Our Research

- Regenerative Medicine
- **Disease Modelling**
- Designer Cells
- Engagement, Ethics and Policy Program
- Accelerated Research Program
- Previous Research Programs

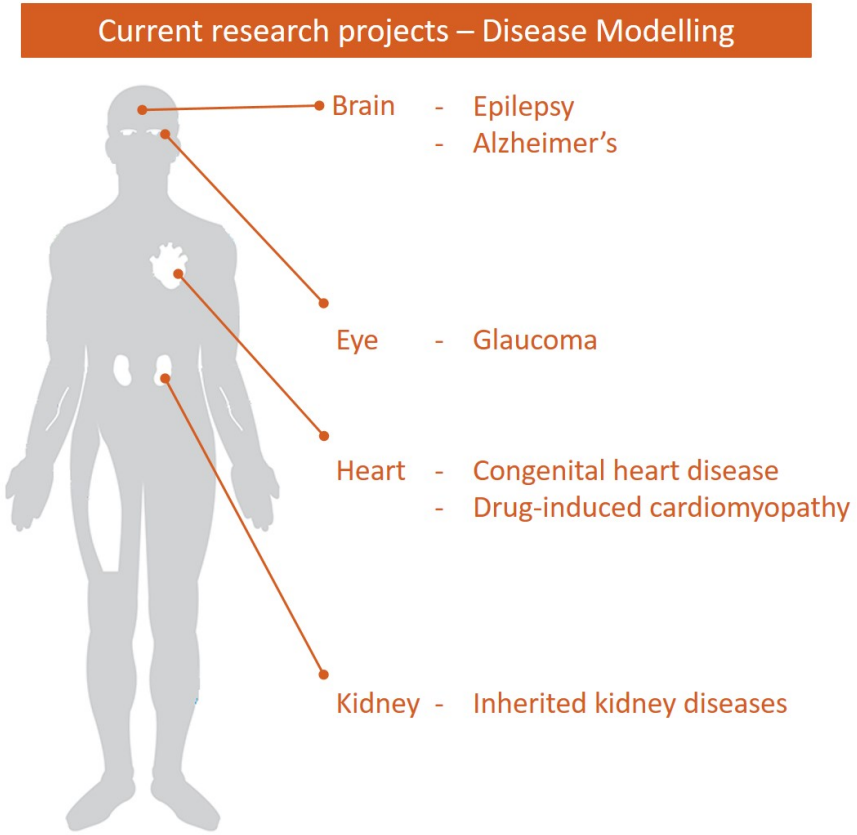
Download a PDF copy of this content

DISEASE MODELLING

Disease Modelling is one of three pillars of research in Stem Cells Australia.

The Disease Modelling program is creating tissues from patient-derived stem cells to provide a platform for determining the causes of disease, for developing diagnostic tools and for testing potential new drugs.

Current translational projects include research in diseases affecting the brain, eye, heart and kidney.



2.1 Heart – Modelling congenital heart disease using induced pluripotent stem cells

Richard Harvey (University of New South Wales/Victor Chang Cardiac Research Institute)

Hypoplastic left heart (under-development of the left side of the heart) is one of the most severe forms of congenital heart disease and patients often have a poor prognosis follow current surgical treatments. This project aims to understand mechanisms contributing to this condition, using cardiomyocytes produced from patient-derived induced pluripotent stem cells to assess gene expression profiles, responses to metabolic stresses and effects of drugs that stimulate cardiomyocyte proliferation.

2.2 Heart – Screening platform for drugs that stimulate proliferation of cardiomyocytes

Enzo Porello (Murdoch Children's Research Institute), Dave Elliott (Murdoch Children's Research Institute)

Heart failure has many causes, including ischemic injury, congenital disorders, cardiomyopathies and acquired heart disease (such as drug toxicity). This project will use gene-editing techniques to identify key genes and cellular processes implicated in the proliferation of human heart cells, which is a potential strategy to treat heart failure. It will use human cardiomyocytes from induced pluripotent stem cell derived from healthy and diseased patients. Gene

candidates implicated in cardiomyocyte proliferation will be validated in animal models and in human cardiac organoids and will be the basis for future drug discovery programs for new therapeutics for heart failure.

