CLEM JONES CENTRE FOR REGENERATIVE MEDICINE

RESEARCH HIGHLIGHTS - 2019

The Clem Jones Centre for Regenerative Medicine continued to support studies in stem cell biology and regenerative medicine with an emphasis on translational research for therapeutic benefit. In 2018, research was supported by funding from the NHMRC, the Clem Jones Foundation and philanthropic donations. The Centre benefitted for the first time from the Cora Cutmore Bequest awarded to Bond University to support stem cell research.

Associate Professor Nigel Barnett

Centre staff have expertise in stem cell differentiation and isolation, tissue organogenesis and regeneration, tissue engineering and surgery for transplantation. Two main research themes of research include: (1) development of a stem cell therapy for age-related macular degeneration (AMD), and (2) spleen as an alternative site for hematopoiesis.

A highlight for the year was the engagement of Associate Professor Nigel Barnett, a vision scientist with extensive experience in retinal physiology in diseases like AMD, diabetic retinopathy and glaucoma. The Centre now has seven research staff and three higher degree research students. In 2018, PhD student Christie Short won the HSM Best Lightning Oral presentation entitled: Improving hematopoietic recovery following high-dose irradiation and stem cell transplantation.

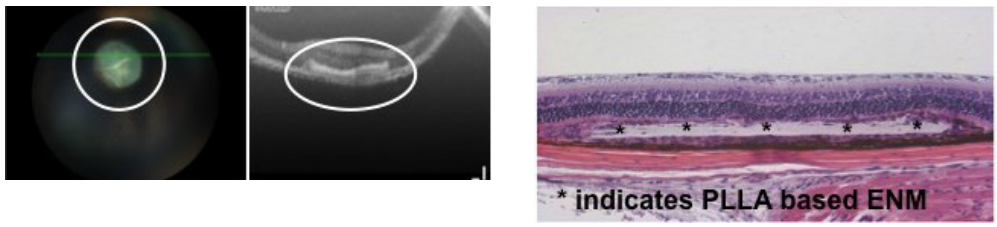
A Cell Laboratory was established this year and new equipment acquired through an NHMRC Equipment grant to Dr Jon Tan. Associate Professor Barnett was successful in an application for a Research Infrastructure Block Grant to purchase a Phoenix Micron IV Retinal Imaging System to expand the Vision Laboratory. Single cell gene expression profiling was introduced into the Centre for analysis of stem cells and their development.

Centre and Research Office staff attended an Equipment Grant presentation by Karen Andrews MP (left) to Deputy Vice Chancellor (Academic) Professor Keitha Dunstan (right).

Stem cell therapy for AMD

The goal has been to prepare a cell-on-membrane construct for implantation of retinal cells into the eye to replace cells damaged by AMD. A biodegradable, electrospun membrane which is thin and porous was used to transfer and support a layer of retinal pigment epithelial (RPE) cells. A fast, efficient, clinical-grade procedure was developed to make pure populations of RPE cells and photoreceptors from pluripotent stem cells. The Centre holds patents on membrane technology, and patents under application for retinal cell development from stem cells. Cell-on-membrane constructs have been engineered and surgical procedures perfected to implant constructs into the rat eye.

Pilot studies to test the effectiveness of implantation in vision-impaired rats have been conducted with a view to development of implants for AMD patients.



images: Successful insertion of a PLLAA based electrospun nanofibrous membrane (ENM) into the rat eye.

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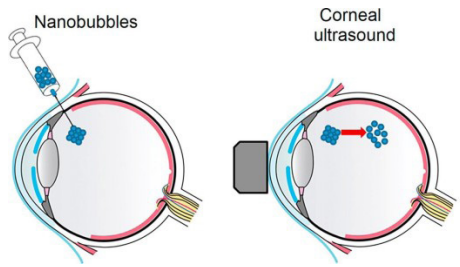
Spleen as an alternative site for hematopoiesis

Spleen plays a very important role in supporting hematopoiesis or blood cell production in response to infection and physiological stressors like exercise, pregnancy, blood loss and bone marrow failure. The spleen supports more restricted blood cell production than bone marrow, and acts as a constant source of myeloid cells for wound healing and tissue repair. A new activity in the Centre has been the investigation of the hematopoietic stem cells (HSC) present in spleen and bone marrow, their heterogeneity and characteristics, and the changes they adopt following stress, infection and ageing. For example, HSC in aged individuals show bias in their production of myeloid cells over lymphoid cells. The Centre has developed capacity to study HSC using the most advanced technology and extending this to studies in the Centre involving hemangiogenic, neural retinal and mesenchymal stem cells.

Significant recent findings by Centre staff

Ultrasound-responsive nanobubbles for enhanced intravitreal drug migration, *Published in European Journal of Pharmaceutics and Biopharmaceutics by Barnett and collaborators.*

Intravitreal injection of anti-angiogenic agents is currently the preferred treatment for neovascular retinal diseases like wet AMD. However, the intravitreal route faces many challenges including non-specific distribution and premature clearance of therapeutics from ocular tissues. Nanobubbles and ultrasound may improve the outcome of intravitreal drug administration by influencing the directionality of drug-containing particle migration. Centre staff and their collaborators have shown that repeated cycles of corneal ultrasound can improve the migration of injected nanobubbles deeper into the posterior regions of the vitreous humour towards the retina, while causing no observable acute damage to the ocular tissues.



Successful insertion of a PLLA based electrospun nanofibrous membrane (ENM) into the rat eye.

Identification of stromal cells in spleen which support myelopoiesis, *Published in Frontiers in Cellular and Developmental Biology by Lim and O'Neill.*

This study identified for the very first time a stromal cell type in spleen which supports myelopoiesis. Heterogeneity has been found within this subset which also relates to variation in myelopoietic-support capacity. The significance of this finding lies in our understanding of how stromal cells in spleen support hematopoiesis, and in the potential to utilise spleen as an alternative site for hematopoiesis particularly during HSC transplantation.

Determinants of postnatal spleen tissue regeneration and organogenesis, *npj Regenerative Medicine by Tan and Watanabe.*

The spleen plays an important role in immunity to blood-borne pathogens and cancer cells and also supports blood cell formation or extramedullary hematopoiesis at times of stress.

Spleen is also known to have unusual regenerative capacity which makes it an important candidate for formation of artificial or ectopic spleen tissue. Centre staff have identified the spleen organiser cell (SPo) that controls tissue regeneration. These cells co-exist with known lymphoid tissue inducer cells (LTi) cells throughout spleen development from embryo to the adult. They become organised around the white pulp or lymphoid region of adult spleen surrounding the central arteriole (CA). SPo can be isolated through cell sorting and used as grafts to produce new spleen tissue characterised by the formation of T and B cell regions supported by a mesenchymal stromal (MS) network.

The discovery of the SPo, and its importance in hematopoietic tissue regeneration, represents a landmark finding with potential for therapeutic application in patients with comprised bone marrow.