2021-22 ANNUAL REPORT

AUSTRALIAN VISION RESEARCH

australianvisionresearch.org

The Ophthalmic Research Institute of Australia trading as
Australian Vision Research is registered with the
Australian Charities and Not-for-profits Commission (ACNC) ABN 37008393146

Eye research changing lives.

Our Vision.

We seek to alleviate the burden from blindness and vision impairment through research that discovers new knowledge and improves patient outcomes and clinical practice.

Our Mission.

We support eye and vision research that prevents and treats disorders and discovers new knowledge in partnership with RANZCO and our stakeholders.

Contents.

Chair's report.

Dear Colleagues,

One of the joys of writing this report is to look back over the year and review the accomplishments of Australian Vision Research and thank those who have contributed. The past fiscal year was again impacted by COVID which created challenges and brought opportunities. Some of the highlights were:

1. Memorandum of understanding (MOU) with Royal Australian and New Zealand College of Ophthalmologists

The relationship between Australian Vision Research and RANZCO was further strengthened with the signing of our first MOU. The MOU outlines how the two organisations will work closely together to support ophthalmology and ophthalmic research.

2. Funding support to Ophthalmic research

In 2021, Australian Vision Research awarded $539,258 in funding for 2022 for 11 ophthalmic research projects from across Australia. Our Research Advisory Committee, Chaired by Professor Alex Hewitt with Associate Professor Samantha Fraser-Bell as Secretary, coordinated the grant application process, peer-review and conflict of interest management, both online and in person, with the assistance of our volunteer panel members and over 70 'expert' international and national reviewers. High quality research in a wide variety of areas of ophthalmology were supported including in pseudoexfoliation syndrome, retinal dystrophies, bacterial keratitis, uveal melanoma, macular degeneration, glaucoma, retinal vascular diseases, gene therapy and myopia.

Priming grants were awarded to two teams, supporting RANZCO fellows who are new to research, with the Australian Vision Research Board providing strategic advice during grant preparation.

The robust grant review process ensured Australian Vision Research funds were awarded to the projects best able to support Australian ophthalmology to discover new knowledge and improve outcomes for patients; as well as promoting excellence in Australian ophthalmology internationally and to the public. The outcomes from the grant funding are reported each year in our annual report.

3. New CEO appointed

Phillip Cenere was appointed in March 2022 and has brought a wealth of knowledge and expertise to Australian Vision Research. Phillip has extensive experience as a board and management consultant and has served in senior leadership roles within universities including Associate Vice Chancellor, CEO, Executive Dean and Professor.

4. Governance strengthened

The major governance review which started in the prior fiscal year was continued this year. Past policies and agreements were reviewed to ensure that Australian Vision Research remains recognised under the Australian Charities and Not-for-Profits Commission (ACNC) as a Health Promotion Charity (HPC). The review also enabled the digital archiving of our historical documents. As a compliant HPC we have tax deductibility (DGR) for all donations and publish all our reports online; they can be accessed on the commission's website at ORIA ACNC.

5. Donors supporting ophthalmic research

The generosity and support of our donors is critical to Australian Vision Research's funding of impactful ophthalmic research. Australian Vision Research is grateful for bequests and donations received including from the NSW Branch of RANZCO, Australian and New Zealand Society of Retinal Specialists (ANZSRS) and the Perth Eye Foundation, along with the DW Fund.

6. Member engagement

Our Annual General Meeting, Annual Report, symposium at RANZCO annual congress, newsletter, and social media channels have enabled Australian Vision Research to communicate with our members, stakeholders, the profession and community. Please Follow us on Twitter, Facebook, and LinkedIn to stay in touch.
For the coming fiscal year, Australian Vision Research looks forward to working with RANZCO to increase our support for RANZCO fellows to conduct ophthalmic research and completing our strategic and governance review. In 2023, we look forward to celebrating our 70th year.

Thank you to the Research Committee Chair Prof Alex Hewitt, Secretary A/Prof Samantha Fraser Bell, Treasurer Clin. A/ Prof Paul Healey, Honorary Secretary A/Prof Richard Mills, the Board, Research Advisory Committee, our volunteer reviewers, the RANZCO staff and all our members for their hard work and continued support over the year. As well as thank you to Phillip Cenere our new CEO.

Professor Stephanie Watson, OAM
Chair

RANZCO's president report.

RANZCO's mission is to lead eye care by setting and improving standards, providing lifelong education, promoting research and innovation and advocating on behalf of patients, their communities and our membership.

Across the 2021-2022 financial year, the College went through some major changes and 'firsts'.
As with most organisations, the disruptions of COVID-19 were frequent and felt across many areas.

Our Annual Scientific Congress had been postponed to October 2021 but was instead run as a fully virtual event in late February 2022. The virtual format was a first for the Congress and allowed for plenty of interaction between delegates. Although it is not a format we intend to repeat, it was highly successful and will pave the way for more interactive formats of presentations in the future.

The Congress was the platform for the launch of the consultation for Vision 2030 and beyond. The plan focuses on six key areas:

- Service Delivery
- Workforce and Training
- Aboriginal and Torres Strait Islander Healthcare
- Preventative Healthcare
- Global Eye Health
- Sustainability

A lot of stakeholder engagement and consultation followed the Congress, with key Fellows and staff meeting with RANZCO Branch Chairs, Special Interest Group, key politicians and bureaucrats in health and external bodies such as the Australian Indigenous Doctors' Association.

Through a coordinated and concerted effort, it is hoped Vision 2030 and beyond will address key areas of health inequity in Australia and further afield.

RANZCO's advocacy efforts also included a campaign to leverage the combined influence of RANZCO Fellows in the lead-up to the Australian Federal election. RANZCO asked individual Fellows to write to their local MP highlighting a particular eye health care issue that required federal government attention. The main objective was not to seek election commitments, but rather to help set the scene for post-election strategies, raising the voices of ophthalmologists and the profession, also cultivating ground for future advocacy.

Pre-election activities also involved formal correspondence from myself to key politicians and Ministers, including the cross benchers highlighting priority areas that require attention at the federal level. The College is now planning follow-up on those communications and resulting interactions to further develop established, and commence new, relationships with relevant Ministers.

On the research front, RANZCO has carried out the following activities:

1. Evaluation of virtual accreditation of medical specialist training sites for ophthalmology in Australia and New Zealand

2. Examination of the relationship between trainee attitude towards virtual reality simulator in ophthalmology and their microsurgical skills

3. Examination of the RANZCO Advanced Clinical Examinations (RACE)

4. Considered training and workforce development to enhance rural and remote ophthalmology practice in Australia

5. Evaluation of the RANZCO Specialist Training Program (STP)

RANZCO The Royal Australian and New Zealand College of Ophthalmologists
THE LEADERS IN COLLABORATIVE EYE CARE

RANZCO published or facilitated papers including:

• Allen P, Jessup B, Khanal S, Baker-Smith V, Obamiro K, Barnett T. Distribution and Location Stability of the Australian Ophthalmology Workforce: 2014-2019. Int J Environ Res Public Health. 2021;18(23):12574.

•Khanal S, Gole G, Kaufman D. Evaluation of virtual accreditation of medical specialist training sites for ophthalmology in Australia and New Zealand during the COVID-19 pandemic. Australian Health Review;2022, https://doi.org/10.1071/AH22031.

•Gill HK, Niederer RL, Danesh-Meyer HV. Gender differences in surgical case volume among ophthalmology trainees. Clin Exp Ophthalmol. 2021;49(7):664-671. doi:10.1111/ceo.13969

•Gin, C., Reyna, J., Khanal, S. & Chakrabarti, R. (2022). Trainee Attitude Towards Virtual Reality Simulation (VRS) to Acquire Microsurgical Skills in Ophthalmology. In T. Bastiaens (Ed.), Proceedings of EdMedia + Innovate Learning (pp. 753-758). New York City, NY, United States: Association for the Advancement of Computing in Education (AACE). https://www.learntechlib.org/primary/p/221369/.

•Reyna, J.,Khanal, S., Baker-Smith, V. & Cooper, E. (2021). A systematic approach to learning design for supervisor training in Ophthalmology Education. In Gregory, S., Warburton, S., & Schier, M. (Eds.), Back to the Future. Proceedings ASCILITE 2021 in Armidale (pp. 32–36). https://doi.org/10.14742/ascilite2021.0104

•A range of research pieces from the Chair of RANZCO's Sustainability Committee, Dr Jesse Gale, and a further 17 published articles and conference papers with contributions from RANZCO Senior Learning Designer, Dr Jorge Reyna.

An important contribution from RANZCO in this space is the **RANZCO Data Access Policy** which enables external researchers access to RANZCO data for research and the above publication. At least two other projects have been approved under this policy and we anticipate more papers to be published using RANZCO data soon.

The RANZCO Human Research Ethics Committee provides a cost-effective way for ophthalmologists in private practices, who do not have access to institutional ethics committees, to seek ethics approval for their research activities and facilitate research partnerships between research institutes and private practices.

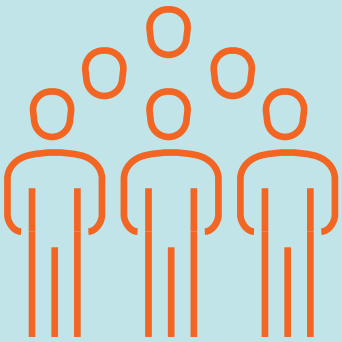
RANZCO has promoted research through initiatives such as the Women in Ophthalmology's 10-minutes of science podcast series and donations to Australian Vision Research from the NSW Branch ($50,000) and ANZSRS ($50,000). Additionally, a trainee has started on the VTP/PhD pathway this year, demonstrating RANZCO's commitment to producing future ophthalmology researchers.

RANZCO has also welcomed a new CEO during the past financial year. Mr Mark Carmichael took over from Dr David Andrews, with a short gap between David finishing and Mark starting. We were fortunate that the RANZCO Board could have its first face-to-face meeting in nearly two-and-half years in May. This was also an excellent opportunity for the whole Board to meet with Mark and share our vision of the future.

