



Annual Report for CLEM JONES CENTRE FOR REGENERATIVE MEDICINE, BOND UNIVERSITY – 2022

Mission Statement

The Centre was established to investigate the therapeutic use of stem cells in tissue repair and disease. Research excellence is combined with clinical translation to differentiate, develop and transplant stem cells for patient benefit.

An important long-term translational project has been the application of stem cell therapy to the improvement of vision in age-related macular degeneration (AMD).

The Centre supports research and teaching in the broader field of regenerative medicine and stem cell biology, combining stem cell science, biomaterials, tissue engineering and tissue regeneration, novel drugs to control inflammation, and advanced surgery.

Advisory Circle - Terms of Reference

An Advisory Circle was established in 2022 to advise the Director on achieving the mission of the Centre. Members of the inaugural Circle include Dr Darryl Gregor (Chair), Peter Johnston, Dr Robert Bourke, Professor Helen O'Neill (as Centre Director) and Professor Nick Zwar (as Dean HSM). Terms of Reference for the Advisory Circle were identified:

- As a source of independent advice to the Centre Director
- To ensure that research is relevant, top quality and international
- To advise on building linkages with industry, government and the wider community
- To advise on engagement for philanthropy

An Operational Plan for the Centre

A set of objectives for research outcomes was drawn up midyear and then became the subject of discussion at a year-end Planning Day. This successful event drew together all staff to review achievements in the year and to set in place new project priorities and plans for 2023. The operational plan going forward also includes greater networking for philanthropy. With the assistance of the Office of Engagement, Sarah Rainbird was employed as a consultant to advise on

philanthropy, prepare a Fundraising Capability Review, a Case for Support and to hold a workshop on fundraising. Following her involvement, a donation site was established on our webpage, a flyer was printed for distribution and fundraising booklet have been prepared.

Forward projects supported by the Centre

1. Methodologies for production of clinical grade retinal cells from pluripotent stem cells. This work has now been extended to include production of retinal pigment epithelial cells, photoreceptors, neural retinal cells and retinal organoids. The goal is development of cell differentiation methods which are efficient and fully defined, and can produce cells in numbers suitable for clinical use. Collaborations established this year now ensure a supply of clinical grade human induced pluripotent stem cells from super-donors with a view to production of cell banks of retinal cells of known histocompatibility type.
2. Development of surgical procedures for transplantation of stem cell-derived retinal cells for tissue regeneration. In terms of developing a cell therapy for macular degeneration, this will involve implantation of cell-on-membrane constructs into vision-impaired animals and eventually humans. Electrospun nanofibre membranes are prepared to exact specification and used to support monolayer growth of stem cell-derived retinal pigment epithelial cells. Pre-clinical studies will test cell survival, regeneration of the retina, impact on disease progression and recovery of vision.
3. Development and testing of novel drugs to enhance the survival of retinal cells within the hostile environment of the diseased eye. Drug therapy involves the delivery of enhanced antioxidant compounds, and the reduction of inflammatory responses within the retina using a range of novel anti-inflammatory drugs. This work has been extended from investigation *in vitro* to studies on animal models with impaired vision. The eventual goal is development of drugs which can condition the diseased eye for better acceptance of cell implants for vision recovery.

Research Highlights in 2022

- Development of differentiation protocols for production of Rod and Cone photoreceptors *in vitro*. Jason Limnios and Davinia Beaver
- Australian patent awarded in December 2022 on Jason Limnios' procedure for differentiating retinal pigment epithelial cells from pluripotent stem cells.

Significant contributions

Centre staff were active in supervision of 3 PhD, 2 Masters students, and 2 MD students across 2022. Helen O'Neill gave a lecture during Research Week showcasing vision research in the Centre. Jon Tan lectured on Regenerative Medicine in 2 courses delivered by the Biomedical Sciences Program at Bond. Jason Limnios has worked diligently toward greater public awareness of the Centre research. He has also fostered connections with Guide Dogs Australia and the Blind Cricket Association to advance fundraising and public awareness of macular degeneration and blindness.

Research productivity

Papers in press and under submission

1. Tran, V. and **O'Neill, H.C.** (2022) Role of SVEP1 in stroma-dependent hematopoiesis *in vitro*. *Frontiers in Cellular and Developmental Biology*, **9**:760480. <https://doi.org/10.3389/fcell.2021.760480>
2. Petvises, S., Tran, V., Hey, Y-Y., Talaulikar, D., O'Neill, T.J., **Tan, J.** and **O'Neill, H.C.** (2022) Extramedullary hematopoiesis: mesenchymal stromal cells from spleen provide an *in vitro* niche for myelopoiesis. *In vitro Cellular and Developmental Biology – Animal*, 31 May 2022, <https://doi.org/10.1007/s11626-022-00693-8>
3. Patel, K., **Beaver, D.**, Gruber, N., Printezis, G., & Giannopulu, I. (2022). Mental imagery of whole-body motion along the sagittal-anteroposterior axis. *Scientific Reports*, **12**(1), [14345]. <https://doi.org/10.1038/s41598-022-18323-4>
4. **O'Neill, H.C.** and **Lim, H.K.** (2023) Skeletal stem/progenitor cells provide the niche for extramedullary hematopoiesis in spleen. *Frontiers in Physiology* **14**:1148414. <https://doi.org/10.3389/fphys.2023.1148414>
5. **Mammone, T.** (Author). (2022). 3MT - A picture tells 80,000 words. Digital or Visual Products <https://vimeo.com/735304049>
6. **Beaver, D.**, **O'Neill, H.C.** and **Limnios, I. J.** (2023) A Treatment Within Sight: Challenges in the development of stem cell-derived photoreceptor therapies for retinal diseases. *Frontiers in Transplantation*, Submitted.
7. **Rayner, C.R.**, **Bottle, S.E.**, Martyn, A.P. and **Barnett, N.R.** (2023) Preserving Retinal Structure and Function with the Novel Nitroxide Antioxidant, DCTEIO. *Neurochemical Research*, Submitted.
8. **Rayner, C.R.**, **Bottle, S.E.**, Tong, J., Thomas, K. and **Barnett, N.R.** (2023) Comparative antioxidant properties of novel NSAID-Nitroxide hybrid compounds in retinal cells. In preparation.
9. **Toto, R.**, Byambasuren, O. and **Barnett, N.L.** (2023) Oxidative stress and inflammation in neovascular Age-related Macular Degeneration and advancements in drug therapy. *International Journal of Molecular Sciences*, In preparation.