2.3 Eye – Using patient-derived stem cells to improve early diagnosis of glaucoma

Alice Pébay (University of Melbourne), Alex Hewitt (University of Tasmania)

Glaucoma causes the death of the nerve cells in the retina that communicate what the eye sees to the brain. It is the leading cause of irreversible blindness worldwide and one subtype, primary open-angle glaucoma, is the leading form and has no symptoms in its early stages. This project will determine gene expression profiles of single retinal ganglion cells derived from induced pluripotent stem cells created from human subjects to develop a better risk assessment tool for early glaucoma diagnosis.

2.4 Blood – Building better models of blood cancer

Andrew Elefanty (Murdoch Children's Research Institute), Susie Nilsson (CSIRO/Monash University), Christine Wells (University of Melbourne)

Leukaemias are the commonest cancer world-wide in children and many are acute. To improve survival rates, the genetic changes in leukaemias from individual patients have been documented in detail. This has shown that each patient has a mixed population of leukeamic cells, each with different collections of genetic changes. This project will characterise the importance of different combinations of leukaemia mutations by introducing these changes into blood cells created from human pluripotent stem cells. This will develop human leukaemic cells that are suitable for evaluating existing and new anti-leukaemia therapies.

2.5 Brain - Developing models of Alzheimer's disease to test new therapies

Ernst Wolvetang (University of Queensland)

All people with Down syndrome develop early-onset Alzheimer's disease. It is possible to model Alzheimer's disease in a dish by differentiating induced pluripotent stem cells derived from Down syndrome patients into neurones, microglia and astrocytes and forming brain organoids. Matched cells and organoids with the extra chromosome removed can be created by gene-editing. This project will use these approaches to investigate how different factors implicated in Alzheimer's affect the behaviour and pathology of the different brain cell types and to test potential drugs candidates.

2.6 Brain – Better cell models for identifying new therapeutic agents for neurodegenerative diseases

Colin Pouton (Monash University), John Haynes (Monash University)

Drug discovery programs have not yet identified therapies that reduce the rate of progression of serious neurodegenerative diseases, such as Parkinson's and Alzheimer's. In part this is because the biological models used in drug development programs are inadequate. This project will use neurons and microglia derived from human pluripotent stem cells to screen for small molecules that upregulate expression of neuroprotective genes. Sophisticated small molecule libraries will provide the base for a future medicinal chemistry/drug discovery program.

2.7 Brain – Using stem cell-derived neurones for drug discovery in inherited epilepsies

Steve Petrou (Florey Institute of Neuroscience/University of Melbourne)

Inherited epilepsies are severe early-onset disorders in children that often do not respond to current drug treatments. The genetic bases of these diseases are increasingly better understood. This has enabled the use of neurones derived from induced pluripotent stem cells made from patient skin samples for drug screening programs. This project is using such cells, and matched cells with their genetic defects corrected, to test potential drug candidates and other novel therapies such as antisense oligonucleotides.

2.8 Kidney – Developing a model of inherited kidney disease in a dish for drug screening

Melissa Little (Murdoch Children's Research Institute/University of Melbourne), Lorna Hale (Murdoch Children's Research Institute), Cathy Quinlan (Royal Children's Hospital)

Congenital nephrotic syndrome is a very early onset and severe condition with no treatment. It is caused by a number of genetic defects which produce varying severity of disease. This project uses a robust protocol for generating human kidney organoids from induced pluripotent cells. Organoids derived from children with the disease are providing a model to create a sophisticated system to screen potential therapeutic compounds.

The research conducted by Stem Cells Australia is funded through an Australian Research Council Special Research Initiative which provides funding for new and emerging fields of research and builds capacity in strategically important areas.