Prof Nitin Verma,
RANZCO President

RANZCO The Royal Australian and New Zealand College of Ophthalmologists
THE LEADERS IN COLLABORATIVE EYE CARE

Thanks to our reviewers.



Australian Vision Research would like to thank all our external reviewers who kindly gave insight and advice to help with the allocation of the 2021-2022 grants. Thank you for gifting your time to advance eye research! Your work is invaluable.

Dr Alex Muntz
A/Prof Andrew White
Dr Anna King
Dr Anthony Hall
Dr Ashley Franks
Dr Ashley Kras
Dr Ayub Zuhair
Dr Brent Gaskin
Dr Caroline Catt
A/Prof Chandra Balaratnasingam
Dr Christine Younan
Dr Clare Fraser
Prof Colin Green
Dr Con Petsoglou
A/Prof Elizabeth Berger
Dr Francis Hunter
A/Prof Fred Chen
A/Prof Gerald Liew
Prof Gerard Sutton
Dr Glyn Chidlow
Dr Grace Lidgerwood
Prof Graham Lee
Prof Greg Neely
A/Prof Guei-Sheung Liu
Dr Hemal Mehta
A/Prof Isabelle Jalbert
Dr Jacqueline Beltz
Prof Jamie Craig
Dr Jennifer Arnold
A/Prof Jie Zhang
Dr Jing You
Dr Johanna Jones
Dr Jonathan Astin
Prof Justine Smith
Dr Kathryn Burdon
Prof Keith Martin
Dr Kelvin Teo
Dr Li-Anne Lim
Dr Leo Sheck
Dr Logan Mitchell
Dr Maciej Daniszewski
Dr Mark Gillies
Dr Matthew Simunovic
A/Prof Michael Coote
Prof Mingguang
Dr Ming-Lee Lin
Dr Mohammed Ziaei
Dr Mohd Khairul Nizam Mohd Khalid
A/Prof Owen Siggs
Dr Penny Allen
A/Prof Puya Gharahkhan
Dr Rachael Heath Jeffery
Dr Rasha Altaie
A/Prof Raymond Wong
Dr Rod O'Day
Dr Rosie Dawkins
Dr Samuel McLenachan
Dr Sandy Hung
A/Prof Sanjwick Remasinghe
Dr Sarah Hull
Dr Shweta Kaushik
Adjunct Prof Stephen Klyce
Dr Sophia Zagora
Dr Srujana Sahebjada
Prof Stuart Graham
Dr Thomas Campbell
Dr Yuan Zhou

Thanks to our partners.

Australian Vision Research could not do the work we do without the support of partners and individual supporters who are committed to the advancement eye health and the ophthalmic medical practice.

During the 2021 and 2022, we were pleased to have partnered with The Perth Eye Foundation, the Australian and New Zealand Society of Retinal Specialists, RANZCO and RANZCO NSW Branch.

We would like to offer a special thank you to all our generous partners and donors, including the DW Fund, whose generosity helped fund such important research projects over the year.

Grants Awarded 2021 for 2022.

CHIEF INVESTIGATOR	OTHER INVESTIGATORS	GRANT NAME	RESEARCH PROJECT TITLE	AMOUNT
Prof Jamie Craig	A/Prof Owen Siggs, Dr Joshua Schmidt, Dr Sean Mullany	ORIA Grant	Is pseudoexfoliation syndrome triggered by viral infection?	$49,494
Dr Robyn Jamieson	Prof John Grigg	ANZSRS Grant	Therapies for the cone-rod dystrophies	$50,000
Prof Stephanie Watson	Prof Monica Lahra, A/Prof Richard Mills, Dr Steve Wiffen, Dr Maria Cabrera- Aguas, Dr Evan Wong, Dr Jonathan Chung-Wah-Cheong	ORIA Grant	The Bacterial Ocular Surveillance System (BOSS)	$50,000
A/Prof Fan Fan Zhou	A/Prof Robert Max Conway, A/Prof Svetlana Cherepanoff	Priming Grant	Develop novel therapy for human Uveal Melanoma	$49,904
Dr Ling Zhu	Prof Mark Gillies, Dr Ting Zhang	ORIA Grant	Targeting Nrf2-MAFF pathway in Müller cells to treat macula degeneration	$49,856
A/Prof Vivek Gupta	Prof Stuart Graham, A/Prof Mehdi Mirzaei	ORIA Grant	Amyloid and Tau targeting to protect Retinal Ganglion Cell and Optic Nerve in glaucoma	$49,856
Prof Kathryn Burdon	Clinical Prof Nitin Verma, Dr Rajya Gurung, Clinical Prof Brendan Vote, Dr Bennet McComish	Humbley Foundation Grant	VEGF intraocular injections for diabetic macular oedema	$48,430
Dr Ayub Qassim	John Landers, Henry Marshall	ORIA Grant	Identifying cardiovascular disease parameters with high clinical relevance in primary open-angle glaucoma	$49,718
A/Prof Peter van Wijngaarden	Dr Xavier Hadoux, A/Prof Lyndell Lim, Dr Amy Cohn, Darvy Dang	ORIA Grant	Hyperspectral retinal imaging perfusion maps for retinal vascular diseases	$49,994
Dr Devaraj Basavarajappa	Dr Nitin Chitranshi, Dr Deepa Viswanathan	NSW RANZCO Grant	The next generation of medicine-Gene therapy for glaucoma	$49,811.20
Dr Jessica Mountford	Dr Livia Carvalho, Dr Patricia Jusuf, Dr Antony Clark	Perth Eye Foundation Grant	Establishing zebrafish morpholino as a model to study early-onset myopia.	$42,194.33
Total for 2021 - 2022				**$539,258**

Progress reports from the previous year.

Hardie Anselmi Bequest Grant

Development of a novel hybrid vision restoration strategy

Chief Investigator: A/Prof Chi Luu
Co-investigators: A/Prof Penelope Allen, A/Prof Mohit Shivdasani

Aim
To determine whether retinal stimulation using a combination of light and electrical current (hybrid stimulation) will improve neural activation in the visual cortex compared to stimulation using light alone in eyes treated with optogenetic gene therapy.

Methods
Optogenetic gene therapy targeting the retinal ganglion cells was delivered intravitreally to one eye of a normal sighted preclinical model. Four weeks post-injection, neural activity in the visual cortex in response to light and hybrid stimulation was recorded using multi-unit recording techniques.

Key Results
The initial results showed that hybrid stimulation produced a greater neural activity in the visual cortex compared to stimulation with light alone (Figure 1).

Conclusion
Neural activation in the visual cortex can be improved by combining light and electrical stimulation.

Implications for Clinical Practice/Science and Future Research
The findings warrant further research into a hybrid stimulation approach for retinal stimulation.

Lay summary of outcomes
The findings from our research project indicate that stimulating the retina with light and electrical current enhances neuronal activation in the visual cortex.

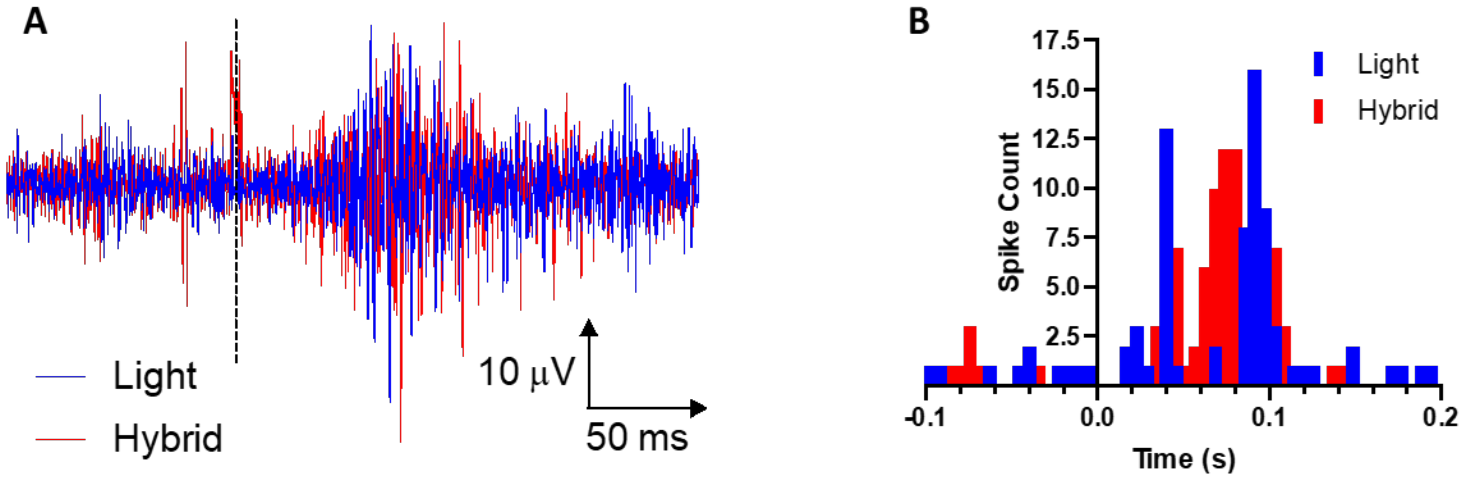


***Figure 1**: Efficacy of hybrid stimulation. (A) An example of one recording channel in the visual cortex depicting multiunit activity in response to a single pulse of retinal stimulation with light alone (blue) versus hybrid stimulation (red) of the same eye. Dashed line indicates onset of stimulation. (B) Peristimulus time histogram of multiunit visual cortex activity in response to light and hybrid stimulation. Hybrid stimulation is associated with a greater activity in the visual cortex compared to light stimulation.*

Perth Eye Foundation Grant

Applying machine learning to efficiently analyse fundus autofluorescence images in preparation for gene therapy