Conference Abstracts

1. **Beaver, D.**, **O'Neill, H.C.** and **Limnios, I. J.** (2022) Development of a small molecule protocol for the differentiation of human pluripotent stem cells (hPSCs) to photoreceptors. *NSW Stem Cell Network*, Sydney, Australia.
2. **Beaver, D.**, **O'Neill, H.C.** and **Limnios, I. J.** (2023) Development of a small molecule protocol for the differentiation of human pluripotent stem cells (hPSCs) to photoreceptors. *International Society of Eye Research*, Gold Coast, Australia.
3. **Mammone, T.**, **O'Neill, H.C.**, and **Barnett, N.** (2023) Hyperreflective foci in a rat model of choroidal neovascularization. *International Society of Eye Research*, Gold Coast, Australia.
4. **Toto, R.**, **Mammone, T.**, **Bottle, S.**, **Byambasuren, O.** and **Barnett, N.L.** (2023) Effect of novel nitroxide-corticosteroid hybrid compounds on retinal vasculature in a rodent model of laser-induced age-related macular degeneration. *International Society of Eye Research*, Gold Coast, Australia.
5. **Barnett, N.L.**, **Rayner, C.L.** and **Bottle, S.E.** (2023) Preserving post-ischaemic retinal function and structure with the novel nitroxide antioxidant, DCTEIO. *International Society of Eye Research*, Gold Coast, Australia.

Confirmation of Candidature for HDR students

Rimaz Toto MSc
 Davinia Beaver MSc conversion to PhD

Grants held in 2021

2022	Nosegay Investment Trust (\$40,000)
2021-2024	Clem Jones Foundation (\$300,000)
2022	RIBG equipment funding: Tissue culture incubator (\$9800); Animal technician support (\$18,000).
2021-2024	NHMRC Ideas Grant APP2002239 (\$1,189,692). Investigating microRNAs as key regulators in a novel communication pathway driving retinal degeneration.
2020-2023	NHMRC Ideas Grant APP1168742 (\$683,062). Retinal stem cell therapy in the immune-privileged eye.
2022	Cutmore Bequest for Stem Cell Research (ongoing support).

Centre staff and students

Professor Helen O'Neill, Centre Director
 Associate Professor Nigel Barnett, Associate Professor
 Dr Jonathan Tan, Assistant Professor
 Dr Jason Limnios, Senior Postdoctoral Research Fellow
 Dr Naghmed Abbasi, Postdoctoral Research Fellow
 Karin Tourle, Senior Research Assistant, Centre Manager
 Cassie Rayner, Senior Research Assistant
 Christie Short, PhD student: Supervisors Tan & O'Neill
 Teresa Mammone, PhD student/Senior Research Assistant: Supervisors Barnett & O'Neill
 Jessica Smith, PhD student/Research Assistant: Supervisors (Moro) & Tan
 Minnie Kim, PhD student: Supervisors Levonis, Schweiker & Tan
 Rimaz Toto, MSc student: Supervisor Barnett
 Davina Beaver, Research Assistant/MSc student: Supervisors Limnios & O'Neill
 Amber Rucinski, Research Assistant/MD student: Supervisor Tan & Limnios
 Alex Grainger, MD student: Supervisors: Tan & Limnios
 Macarena Gonzalez, Research Assistant/Medical student
 Aiden McKeon, Research Assistant/PhD student

Collaborators

Professor Alan Trounson (Cartherics, Monash)
 Professor Richard Boyd (Cartherics, Monash)
 Professor Mike Robinson (Miami U)
 Professor Katia Del-Tsonis (Miami U)
 Professor James Hurley (Univ of Washington)
 Professor Steven Bottle (QUT)
 Associate Professor Riccardo Natoli (ANU)
 Professor Traian Chirila (QLD Eye Institute)
 Professor Takeshi Watanabe (Kyoto)
 Dr Robert Bourke (Eye Specialist institute)
 Dr Lewis Lim (Eye Specialist institute)
 Dr Silvio Tiziano (CCRM)
 Dr Chih-Wei Teng (CCRM)
 Dr Hong Lim (QIMR)

Visitors to the Centre

Emeritus Professor David Vaney (UQ)
 Associate Professor Chris Layton (UQ)

Associate Professor Riccardo Natoli (ANU)
Professor Steven Bottle (QUT)
Dr Silvio Tiziani (CEO, CCRM)
Dr Chih-wei Teng (COO, CCRM)
Mr Don Cutmore
Ms Janet Price
Ms Roz Bull