive income, statement of changes in equity and statement of cash flows for the year then ended, and notes to the financial statements, including a summary of significant accounting policies, and the directors' declaration.

In our opinion, the accompanying financial report of The Ophthalmic Research Institute of Australia has been prepared in accordance with Div 60 of the *Australian Charities and Not-for-profits Commission Act 2012,* including:

(i) giving a true and fair view of the registered entity's financial position as at 30 June 2019 and of its financial performance for the year then ended; and

(ii) complying with Australian Accounting Standards and Div 60 of the *Australian Charities and Not-for-profits Commission Regulation 2013*.

Basis for Opinion

We conducted our audit in accordance with Australian Auditing Standards. Our responsibilities under those standards are further described in the *Auditor's Responsibilities for the Audit of the Financial Report* section of our report. We are independent of the registered entity in accordance with the ethical requirements of the Accounting Professional and Ethical Standards Board's APES 110: *Code of Ethics for Professional Accountants* (the Code) that are relevant to our audit of the financial report in Australia. We have also fulfilled our other ethical responsibilities in accordance with the Code.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Information Other than the Financial Report and Auditor's Report Thereon

The directors are responsible for the other information. The other information comprises the information included in the registered entity's annual report for the year ended 30 June 2020, but does not include the financial report and our auditor's report thereon. Our opinion on the financial report does not cover the other information and accordingly we do not express any form of assurance conclusion thereon. In connection with our audit of the financial report, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the financial report or our knowledge obtained in the audit or otherwise appears to be materially misstated. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report in this regard.

Responsibilities of the Directors for the Financial Report

The directors of the registered entity are responsible for the preparation of the financial report that gives a true and fair view in accordance with Australian Accounting Standards and the *Australian Charities and Not-for-profits Commission Act 2012* and for such internal control as the directors determine is necessary to enable the preparation of the financial report that gives a true and fair view and is free from material misstatement, whether due to fraud or error.

In preparing the financial report, the directors are responsible for assessing the registered entity's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the directors either intend to liquidate the registered entity or to cease operations, or have no realistic alternative but to do so.

Auditor's Report

INDEPENDENT AUDITOR'S REPORT TO THE MEMBERS OF THE OPHTHALMIC RESEARCH INSTITUTE OF AUSTRALIA

Auditor's Responsibilities for the Audit of the Financial Report

Our objectives are to obtain reasonable assurance about whether the financial report as a whole is free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with the Australian Auditing Standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of this financial report.

As part of an audit in accordance with the Australian Auditing Standards, we exercise professional judgement and maintain professional scepticism throughout the audit. We also:

- Identify and assess the risks of material misstatement of the financial report, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the registered entity's internal control.
- Evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by the directors.
- Conclude on the appropriateness of the directors' use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the registered entity's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the financial report or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause the registered entity to cease to continue as a going concern.
- Evaluate the overall presentation, structure and content of the financial report, including the disclosures, and whether the financial report represents the underlying transactions and events in a manner that achieves fair presentation.

We communicate with the directors regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.

Orr Martin & Waters

ORR MARTIN & WATERS
Chartered Accountants

L R Gilmour

L R Gilmour

461 Whitehorse Road Balwyn Vic 3103

Dated this 9th day of December 2020

Liability limited by a scheme approved under Professional Standards Legislation


ORIA