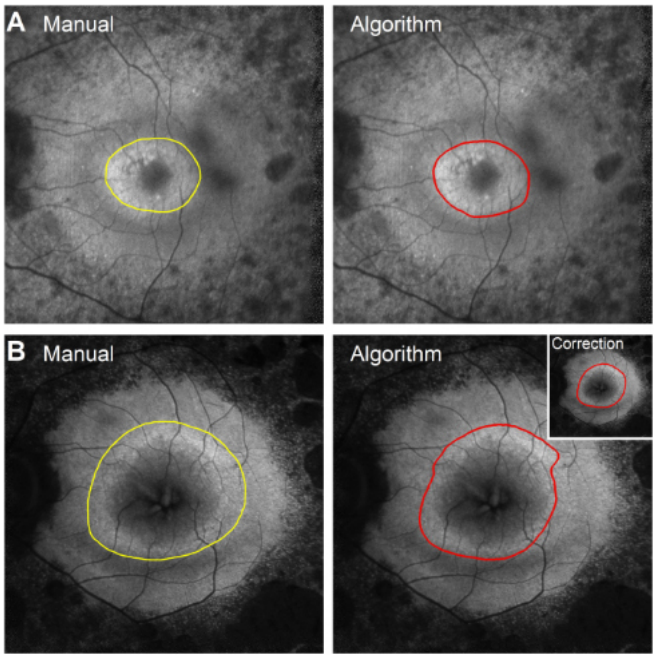
Chief investigator: Dr Jason Charng
Co-investigators: Dr David Alonso-Caneiro, Prof David Mackey



Aim
Eyes with retinitis pigmentosa (RP) show a characteristic hyperautofluorescent ring (HAR) with fundus autofluorescence (FAF) imaging, we aim to develop a machine-learning based algorithm that marks and quantifies the HAR.

Method
2255 FAF images from RP eyes were extracted and the HAR was manually segmented for each image. The delineated images were then utilised to develop and validate the machine learning algorithm.

Key Results
In most cases, HAR marking by the algorithm was similar to human delineation (Fig 1A). However, human segmentation was more accurate in minor instances of low image quality and/or indistinct boundary (Fig 1B). Hence a manual correction functionality has been introduced into the program (Fig 1B, inset).



Conclusion
The machine learning algorithm was able to segment HAR in RP eyes, comparable to human marking. Manual correction was required in a minority of images.

Implications and future research
With the generous support from Perth Eye Foundation, the developed algorithm can be immediately deployed into the clinic for accurate and quick analysis of HAR in RP. More importantly, given the potential of HAR as a trial endpoint in RP gene therapy, the program will facilitate efficient analysis of FAF images.

Publications arising from this work:
Charng et al. A wavelength-agnostic, deep-learning algorithm segmenting the hyperautofluorescent ring in retinitis pigmentosa. The Association for Research in Vision & Ophthalmology 2022 Annual Meeting.

Lay summary of outcomes
Retinitis pigmentosa (RP) causes irreversible blindness and there is no treatment to date. With the generous support from Perth Eye Foundation, we developed an artificial-intelligence system that accurately assesses the structure of eyes with RP, which will aid clinical decision-making and data analysis in clinical trials.

Figure caption:
A: An example of comparable manual (yellow outline) and machine learning (red outline) segmentation of a hyperautofluorescent ring.
B: An example of dissimilar segmentation between the two methods due to indistinct temporal boundary. Machine learning segmentation required manual adjustment (inset).

Richard and Ina Humbley Foundation Grant

Transcriptomic and proteomic retinal pigment epithelium signatures of age related macular degeneration

Chief investigator: Dr Grace Lidgerwood
Co-investigators: Dr Mehdi Mirzaei, Prof Alex Hewitt, Prof Alice Pébay

Aim
To establish the proteomic profile of RPE cells from a large study of age-related macular degeneration geographic atrophy (GA) patients and healthy controls to identify molecular differences associated with the disease.

Methods
Fibroblasts from 79 individuals (43 geographic atrophy and 36 controls) were reprogrammed into iPSCs and differentiated to mature and functional retinal pigment epithelium (RPE) cells, the tissue that is affected in GA. All samples were harvested after 90-days, and the proteome was determined using liquid chromatography mass spectrophotometry (LC-ESI-MS/MS) and computational analysis.

Key Results
The study found that 234 proteins were significantly differentially expressed between geographic atrophy and control RPE. The GA dataset was highly enriched in pathways associated with mitochondrial and metabolite functions (including lipid synthesis, gluconeogenesis, cholesterol, and glucose metabolism).

Conclusion
The results suggest changes to metabolic homeostasis is a feature of GA.

Implications for Clinical Practice/Science and Future Research
The study identified mitochondrial-associated pathways as significantly altered in disease, and this may lead to therapeutic discovery in future follow-up research. We are currently examining mitochondrial function in GA-affected RPE cells. Optimisation of assays that measure functional changes in the mitochondria is underway, and approaches to mimic the disease features in vitro by incorporating aspects of stress and biological aging are being explored.

Lay summary of outcomes
Our study explored how complex molecules (proteins) differ between late-AMD and healthy individuals. Analysing stem cell derived retinal cells from 79 patients, we identified 234 proteins associated with disease. A significant proportion were associated with energy metabolism, suggesting it is a key feature of the disease.

Esme Anderson Grant

Neuroprotection of Retinal Ganglion Cells by Photobiomodulation

Chief investigator: Professor Robert Casson

Aim
The retinal ganglion cells (RGCs) are the cells at the back of the eye that degenerate in glaucoma: we are investigating photobiomodulation (PBM) as a novel therapy to prevent loss of these cells.

Methods
We are assessing PBM in cell culture models and in animal models of glaucoma.

Key Results
To date, we have demonstrated a protective effect of PBM in our cell culture models and have shown that PBM influences the energy metabolism of the cell by acting on the cell's powerhouse: the mitochondria.

Conclusions
PBM favourably influences mitochondrial function in retinal cells and protects cells from degeneration induced by metabolic stressors.

Clinical Implications
Based on previous ORIA-funded research, we have previously shown that PBM rescues light-sensitive retinal cells (photoreceptors). We demonstrated this effect in the lab and completed a Phase I first-in-human trial in patients with retinitis pigmentosa. The current research expands on this ORIA-funded work and has provided encouraging results indicating that PBM may be applicable to glaucoma. The next steps are to assess PBM in the animal models of glaucoma with a view to demonstrating safety and efficacy and proceeding to a Phase I clinical trial in glaucoma. If successful, the research has the potential to provide a novel treatment in addition to eye pressure lowering therapy in glaucoma.

Publications/Presentations
Presented at the Optic Nerve Meeting in Obergurgl December 2022.

Lay summary of outcomes
Low energy red light therapy shows promise as a new therapy for glaucoma.

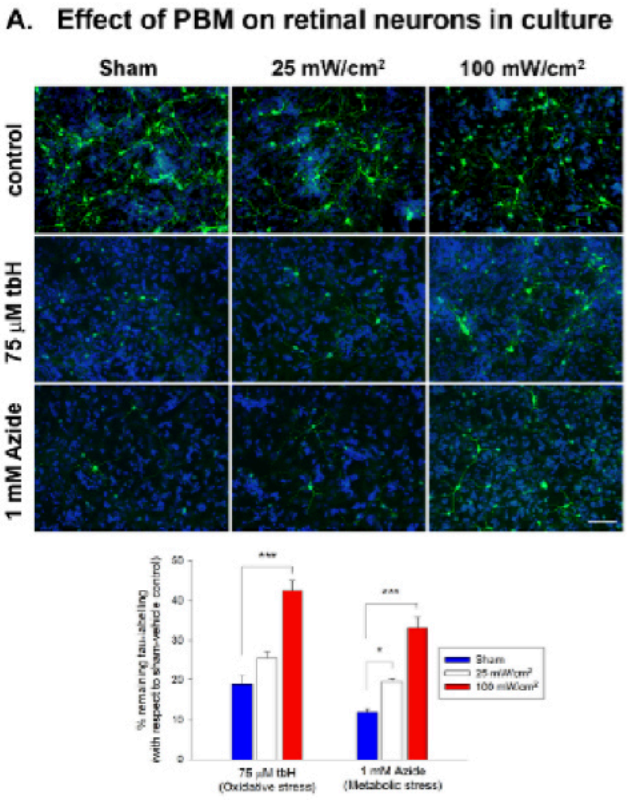
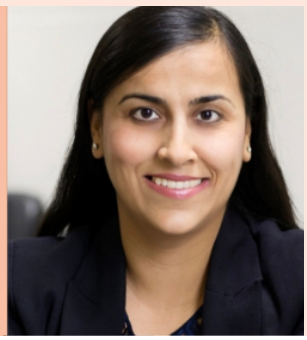


Fig. 1 *Effect of PBM on retinal cultures. (A) Effect of PBM on survival of tau-immunolabelled retinal neurons subjected to oxidative stress (tbH) or metabolic stress (sodium azide). PBM laser application at both 25 and 100 mW/cm2 augmented survival of retinal neurons in both injury settings. Scale bar: 50 µm. Data are expressed as mean ± SEM. ***p<0.001, *p<0.05 by one-way ANOVA plus Tukey's post hoc test, where n=6 determinations, from separate cultures.*

Australia and New Zealand Eye Foundation Grant

South Western Eye and Diabetes Deep Learning Algorithm (SWEDDLA) Study

Chief Investigator: Dr Shweta Kaushik
Co-investigators: Professor David Simmons, Dr Chee L. Khoo, Dr Marko Andric, Dr Kate McBride, Dr Jason R. Daley, Ms Xingdi Wang, Dr Vallimayil Velayutham, Dr Uchechukwu Levi Osuagwu



Aim
To test whether an Artificial Intelligence algorithm, created in Australia, can diagnose vision-threatening diabetic eye disease with similar accuracy to eye specialists.

Methods
We took retinal colour photographs and retinal scans of persons with diabetes, and compared the grading of photographs by the Artificial Intelligence algorithm we created with the grading by eye specialists.

