



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

Prof. HC O'Neill – Cutmore Distinguished Professorship of Stem Cell Research

Current 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 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 superdonors 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 strategies include the delivery of enhanced antioxidant compounds, and the reduction of inflammatory responses within the retina using a range of novel anti-inflammatory drug types. 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.
4. Regeneration of spleen tissue as a site for extramedullary hematopoiesis. The unusual capacity of spleen to regenerate offers opportunity to provide new environments to support hematopoiesis with ageing. The spleen provides niches for hematopoietic stem/progenitor cells and supports myelopoiesis, particularly following periods of stress. Previous work has determined the spleen organiser cells and identified the requirement for an endothelial spleen organiser cell as well as a specific stromal cell subset in tissue regeneration. Future work aims to determine

transplantation procedures which provide outgrowth of spleen tissue which fully support hematopoiesis and immune functions unique to spleen. Importantly the B1a B cell composition of regenerating spleen is under investigation.

Research Highlights in 2021

- Nigel Barnett won a 4-year \$683,062 NHMRC Ideas grant (2021-2024) with his collaborators at ANU and UQ: 'Investigating microRNAs as key regulators in a novel communication pathway driving retinal degeneration.'
- Naghmed Abbasi, who recently graduated with a PhD from Griffith University, joined the Centre as a Research Fellow in Biomaterials and Tissue Engineering.
- Helen O'Neill was awarded the Vice-Chancellor's Award for Excellence in Research.
- Centre Research was selected for showcasing during Research Week at Bond University. The event was open to the public and provided a forum for networking with the local clinical and philanthropic community.

Significant contributions

Centre staff were active in supervision of 3 PhD, 2 Masters students, 1 Honours and 2 MD students across 2021. Three staff gave public lectures during Research Week as part of the Centre Showcase on Vision Research. Nigel Barnett served on an NHMRC Ideas Grant Review panel. Jon Tan lectured on Regenerative Medicine in 2 courses delivered by the Biomedical Sciences Program at Bond. Jason Limnios contributed three media presentations to the general public including a podcast for Life Science Queensland on regenerative therapies to treat vision loss, an Expert Opinion on 'iBlastoids: making human embryos from skin cells', and a Science Education programme on ABC Radio about "Cloning stem cells and reprogramming".

Research productivity across 2021

In 2021, researchers published four major research papers and presented papers at four conferences. Several papers are also in preparation or under submission.

Papers

Shen W, Lee SR, Mathai AE, Zhang R, Du J, Yam MX, Pye V, Barnett NL, Rayner CL, Zhu L, Hurley JB, Seth P, Hirabayashi Y, Furuya S, Gillies MC. (2021) Effect of selectively knocking down key metabolic genes in Muller glia on photoreceptor health. *Glia* 69(8):1966-1986.

Limnios IJ, Chau YQ, Skabo SJ, Surrao DC, O'Neill HC (2021). Efficient differentiation of human embryonic stem cells to retinal pigment epithelium under defined conditions. *Stem Cell Research and Therapy* 12(1):248.

Greferath U, Huynh M, Jobling AI, Vessey KA, Venables G, Surrao D, O'Neill HC, Limnios IJ, Fletcher EL. (2021) Dorsal-Ventral Differences in Retinal Structure in the Pigmented Royal College of Surgeons Model of Retinal Degeneration. *Frontiers in Cellular Neuroscience* 14:553708.

Tran V, O'Neill HC. (2021) Role of SVEP1 in stroma-dependent hematopoiesis *in vitro*. *Frontiers in Cellular and Developmental Biology* 2021: 760480.

Grants held in 2021

- 2021 Nosegay Investment Trust (\$40,000)
- 2021-2024 Clem Jones Foundation (\$300,000)
- 2021 Early Career Researcher Grant to Jason Limnios (\$4860)
- 2021 RIBG equipment funding: Nikon software for microscopy; Animal technician support; Equipment for ophthalmic surgery (\$35,667)
- 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 immunoprivileged eye.
- 2021 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, 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
 Jason Tong, MPhil student (UQ): Supervisor Barnett
 Davina Beaver, MSc student/Research Assistant: Supervisors Limnios & O'Neill
 Dayna Bushell, Honours student: Supervisor (Moro) & Tan
 Lucy Yuan, Research Assistant/Medical Student
 Amber Rucinski, Research Assistant/MD student (Supervisor Tan)
 Alex Grainger, MD student (Supervisor Tan)
 Eleanor West, Research Assistant/PhD student
 Macarena Gonzalez, Research Assistant/Medical student

Partner organisations

Centre for Commercialisation of Regenerative Medicine (Toronto, Melbourne)
 Cartherics Pty Ltd (Monash, VIC)

Collaborators

Professor Alan Trounson (Cartherics, Monash)
 Professor Richard Boyd (Cartherics, Monash)
 Professor Mike Robinson (Miami U)
 Professor Del Rio-Tsonis (Miami U)
 Professor James Hurley (Univ of Washington)
 Professor Steven Bottle (QUT)
 Associate Professor Riccardo Natoli (ANU)
 Professor Chen Chen (UQ)

Professor Takeshi Watanabe (Kyoto)

Visitors to the Centre

Professor Damien Harkin (QUT)
Professor Steven Bottle (QUT).
Associate Professor Anthony Kwan (QEI/UQ)
Dr Silvio Tiziani (CEO, CCRM)
Dr Chih-wei Teng (COO, CCRM)
Mr Don Cutmore
Ms Janet Price
Ms Roz Bull

Moving forward into 2022

The Centre now has 8 research staff and 7 student research assistants all with complimentary skills across vision science, stem cell biology, molecular biology, immunology and transplantation biology. The Centre now has a fully equipped vision physiology lab, stem cell and cell isolation laboratories and an animal holding facility so that all experimentation on animals can be performed on site.

Across 2021, the main source of funding for the Centre was the Cutmore Bequest, Bond University and an NHMRC grant supporting preclinical testing of a stem cell therapy for AMD. The Centre was fortunate to receive a further trench of funding from the Clem Jones Foundation (\$300K) beginning in July 2021 and extending for three years.

Across 2021, strategic planning for new grant applications and projects was emphasized. The Centre was successful in three applications for Research Infrastructure Block Grant funding to purchase new equipment. These led to award of matched funding for 'HSM Animal Holding Room Support', 'Multifocal Electroretinography Equipment' and 'Workstation for the Confocal Microscope'.

The Centre has been working with the Office of Engagement to seek philanthropic funding to a cell therapy for macular degeneration through to the proof-of-concept stage. With increased funding, the Centre would recruit more researchers to support excellent stem cell research and to develop an active, collaborative team.