FUNCTIONAL GENOMICS DRIVE REGENERATIVE MEDICINE

Wolvetang Group

www.aibn.uq.edu.au/ernst-wolvetang

Focus

The Wolvetang Group is working towards solving neurological diseases by understanding the relationships between genes and neurological abnormalities.

Primarily focussed on utilising stem cells to this end, Professor Ernst Wolvetang said the scope of the laboratory's work ranges from common disorders such as Alzheimer's disease, to rarer conditions such as forms of childhood leukodystrophy.

"We harvest cells from patients and reprogram these into induced pluripotent stem cells, essentially bringing them back to a fetal state, which then allows them to make all the different cell types in the body," Professor Wolvetang said.

The group is particularly interested in the complex interconnectivity of cells in the brain and how a breakdown in these connections contributes to disease. They use high content real time imaging, gene expression analysis tools, and a range of cell biology techniques in order to identify disease phenotypes.

The group is currently screening for genes that cause demyelinating diseases, where damage to the insulation of nerve fibres in the brain leads to impaired nerve impulses and neurological defects. Using clustered regularly interspaced short palindromic repeats (CRISPR) technology, the group can mutate or correct genes suspected to be involved in a disease.

"Generation of isogenic controls through CRISPR gene correction is essential for seeing disease phenotypes emerge at a gene expression level," he said.

The research is also increasingly engineering mini organoids from human stem cells with the aim of employing these as 3D models for studying diseases in vitro. The construction of these organoides will help develop platforms for screening drugs in a high throughput manner, with the postulation that the results of testing in the cellular environment of an organoide will be more relevant than disease cell types grown in a petri dish.

Highlights

The group built on its strong program in ataxia telangiectasia (A-T), which is a rare disease where sufferers lose motor control as a result of brain cell degeneration. Affecting around 50 people in Australia, primarily children, most patients lose their lives before the age of 20.

"We are working very closely with a patient and parent support group, BrAshA-T, and we are very grateful for the generous philanthropic funding they have provided for our research," Professor Wolvetang said.

As a potential prelude to cellular therapy for this disease, the group is researching how to deliver gene-corrected, patient-specific cells to the brain of a mouse and determine if they integrate and function correctly. Once this capability becomes clinically viable they hope to be able to apply this cell-based therapy to children with A-T and other degenerative brain diseases.

The group had a successful year in publications, co-authoring a number of papers in high impact journals, including *Nature*, *Science*, *Nature Communications*, *Neuron*, *Human Molecular Genetics*, and *PLoS Genetics*.

The group also hosted Cell Reprogramming Australia's 3rd Annual Collaborative Conference in May, and Professor Wolvetang was invited to present a plenary lecture at the Joint Australian- Chinese Academy of Sciences symposium.

The Wolvetang laboratory was also part of a new $1 million initiative with Bioplatforms Australia, led by the Wells Group, to establish a new stem cells data set.

Professor Wolvetang's vision for stem cell based regenerative medicine of the 21st century is exemplified by his engagement with patient advocate groups such as the Mission Massimo Foundation, which aims to eradicate childhood leukoencephalopathies.

"It is at this interface between cutting edge research, patient advocacy, philanthropy, and industry engagement that our stem cell research can make a real difference for children suffering from rare and currently incurable diseases," Professor Wolvetang said.