Key Results
To date we have compared images from 536 people with diabetes, including 35 children. We found 28.7% of the study population had any degree of diabetic eye disease and 5.8% had vision threatening diabetic eye disease. The algorithm was able to diagnose diabetic retinopathy with 91.8% accuracy from retinal photographs and 97.5% from retinal scans. 94.4% of participants would undergo retinal imaging again.

Conclusion
Our algorithm had excellent accuracy for diagnosing diabetic eye disease amongst the cohort that we have recruited so far.

Implications for Clinical Practice/Science and Future Research
This algorithm may be clinically deployable after further point-of-care testing.
Our algorithm is unique as it includes children and combines information from retinal photographs and scans.

Publications/Presentations
Daley JR, Wang X, Simmons D, Osuagwu UL, Vellayutham V, Khoo CL, Heydon P, Liew G, Andric M, Kaushik S. Development of a deep learning algorithm for provision of a South Western Sydney diabetes retinal screening service. [paper] The Royal Australian and New Zealand College of Ophthalmologists (RANZCO) 52rd Annual Scientific Congress, Brisbane, February 2022.

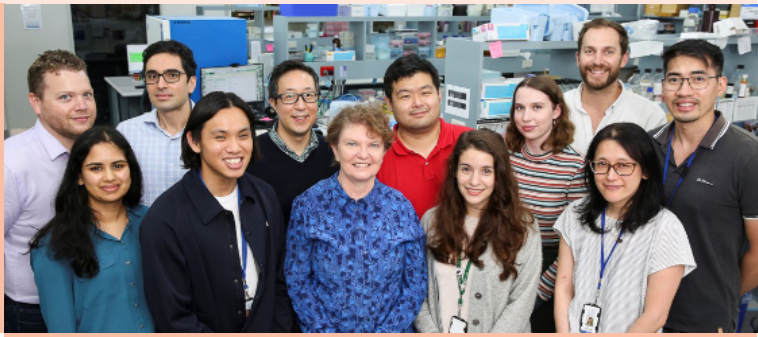
Wang X, Daley JR, Simmons D, Osuagwu UL, Vellayutham V, Khoo CL, Heydon P, Liew G, McBride K, Andric M, Kaushik S. Establishing a diabetes retinal screening service in South Western Sydney: Patient satisfaction with retinal imaging and the correlation between diabetic retinopathy and quality of life. [poster] RANZCO 52rd Annual Scientific Congress, Brisbane, February 2022.

Lay Summary of Outcomes
Diabetic eye disease is highly prevalent in South Western Sydney, greater than reported in other areas of Australia. Our Study's preliminary findings suggest that an Artificial Intelligence program can bring specialist-level accuracy to diabetes hospital and general practitioner clinics, meaning patients can have their diabetes management optimised at the same time as their eye test.

RANZCO NSW Branch Grant

A new inflammatory pathway for modulation in the retinal dystrophies

Chief Investigator: Professor Robyn Jamieson
Co-Investigator: Professor John Grigg



Prof Robyn Jamieson and Eye Genetics Research Unit

Aim
To assess phenotypic impact of a novel inflammatory pathway mutation using human induced pluripotent stem cell (iPSC)-retinal pigment epithelium (RPE) and retinal organoids (ROs) and test knockdown in inherited retinal dystrophies (IRDs).

Methods
Patient-derived inflammatory mutant iPSCs, retinal dystrophy patient iPSCs and controls were differentiated to RPE and ROs and characterised using cytokine, retinal and ciliary markers. CRISPR/Cas9 was used to knockout specific inflammatory factors in patient- derived retinal dystrophy mutant lines, and biomarkers assessed in the differentiated lines.

Key results
Patient-derived inflammatory mutant and retinal dystrophy iPSC-RPE and RO lines were characterised, and cytokine and retinal biomarkers of disease identified. CRISPR/Cas9 gene editing knocked out specific inflammatory factors in patient-derived iPSC lines. Upon differentiation of the patient-derived mutant lines, disease biomarkers were modulated in response to the CRISPR created changes in inflammatory factor expression.

Conclusion
Human iPSCs differentiated to RPE and ROs provide a valuable model system to investigate disease mechanisms in retinal diseases. Investigation of the novel inflammatory pathway reveals biomarkers and approaches useful for development of new therapy applications and evaluation in the retinal dystrophies.

Implications for Clinical Practice/Science and Future Research
iPSC-RPE and RO studies led to eligibility for clinical gene therapy and resolution of previously unsolved genetic variants. Impact of modulation of the novel inflammatory pathway will be investigated in additional types of retinal dystrophies.

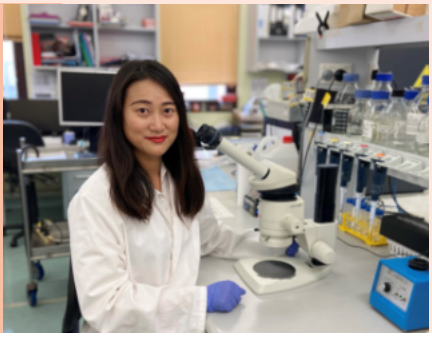
Conference Abstracts
1. Nash BM, et al. ARVO. May, 2021;
2. Chahine Karam F et al. ARVO. May, 2021;
3. Sabri et al, EMCR Symposium (1st Prize), Westmead Precinct, Dec, 2021;
4. Jamieson et al, RANZCO Symposium, Mar 2022

Lay summary of outcomes
Patient-derived stem cells differentiated to retinal tissues are valuable in determining eligibility for novel genetic therapies, understanding disease mechanisms including inflammatory pathways, and testing novel therapies in the IRDs.

RANZCO NSW Branch Grant

Targeting the pentose phosphate pathway in Müller cells to treat photoreceptor degeneration

Chief Investigator: Dr Ting Zhang
Co-investigator: Prof Mark Gillies



Aim
This project aimed to study the role of transketolase (TKT) in maintaining the function and health of Müller cells and the retina.

Methods
We explored the role of TKT in human Müller cells by knocking down its expression in primary cultured Müller cells isolated from the human retina (14 human donors) and cultured under light-induced oxidative stress.

Key results
We found that Müller cells were the primary retinal cell type expressing TKT in the human retina. TKT knockdown and light stress reduced TKT enzymatic activities and the viability of Müller cells. Induced dysfunction of TKT reduced the activity of the pentose phosphate pathway (PPP), which led to the derangement of retinal metabolism and impaired energy supply to Müller cells and the retina.

Conclusions
Müller cell-mediated TKT activity plays a critical protective role in the stressed retina. Knockdown of TKT disrupted the PPP and impaired overall glucose utilisation by Müller cells and made them more vulnerable to light stress by impairing energy supply and antioxidative responses.

Implications for Clinical Practice/Science and Future Research
This study investigated the role of transketolase (TKT) plays in maintaining retinal metabolism and redox homeostasis. We used benfotiamine, a derivative of thiamine (vitamin B1), to boost the activity of TKT, but it did not protect Müller cells exposed to photic stress. We will study further whether activating TKT using mRNA-lipid nanoparticles in Müller cells can restore the retinal redox environment under photic stress. This work may identify a new treatment for photoreceptor degeneration.

RANZCO NSW Branch Grant - continued

Targeting the pentose phosphate pathway in Müller cells to treat photoreceptor degeneration

Chief Investigator: Dr Ting Zhang
Co-investigator: Prof Mark Gillies

Lay summary of outcomes

We found that an enzyme in Müller cells, transketolase (TKT), plays an important antioxidant role in the retina. Disruption of TKT led to impaired glucose metabolism and reduced antioxidative capacity in Müller cells. Boosting TKT may be a way to prevent retinal degeneration.

Publications

Chen Y, Zhang T, Zeng S, Jin K, Xu R, Fan X, Zhang M, Du J, Gillies MC, Zhu L. Disruption of the pentose phosphate pathway in Müller cells makes them more susceptible to light stress by interfering with the oxidative stress-induced NRF2 response. The ARVO Annual Meeting 2021, Image The Kreissig travel grant.

Chen Y, Zhang T, Zeng S, Yam M, Gillies MC, Zhu L. Isolation, Culture, and Identification of Primary Müller Cells from Human Retina. Bio Protoc. 2021 Oct 5;11(19):e4179. doi: 10.21769/BioProtoc.4179. PMID: 34722826

Chen Y, Coorey NJ, Zhang M, Zeng S, Madigan MC, Zhang X, Gillies MC, Zhu L, Zhang T. Metabolism Dysregulation in Retinal Diseases and Related Therapies. Antioxidants (Basel). 2022 May 11;11(5):942. doi: 10.3390/antiox11050942. PMID: 35624805.

Chen Y, Zhang T, Zeng S, Xu R, Jin K, CooreyNJ, Wang Y, Wang K, Lee SR, Yam M, Zhu M, Chang A, Fan X, Zhang M, Du J, Gillies MC, Zhu L. Transketolase in human Müller cells is critical to resist light stress through the pentose phosphate and NRF2 pathways. Redox Biol. 2022 Jun 24;54:102379. doi: 10.1016/j.redox.2022.102379. PMID: 35779441.

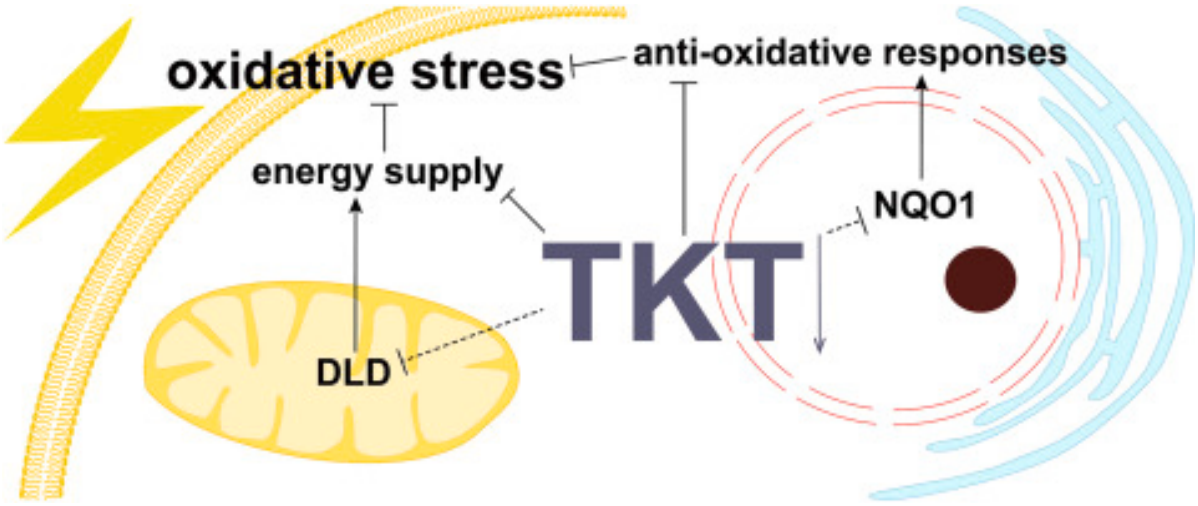


Fig. 1 *Transketolase in human Muller cells is important for combatting oxidative stress.*

R and L Lowe Bequest Grant

Measuring the correlation between innate VEGF expression and therapeutic response in humans

Chief Investigator: Dr Carla Mellough
Co-Investigators: Prof. Piroska Rakoczy,
Prof. Ian J. Constable (FRANZCO, ORIA)

Pending Final Report

Aim

This project will create a human platform that can be used as a tool to study VEGF physiology and assess novel pharmaceutical and gene therapy approaches for the treatment of wet AMD in order to predict clinical outcome

1. Generation and characterisation of patient-specific iPSC cell lines
2. Generation and characterisation of ROs and RPE
3. Measurement of VEGF expression in ROs and RPE under normoxic and hypoxic conditions

Background

Vascular endothelial growth factor (VEGF) is a potent angiogenic factor well known for its role in pathogenic choroidal neovascularisation leading to wet, or 'neovascular', age-related macular degeneration (nAMD), a common cause of vision loss in the elderly. (**2**) The blockade of this factor has been a key therapeutic approach in the management of pathogenic neovascularisation. (**3**) Intravitreally-injected anti-VEGF agents are currently used clinically for the reduction of VEGF in patients and, whilst this therapy has proven to be effective in stabilising vision for the vast majority, the delivery of monthly/bimonthly intravitreal injections which may be required over many years is a significant treatment burden. (**4,5**) In order to determine why some patients are unresponsive to treatment, as well as test less onerous approaches and more accurately predict clinical outcome, the development of a human platform would be an invaluable clinical research tool.

2. Kliffen M et al. Increased expression of angiogenic growth factors in age -related maculopathy. BrJO. 81, 154-162 (1977).

3. Pożarowska D. The era of anti-vascular endothelial growth factor (VEGF) drugs in ophthalmology, VEGF and anti-VEGF therapy. Cent Eur J Immunol. 41, 311-316. (2016).

4.Hussain RM, CiullaTA. Treatment Burden in nAMD:Visual Acuity Outcomes are Associated With Anti-VEGF Injection Frequency. Ophth. Sur., Lasers & Imaging Retina. 48,780-4 (2017).

5. Senra H et al. Experience of Anti-VEGF Treatment and Clinical Levels of Depression and Anxiety in Patients With Wet Age-Related Macular Degeneration. AmJO. 177, 213-224 (2017).

ORIA Priming Grant

Near-infrared Light Photobiomodulation Treatment for Retinal Vein Occlusion Macular Oedema (NIRVO)

Chief Investigator: Dr Elisa Cornish
Co-investigator: A/Prof Samantha Fraser-Bell

Interim Report

Aim
To assess if Near Infra-Red (NIR) laser is effective for eyes with macular oedema from a retinal vein occlusion.

Methods
Twelve 90 second exposure treatments with NIR laser is given over a 4 week period to eyes with reduced vision from a retinal vein occlusion with macular oedema. Visual acuity and anatomy response are included in the outcome measures.

Key Results
Due to COVID lockdown and The University of Sydney's policy on clinical trial recruitment being put on hold, the study has not been completed.

Conclusions
Not available yet. Unfortunately, only 6 patients have completed the NIRVO trial to date. We are recruiting a further 8 patients to complete the study. We are extremely appreciative of the support of the Ophthalmic Research Institute of Australia and look forward to sharing our final results with you in the near future.

Our People 21-22.

Our Board.

Prof Stephanie Watson OAM, NSW (Chair)

A/Prof Richard Mills, SA (Honorary Secretary)

A/Prof Paul Healey, NSW (Honorary Treasurer)

Dr Bill Glasson AO, QLD (RANZCO Nominee)

Prof Andrea Vincent, NZ (RANZCO Nominee)

A/Prof Chameen Samarawickrama, NSW

A/Prof Samantha Fraser-Bell, NSW

A/Prof Peter van Wijngaarden, VIC

Dr Jennifer Fan-Gaskin, VIC

Prof Stuart Graham, NSW

Prof David Mackey AO, WA

Dr Richard Stawell AM, VIC

Prof Mark Gillies, NSW

A/Prof George Kong, VIC

Prof Alex Hewitt, TAS

Research Advisory Committee.

Prof Alex Hewitt (Chair)

A/Prof Samantha Fraser-Bell (Secretary)

Dr Graham Wilson (NZ Save Sight Representative)

A/Prof Peter van Wijngaarden

Dr Jennifer Fan Gaskin

A/Prof Michele Madigan

Dr Isabel Lopez Sanchez

Prof Andrea Vincent

Prof Stephanie Watson

Dr John Wood

Dr Livia Carvalho

Prof Robert Casson

Prof Trevor Sherwin

Dr Carla Mellough

CEO.

Phillip Cenere

Directors' report.

30 June 2022

The directors present their report on The Ophthalmic Research Institute of Australia operating as Australian Vision Research for the financial year ended 30 June 2022.

1. General information

Directors

The names of the directors in office at any time during, or since the end of, the year are:

Names	Position
Prof Stephanie Watson, NSW Chair	Chair
Prof Mark Gillies, NSW	Vice Chair (Resigned 21/6/2022)
Prof Richard Mills, SA	Honorary Secretary
A/Prof Paul Healey, NSW	Honorary Treasurer
Dr Jennifer Fan Gaskin. Vic	Board Member
A/Prof Sam Fraser Bell, NSW	Board Member
Prof Stuart Graham, NSW	Board Member
A/Prof Alex Hewitt TAS	Board Member
Dr George Kong, VIC	Board Member
Prof David Mackey, WA	Board Member
Dr Charmeen Samarawickrama, NSW	Board Member
A/Prof Andrea Vincent, New Zealand	Board Member (Resigned 29/10/2022)
A/Prof Peter Van Wijngaarden Vic	Board Member
Dr Richard Stawell AM Vic	Board Member (Elected 30/6/2022)
Dr William (Bill) Glasson AO, QLD	RANZCO Nominee (Elected 30/6/2022)
Dr Matthew Simunovic NSW	Board Member (Elected 30/10/2022)

Directors have been in office since the start of the financial year to the date of this report unless otherwise stated.

Principal activities

The principal activity of The Ophthalmic Research Institute of Australia during the financial year was to provide funds for ophthalmic research.

No significant changes in the nature of the Company's activity occurred during the financial year.

Members' guarantee

The Ophthalmic Research Institute of Australia is a company limited by guarantee. In the event of, and for the purpose of winding up of the company, the amount capable of being called up from each member and any person or association who ceased to be a member in the year prior to the winding up, is limited to $ 10 for members that are corporations and $ 10 for all other members, subject to the provisions of the company's constitution.

Significant changes

No significant change in the nature of these activities occurred during the year.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

Directors' Report

30 June 2022

Operating results and review of operations for the year

Operating result

The deficit of the Company for the financial year after accounting for other comprehensive income was $ (1,675,981) (2021: $ 2,126,787 surplus).

Meetings of directors

During the financial year, 2 meetings of directors (including committees of directors) were held. Attendances by each director during the year were as follows:

	Directors' Meetings	
	Number eligible to attend	Number attended
Prof Stephanie Watson, NSW Chair	2	2
Prof Mark Gillies, NSW	2	2
Prof Richard Mills, SA	2	2
A/Prof Paul Healey, NSW	2	2
Dr Jennifer Fan Gaskin. Vic	2	2
A/Prof Sam Fraser Bell, NSW	2	2
Prof Stuart Graham, NSW	2	2
A/Prof Alex Hewitt TAS	2	2
Dr George Kong, VIC	2	2
Dr Charmeen Samarawickrama, NSW	2	2
A/Prof Andrea Vincent, New Zealand	2	2
A/Prof Peter Van Wijngaarden Vic	2	2
Dr Richard Stawell AM Vic	-	-
Dr William (Bill) Glasson AO, QLD	-	-
Dr Matthew Simunovic NSW	-	-

Indemnification and insurance of officers and auditors

No indemnities have been given or insurance premiums paid, during or since the end of the financial year, for any person who is or has been an officer or auditor of The Ophthalmic Research Institute of Australia.

2. Other items

Events after the reporting date

No matters or circumstances have 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.

Future developments and results

Likely developments in the operations of the Company and the expected results of those operations in future financial years have not been included in this report as the inclusion of such information is likely to result in unreasonable prejudice to the Company.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

Directors' Report
30 June 2022

2. Other items

Benefits received directly or indirectly by directors

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.

Some board members were investigators on some grants for 2021/2022. AVR has stringent governance processes for managing conflicts of interest during the allocation of grants. All grants are evaluated by AVR's Research Advisory Committee (RAC). The RAC consists of leading research ophthalmologists and vision scientists from Australia and New Zealand. The RAC members are selected annually by the executive. They are joined by reviewers from around the world to conduct the annual grant application review

Auditor's independence declaration

The lead auditor's independence declaration in accordance with section 307C of the *Corporations Act 2001*, for the year ended 30 June 2022 has been received and can be found on page 4 of the financial report.

Signed in accordance with a resolution of the Board of Directors:

Stephanie Watson (Mar 20, 2023 10:26 GMT+11)

Director: .....
Prof Stephanie Watson, NSW Chair

P Healey (Mar 20, 2023 11:21 GMT+11)

Director: .....
A/Prof Paul Healey, NSW

Dated 20/03/2023

20/03/2023

Auditor's Declaration.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

BANKS GROUP

Auditor's Independence Declaration under Section 307C of the Corporations Act 2001 to the Directors of The Ophthalmic Research Institute of Australia

I declare that, to the best of my knowledge and belief, during the year ended 30 June 2022, there have been:

(i) no contraventions of the auditor independence requirements as set out in the *Corporations Act 2001* in relation to the audit; and

(ii) no contraventions of any applicable code of professional conduct in relation to the audit.

Andrew Fisher FCA, Partner (auditor registration number 306364) on behalf of
Banks Group Assurance Pty Ltd, Chartered Accountants
Authorised audit company registration number 294178 (ACN 115 749 598)

20 March 2023

Banks Group | Accountants | Auditors | Advisers
801 Glenferrie Road, Hawthorn VIC 3122 (Locked Bag 50, Hawthorn VIC 3122) Australia
T +61 3 9810 0700 **F** +61 3 9815 1899 **E** reception@banksgroup.com.au www.banksgroup.com.au

Statement of Profit or Loss.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

Statement of Profit or Loss and Other Comprehensive Income
For the Year Ended 30 June 2022

	2022	2021
	$	$
Investment Income	**572,482**	514,849
Trust Distribution Income	**13,035**	22,617
Membership Fee Income	**178,035**	172,965
Donation Income	**51,000**	294,203
Realised gain on disposal of investments	**151,780**	113,019
Other Income	**7,334**	7,893
Total Income	**973,666**	1,125,546
Administrative expenses	**(379,000)**	(276,528)
Grants awarded	**(539,258)**	(428,853)
Employee Expenses	**(125,537)**	(94,056)
(Deficit) / Surplus before income tax	**(70,129)**	326,109
Income tax expense	**-**	-
(Deficit) / Surplus for the year	**(70,129)**	326,109
Net fair value movements for available-for-sale financial assets	**(1,605,852)**	1,800,680
Other comprehensive income for the year, net of tax	**(1,605,852)**	1,800,680
Total comprehensive (Deficit) / Surplus for the year	**(1,675,981)**	2,126,789

Statement of Financial Position.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

Statement of Financial Position
As At 30 June 2022

	Note	2022 $	2021 $
ASSETS			
CURRENT ASSETS			
Cash and cash equivalents	4	**2,881,102**	1,802,329
Trade and other receivables	5	**346,092**	398,279
Investments	6	**10,073,132**	12,509,613
TOTAL CURRENT ASSETS		**13,300,326**	14,710,221
NON-CURRENT ASSETS			
Property, plant and equipment		**4,537**	-
TOTAL NON-CURRENT ASSETS		**4,537**	-
TOTAL ASSETS		**13,304,863**	14,710,221
LIABILITIES			
CURRENT LIABILITIES			
Trade and other payables	7	**1,168,262**	897,639
TOTAL CURRENT LIABILITIES		**1,168,262**	897,639
NON-CURRENT LIABILITIES			
TOTAL LIABILITIES		**1,168,262**	897,639
NET ASSETS		**12,136,601**	13,812,582
EQUITY			
Research Fund	8	**2,638,254**	2,638,254
Settled Funds	9	**472,556**	472,556
Financial Asset Revaluation Reserve	10	**262,522**	1,868,374
Capitalised Profit on re-arrangement of investments, capital distribution & transfers	11	**7,426,618**	7,426,618
Retained Surplus	12	**1,336,651**	1,406,780
TOTAL EQUITY		**12,136,601**	13,812,582

Statement of Changes in Equity.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

Statement of Changes in Equity
For the Year Ended 30 June 2022

2022

	Research Fund	Settled Funds	Realised Profits on Capital Distributions and Transfers	Financial Assets reserve	Retained earnings	Total
	$	$	$	$	$	$
Balance at 1 July 2021	**2,638,254**	**472,556**	**7,426,618**	**1,868,374**	**1,406,780**	**13,812,582**
(Deficit)/ Surplus for the year	-	-	-	-	(70,129)	(70,129)
Transactions with owners in their capacity as owners						
Unrealised movement in investments held at year end	-	-	-	(1,605,852)	-	(1,605,852)
Balance at 30 June 2022	2,638,254	472,556	7,426,618	262,522	1,336,651	12,136,601

2021

	Research Fund	Settled Funds	Realised Profits on Capital Distributions and Transfers	Financial Assets reserve	Retained earnings	Total
	$	$	$	$	$	$
Balance at 1 July 2020	2,588,305	472,556	7,313,599	67,694	1,243,639	11,685,793
Surplus for the year	-	-	113,019	-	213,090	326,109
Transactions with owners in their capacity as owners						
Income	-	-	-	1,800,680	-	1,800,680
Transfer to / (from) Reserves	49,949	-	-	-	(49,949)	-
Unrealised movement in investments held at year end	-	-	-	-	-	-
Balance at 30 June 2021	2,638,254	472,556	7,426,618	1,868,374	1,406,780	13,812,582

Statement of Cash Flows.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

Statement of Cash Flows
For the Year Ended 30 June 2022

	Note	2022 $	2021 $
CASH FLOWS FROM OPERATING ACTIVITIES:			
Dividends Received		**278,784**	203,138
Interest Received		**118**	7,650
Trust Distributions		**169,630**	218,932
Other Revenue		**499,300**	180,084
RANZCO - Reimbursement of membership fees		**178,035**	172,965
Commissions		**(89,950)**	(74,285)
Research Grants Paid		**(539,257)**	(525,233)
Payments to suppliers and employees		**(243,833)**	(58,519)
Net cash provided by/(used in) operating activities	20	**252,827**	124,732
CASH FLOWS FROM INVESTING ACTIVITIES:			
Proceeds from re-arrangement of Investments		**-**	22,477,782
Payments for investments		**-**	(23,389,878)
Proceeds from sale of available-for-sale investments		**2,436,480**	-
Loss on sale of investments		**(1,605,853)**	**-**
Purchase of property, plant and equipment		**(4,681)**	-
Net cash provided by/(used in) investing activities		**825,946**	(912,096)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Net increase/(decrease) in cash and cash equivalents held		**1,078,773**	(787,364)
Cash and cash equivalents at beginning of year		**1,802,329**	2,589,693
Cash and cash equivalents at end of financial year	4	**2,881,102**	1,802,329

Notes to the Financial Statements.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

Notes to the Financial Statements
For the Year Ended 30 June 2022

The financial report covers The Ophthalmic Research Institute of Australia as an individual entity. The Ophthalmic Research Institute of Australia is a not-for-profit Company limited by guarantee, incorporated and domiciled in Australia.

The functional and presentation currency of The Ophthalmic Research Institute of Australia is Australian dollars.

Comparatives are consistent with prior years, unless otherwise stated.

1 Basis of Preparation

The financial statements are general purpose financial statements that have been prepared in accordance with the Australian Accounting Standards and the *Corporations Act 2001*.

The financial statements have been prepared on an accruals basis and are based on historical costs modified, where applicable, by the measurement at fair value of selected non-current assets, financial assets and financial liabilities.

Significant accounting policies adopted in the preparation of these financial statements are presented below and are consistent with prior reporting periods unless otherwise stated.

2 Summary of Significant Accounting Policies

2.1. Revenue and other income

Revenue from contracts with customers

The core principle of AASB 15 is that revenue is recognised on a basis that reflects the transfer of promised goods or services to customers at an amount that reflects the consideration the Company expects to receive in exchange for those goods or services. Revenue is recognised by applying a five-step model as follows:

1. Identify the contract with the customer

2. Identify the performance obligations

3. Determine the transaction price

4. Allocate the transaction price to the performance obligations

5. Recognise revenue as and when control of the performance obligations is transferred

Generally the timing of the payment for sale of goods and rendering of services corresponds closely to the timing of satisfaction of the performance obligations, however where there is a difference, it will result in the recognition of a receivable, contract asset or contract liability.

None of the revenue streams of the Company have any significant financing terms.

Notes to the Financial Statements
For the Year Ended 30 June 2022

2 Summary of Significant Accounting Policies

2.1. Revenue and other income

Specific revenue streams

The revenue recognition policies for the principal revenue streams of the Company are:

Investment and Trust Distribution Income

Revenue is recognised upon receipt of the dividend and trust distribution statement is received by the investment manager.

Membership Income

Is recognised when the Company becomes entitled to it.

2.2. Income Tax

The Company is exempt from income tax under Division 50 of the *Income Tax Assessment Act 1997*.

2.3. Goods and services tax (GST)

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 Taxation Office (ATO).

Receivables and payable are stated inclusive of GST.

Cash flows in the statement of cash flows are included on a gross basis and the GST component of cash flows arising from investing and financing activities which is recoverable from, or payable to, the taxation authority is classified as operating cash flows.

2.4. Financial instruments

Financial instruments are recognised initially on the date that the Company becomes party to the contractual provisions of the instrument.

On initial recognition, all financial instruments are measured at fair value plus transaction costs (except for instruments measured at fair value through profit or loss where transaction costs are expensed as incurred).

Financial assets

All recognised financial assets are subsequently measured in their entirety at either amortised cost or fair value, depending on the classification of the financial assets.

Classification

On initial recognition, the Company classifies its financial assets into the following categories, those measured at:

- fair value through other comprehensive income - equity instrument (FVOCI - equity)

Notes to the Financial Statements
For the Year Ended 30 June 2022

2 Summary of Significant Accounting Policies

2.4. Financial instruments

Financial assets

Financial assets are not reclassified subsequent to their initial recognition unless the Company changes its business model for managing financial assets.

Interest income, foreign exchange gains or losses and impairment are recognised in profit or loss. Gain or loss on derecognition is recognised in profit or loss.

Fair value through other comprehensive income

Equity instruments

The Company has a number of strategic investments in listed and unlisted entities over which are they do not have significant influence nor control. The Company has made an irrevocable election to classify these equity investments as fair value through other comprehensive income as they are not held for trading purposes.

These investments are carried at fair value with changes in fair value recognised in other comprehensive income (financial asset reserve). On disposal any balance in the financial asset reserve is transferred to retained earnings and is not reclassified to profit or loss.

Dividends are recognised as income in profit or loss unless the dividend clearly represents a recovery of part of the cost of the investment. Other net gains and losses are recognised in OCI.

Impairment of financial assets

Impairment of financial assets is recognised on an expected credit loss (ECL) basis for the following assets:

- financial assets measured at amortised cost
- investments measured at FVOCI

When determining whether the credit risk of a financial assets has increased significant since initial recognition and when estimating ECL, the Company considers reasonable and supportable information that is relevant and available without undue cost or effort. This includes both quantitative and qualitative information and analysis based on the Company's historical experience and informed credit assessment and including forward looking information.

The Company uses the presumption that an asset which is more than 30 days past due has seen a significant increase in credit risk.

The Company uses the presumption that a financial asset is in default when:

- the other party is unlikely to pay its credit obligations to the Company in full, without recourse to the Company to actions such as realising security (if any is held); or
- the financial assets is more than 90 days past due.

Notes to the Financial Statements

For the Year Ended 30 June 2022

2 Summary of Significant Accounting Policies

2.4. Financial instruments

Financial assets

Credit losses are measured as the present value of the difference between the cash flows due to the Company in accordance with the contract and the cash flows expected to be received. This is applied using a probability weighted approach.

Trade receivables

Impairment of trade receivables has been determined using the simplified approach in AASB 9 which uses an estimation of lifetime expected credit losses. The Company has determined the probability of non-payment of the receivable and multiplied this by the amount of the expected loss arising from default.

The amount of the impairment is recorded in a separate allowance account with the loss being recognised in finance expense. Once the receivable is determined to be uncollectable then the gross carrying amount is written off against the associated allowance.

Where the Company renegotiates the terms of trade receivables due from certain customers, the new expected cash flows are discounted at the original effective interest rate and any resulting difference to the carrying value is recognised in profit or loss.

Other financial assets measured at amortised cost

Impairment of other financial assets measured at amortised cost are determined using the expected credit loss model in AASB 9. On initial recognition of the asset, an estimate of the expected credit losses for the next 12 months is recognised. Where the asset has experienced significant increase in credit risk then the lifetime losses are estimated and recognised.

2.5. Impairment of non-financial assets

At the end of each reporting period the Company determines whether there is evidence of an impairment indicator for non-financial assets.

Where an indicator exists and regardless for indefinite life intangible assets and intangible assets not yet available for use, the recoverable amount of the asset is estimated.

Where assets do not operate independently of other assets, the recoverable amount of the relevant cash-generating unit (CGU) is estimated.

The recoverable amount of an asset or CGU is the higher of the fair value less costs of disposal and the value in use. Value in use is the present value of the future cash flows expected to be derived from an asset or cash-generating unit.

Where the recoverable amount is less than the carrying amount, an impairment loss is recognised in profit or loss.

Reversal indicators are considered in subsequent periods for all assets which have suffered an impairment loss.

Notes to the Financial Statements
For the Year Ended 30 June 2022

2 Summary of Significant Accounting Policies

2.6. Cash and cash equivalents

Cash and cash equivalents comprises cash on hand, demand deposits and short-term investments which are readily convertible to known amounts of cash and which are subject to an insignificant risk of change in value.

3 Critical Accounting Estimates and Judgments

The directors make estimates and judgements during the preparation of these financial statements regarding assumptions about current and future events affecting transactions and balances.

These estimates and judgements are based on the best information available at the time of preparing the financial statements, however as additional information is known then the actual results may differ from the estimates.

The significant estimates and judgements made have been described below.

Key estimates - fair value of financial instruments

The Company has certain financial assets and liabilities which are measured at fair value. Where fair value has not able to be determined based on quoted price, a valuation model has been used. The inputs to these models are observable, where possible, however these techniques involve significant estimates and therefore fair value of the instruments could be affected by changes in these assumptions and inputs.

Key estimates - receivables

The receivables at reporting date have been reviewed to determine whether there is any objective evidence that any of the receivables are impaired. An impairment provision is included for any receivable where the entire balance is not considered collectible. The impairment provision is based on the best information at the reporting date.

4 Cash and Cash Equivalents

	2022	2021
	$	$
Cash at bank and in hand	**2,881,102**	1,802,329
	2,881,102	1,802,329

5 Trade and Other Receivables

	2022	2021
	$	$
CURRENT		
Franking Credit Receivable	**216,847**	212,410
Other receivables	**129,245**	185,869
Total current trade and other receivables	**346,092**	398,279

The carrying value of trade receivables is considered a reasonable approximation of fair value due to the short-term nature of the balances.

Notes to the Financial Statements
For the Year Ended 30 June 2022

5 Trade and Other Receivables

The maximum exposure to credit risk at the reporting date is the fair value of each class of receivable in the financial statements.

6 Investments

	2022 $	2021 $
CURRENT		
Listed shares	**10,073,132**	12,509,613
	10,073,132	12,509,613

7 Trade and Other Payables

	2022 $	2021 $
CURRENT		
Trade payables	**25,181**	14,960
Director of Research - Victoria	**748,443**	618,443
Grants Payable	**294,638**	264,236
Income received in advance	**100,000**	-
	1,168,262	897,639

8 Research Capital Fund

	2022 $	2021 $
General		
Balance 1 July 2021	**2,316,897**	2,266,948
Allocation to Capital		
10% surplus & Imputation Credits and other legacies	-	49,949
Balance as at 30 June 2022	**2,316,897**	2,316,897
Anselmi Estate		
Balance as at 1 July 2021	**290,979**	290,979
Balance as at 30 June 2022	**290,979**	290,979
Ivy May Stephenson Estate		
Balance as at 1 July 2021	**30,378**	30,378
Balance as at 30 June 2022	**30,378**	30,378
Total	**2,638,254**	2,638,254

Notes to the Financial Statements
For the Year Ended 30 June 2022

9 Settled Funds

	2022	2021
	$	$
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 32/3/84)	**56,707**	56,707
Ronald & Lois Lowe	**40,000**	40,000
Total	**472,556**	472,556

10 Financial Assets Reserve

	2022	2021
	$	$
CURRENT		
Opening balance 1 July	**1,868,374**	67,694
Revaluation (decrement)/ increment	**(1,605,852)**	1,800,680
Balance as at 30 June	**262,522**	1,868,374

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

	Balance 30 June 2021	Allocation of Realised Profit/ (loss) on Rearrangement of Investments & Capital Distribution & Transfer	Balance 30 June 2022
	$	$	$
Research Fund			
General	153,433	-	153,433
Anselmi Estate	54,953	-	54,953
Ivy May Stephenson	140	-	140
D.W Research Funds	5,344,969	-	5,344,969
Esme Anderson	1,079,845	-	1,079,845
G.J Williams	185,689	-	185,689
B. Mitchell	183,752	-	183,752
Dame Ida Mann	259,323	-	259,323
Ronald & Loise Lowe	164,514	-	164,514
Total	7,426,618	-	7,426,618

Notes to the Financial Statements
For the Year Ended 30 June 2022

12 Retained Earnings

	2022	2021
	$	$
Accumulated Deficit - 30 June	-	-
Retained income	**1,406,780**	1,243,639
Total Comprehensive (loss) / Income	**(70,131)**	163,141
Total available for appropriation	**1,336,649**	1,406,780

13 Financial Risk Management

The Company is exposed to a variety of financial risks through its use of financial instruments.

The Company's overall risk management plan seeks to minimise potential adverse effects due to the unpredictability of financial markets.

The most significant financial risks to which the Company is exposed to are described below:

Specific risks

- Liquidity risk
- Credit risk
- Market risk - currency risk, interest rate risk and price risk

Notes to the Financial Statements
For the Year Ended 30 June 2022

13 Financial Risk Management

Financial instruments used

The principal categories of financial instrument used by the Company are:

- Trade receivables
- Cash at bank
- Investments in listed shares
- Trade and other payables

	2022 $	2021 $
Financial assets		
Held at amortised cost		
Cash and cash equivalents	**2,881,102**	1,802,329
Trade and other receivables	**346,092**	398,279
Fair value through Other Comprehensive Income		
Revaluation of listed investments	**(1,605,850)**	1,913,699
Total financial assets	**1,621,344**	4,114,307
Financial liabilities		
Trade payables	**25,182**	14,958
Total financial liabilities	**25,182**	14,958

Objectives, policies and processes

The Board of Directors have overall responsibility for the establishment of The Ophthalmic Research Institute of Australia's financial risk management framework. This includes the development of policies covering specific areas such as foreign exchange risk, interest rate risk, liquidity risk, credit risk and the use of derivatives.

Risk management policies and systems are reviewed regularly to reflect changes in market conditions and The Ophthalmic Research Institute of Australia's activities.

The Board of Directors receives monthly reports which provide details of the effectiveness of the processes and policies in place.

Mitigation strategies for specific risks faced are described below:

Liquidity risk

Liquidity risk arises from the Company's management of working capital and the finance charges and principal repayments on its debt instruments. It is the risk that the Company will encounter difficulty in meeting its financial obligations as they fall due.

Notes to the Financial Statements
For the Year Ended 30 June 2022

13 Financial Risk Management

Liquidity risk

The Company's policy is to ensure that it will always have sufficient cash to allow it to meet its liabilities as and when they fall due. The Company maintains cash and marketable securities to meet its liquidity requirements for up to 30-day periods. Funding for long-term liquidity needs is additionally secured by an adequate amount of committed credit facilities and the ability to sell long-term financial assets.

Liquidity needs are monitored in various time bands, on a day-to-day and week-to-week basis, as well a rolling 30-day projection. Long-term liquidity needs for a 180-day and a 360-day period are identified monthly.

At the reporting date, these reports indicate that the Company expected to have sufficient liquid resources to meet its obligations under all reasonably expected circumstances and will not need to draw down any of the financing facilities.

The timing of cash flows presented in the table to settle financial liabilities reflects the earliest contractual settlement dates and does not reflect management's expectations that banking facilities will be rolled forward. The amounts disclosed in the table are the undiscounted contracted cash flows and therefore the balances in the table may not equal the balances in the statement of financial position due to the effect of discounting.

Market risk

Market risk is the risk that the fair value or future cash flows of a financial instrument will fluctuate because of changes in market prices.

Sensitivity analysis

The following table illustrates the sensitivity of the net result for the year and equity to a reasonably possible change in interest rates of +1.00% and -(1.00)% (2021: +1.00%/-1.00%), with effect from the beginning of the year. These changes are considered to be reasonably possible based on observation of current market conditions and economist reports.

The calculations are based on the financial instruments held at each reporting date. All other variables are held constant.

	2022		2021	
	+1.00%	-1.00%	+1.00%	-1.00%
	$	$	$	$
Surplus/ (Deficit) for the year	1,827	(1,827)	2,064	(2,064)
Cash and cash equivalents	28,811	(28,811)	18,023	(18,023)

Notes to the Financial Statements
For the Year Ended 30 June 2022

13 Financial Risk Management

(i) Interest rate risk

Financial instrument composition and maturity analysis

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

	Weighted Average Effective Interest Rate		Non-interest Bearing		Total	
	2022	**2021**	**2022**	**2021**	**2022**	**2021**
	%	**%**	**$**	**$**	**$**	**$**
Financial Assets:						
Cash and cash equivalents	**0.40**	0.40	**2,881,102**	1,802,329	**2,881,102**	1,802,329
Shares	**-**	-	**10,073,132**	12,509,613	**10,073,132**	12,509,613
Receivables	**-**	-	**346,091**	398,279	**346,091**	398,279
Total Financial Assets			**13,300,325**	14,710,221	**13,300,325**	14,710,221
Financial Liabilities:						
Trade and sundry payables	**-**	-	**1,054,369**	897,637	**1,054,369**	897,637
Total Financial Liabilities	**-**	-	**1,054,369**	897,637	**1,054,369**	897,637

(ii) Price risk

Price risk relates to the risk that the fair value or future cash flows of a financial instrument will fluctuate because of changes in market prices of securities held being available-for-sale or fair value through profit and loss.

There is no profit impact, except for investments held at fair value through profit or loss. Equity would increase / decrease as a result of fair value movements through the financial asset reserve.

14 Members' Guarantee

The Company is incorporated under the *Corporations Act 2001* and is a Company limited by guarantee. If the Company is wound up, the constitution states that each member is required to contribute a maximum of $ 10 each towards meeting any outstanding obligations of the Company. At 30 June 2022 the number of members was 10 (2021: 10).

Notes to the Financial Statements
For the Year Ended 30 June 2022

15 Grants Allocated/ Made During the Year

	2022 $	2021 $
Prof Robyn Jamieson	**50,000**	50,000
Prof Robert Casson	**-**	47,100
Dr Jason Charng	**-**	47,800
Dr Elisa Cornish	**-**	50,000
Dr Shweta Kaushik	**-**	49,985
Dr Grace Lidgerwood	**-**	35,000
A/Prof Chi Luu	**-**	48,970
Dr Carla Mellough	**-**	50,000
Dr Tina Zhang	**-**	49,986
Adjustments	**-**	(30)
Dr Jamie Craig	**49,494**	-
Dr Stephanie Watson	**50,000**	-
Dr Fan Fan Zhou	**49,904**	-
Dr Ling Zhu	**49,856**	-
Dr Vivek Gupta	**49,856**	-
Dr Kathryn Burdon	**48,430**	-
Dr Ayub Qassim	**49,718**	-
Dr Peter Van Wijngaarden	**49,994**	-
Dr Devaraj Basavarajappa	**49,811**	-
Dr Jessica Mountford	**42,195**	-
Sub total	**539,258**	428,811
Deduct Contributions from:		
Perth Eye Foundation	**-**	50,000
ANZSRS	**-**	25,000
RANZCO Eye Foundation	**-**	50,000
RANZCO NSW Branch	**-**	150,000
Other	**-**	22,000
Sub total	**-**	297,000
Net	**539,258**	131,853

16 Key Management Personnel Remuneration

The remuneration paid to key management personnel of The Ophthalmic Research Institute of Australia during the year is as follows:

	2022 $	2021 $
Short-term employee benefits	**124,877**	94,056
Long-term benefits	**13,296**	10,816
	138,173	104,872

Notes to the Financial Statements
For the Year Ended 30 June 2022

17 Auditors' Remuneration

	2022 $	2021 $
Remuneration of the auditor Banks Group Assurance Pty Ltd (2021: Orr Martin and Waters), for:		
- auditing or reviewing the financial statements	**8,000**	8,000
Total	**8,000**	8,000

18 Fair Value Measurement

The Company measures the following assets and liabilities at fair value on a recurring basis:

- Financial assets
  - Listed Shares

Fair value hierarchy

AASB 13 *Fair Value Measurement* requires all assets and liabilities measured at fair value to be assigned to a level in the fair value hierarchy as follows:

Level 1	Unadjusted quoted prices in active markets for identical assets or liabilities that the entity can access at the measurement date.
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 table below shows the assigned level for each asset and liability held at fair value by the company:

30 June 2022	**Level 1 $**	**Level 2 $**	**Level 3 $**	**Total $**
Recurring fair value measurements				
Financial assets				
Listed Shares	**10,073,132**	**-**	**-**	**10,073,132**

30 June 2021	**Level 1 $**	**Level 2 $**	**Level 3 $**	**Total $**
Recurring fair value measurements				
Financial assets				
Listed Shares	12,509,613	-	-	12,509,613

Notes to the Financial Statements
For the Year Ended 30 June 2022

18 Fair Value Measurement

Transfers between levels of the hierarchy

There were no transfers between levels of the fair value hierarchy.

19 Contingencies

In the opinion of the Directors, the Company did not have any contingencies at 30 June 2022 (30 June 2021:None).

20 Cash Flow Information

Reconciliation of result for the year to cashflows from operating activities

	2022	2021
	$	$
Net surplus/ (deficit)	**(1,675,981)**	2,126,787
Cash flows excluded from profit attributable to operating activities		
Non-cash flows in profit:		
- depreciation	**144**	835
- fair value movements on investments	**1,605,853**	(1,800,680)
- (gain)/loss on rearrangement of investments	**-**	113,018
Changes in assets and liabilities:		
- increase/decrease in trade and other receivables	**152,184**	(318,819)
- increase/ decrease in trade and other payables	**10,226**	(30,029)
- increase/decrease in grants payable	**30,401**	(96,380)
- increase/decrease in allocation to Director of Research - Victoria	**130,000**	130,000
Cashflows from operations	**252,827**	124,732

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 2022 from the foundation was $23,000.

Notes to the Financial Statements
For the Year Ended 30 June 2022

22 Events after the end of the Reporting Period

No matters or circumstances have 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.

23 Statutory Information

The principal place of business of the company is:
The Ophthalmic Research Institute of Australia
94-98 Chalmers St
Surrey Hills NSW 2010

Directors' Declaration.

The Ophthalmic Research Institute of Australia

ABN 37 008 393 146

The directors of the entity declare **that:**

1. The financial statements and notes, as set out on pages 5 to 23, are in accordance with the *Corporations Act 2001* and:

   (a) comply with Australian Accounting Standards; and

   (b) give a true and fair view of the financial position as at 30 June 2022 and of the performance for the year ended on that date of the entity.

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

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

Stephanie Watson (Mar 20, 2023 10:26 GMT+11)

Director .....
Prof Stephanie Watson, NSW Chair

P Healey (Mar 20, 2023 11:21 GMT+11)

Director .....
A/Prof Paul Healey, NSW

Dated 20/03/2023

20/03/2023

Independent Audit 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 Company), which comprises the statement of financial position as at 30 June 2022, the statement of profit or loss and other comprehensive income, the statement of changes in equity and the 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 Company is in accordance with the *Corporations Act 2001*, including:

(i) giving a true and fair view of the Company's financial position as at 30 June 2022 and of its financial performance for the year ended; and

(ii) complying with Australian Accounting Standards and the *Corporations Regulations 2001*.

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 Company in accordance with the auditor independence requirements of the *Corporations Act 2001* and the ethical requirements of the Accounting Professional and Ethical Standards Board's APES 110 *Code of Ethics for Professional Accountants (including Independence Standards)* (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 confirm that the independence declaration required by the *Corporations Act 2001*, which has been given to the directors of the Company, would be in the same terms if given to the directors as at the time of this auditor's report.

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

Responsibilities of Directors for the Financial Report

The directors of the Company are responsible for the preparation of the financial report that gives a true and fair view in accordance with Australian Accounting Standards and the *Corporations Act 2001* 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 Company'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 Company or to cease operations, or have no realistic alternative but to do so.

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 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 the financial report.

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The Ophthalmic Research Institute of Australia

Independent Audit Report to the members of The Ophthalmic Research Institute of Australia

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 Company'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 Company'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 Company 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.

We also provide the directors with a statement that we have complied with relevant ethical requirements regarding independence, and to communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, actions taken to eliminate threats or safeguards applied.

Banks Group Assurance Pty Ltd, Chartered Accountants
Authorised audit company number 294178 (ACN 115 749 598)

Andrew Fisher FCA, Partner
Registration number 306364

Melbourne, Australia

Date: 20 March 2023

21-22 ANNUAL REPORT

AUSTRALIAN VISION RESEARCH

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