



At the frontier of tomorrow's medicine



Australian Government
Australian Research Council

Milestones in Australian stem cell research

1960s

- Factors that control blood cell development identified (Don Metcalf)

1980s

- Australia pioneers IVF technology, first donor egg and frozen embryo pregnancies (Carl Wood & Alan Trounson)
- Stem cells discovered in mouse brain (Perry Bartlett)
- New methods to mobilise blood stem cells transforms bone marrow transplants (Chris Juttner & Luen Bik To; Don Metcalf & Uli Dührsen)
- Factor that controls mouse embryonic stem cell growth identified (Nic Gough)

1990s

- Approval of drug to fight infection and support blood stem cell transplant based on Metcalf discovery (Amgen)

What are stem cells?

There are more than 200 different types of cells in the human body. Each of these has a specific job. For example, red blood cells carry oxygen. By contrast, stem cells are unspecialised and are capable of 1) making a copy of themselves, and 2) creating the more specialised cells needed to replace those lost to injury, disease and daily wear and tear. There are two main types of stem cells. Tissue stem cells are found in many of our organs but can usually only create cells of that organ. Pluripotent stem cells can be coaxed to form any cell type in the body.



2000s

- Forefront of stem cell isolation from human embryos, first to differentiate these stem cells to nerves (Ben Reubinoff, Alan Trounson & Martin Pera)
- Legislation introduced to regulate research involving human embryos
- Australian Stem Cell Centre – Biotechnology Centre of Excellence – established by Australian Government
- Identification of marker to improve isolation of stromal cells, founding IP for biotech company Mesoblast (Stan Gronthos & Paul Simmons)
- Isolation and expansion of regenerative cells from human nose (Alan Mackay-Sim)
- Australian Regenerative Medicine Institute launched
- Generation of human embryonic stem cells that are engineered to provide readout on growth and development (Andrew Elefanty & Ed Stanley)
- Breast stem cells identified, leading to greater understanding of how errors lead to breast cancer (Jane Visvader)
- Australasian Society for Stem Cell Research incorporated



2010s

- Stem cells grown on therapeutic contact lens restores sight in blinding corneal disease (Stephanie Watson & Nick Di Girolamo)
- Stem Cells Australia – ARC Special Research Initiative – commences
- New type of stem cell identified in the adult heart (Richard Harvey)
- Discovery of novel protein reveals how cancer develops in liver and pancreas (Martin Pera)
- Launch of Stemformatics, a platform to share and visualise stem cell data (Christine Wells)
- Blueprint for development of early mouse embryo described (Patrick Tam)
- Key contribution to international effort to understand reprogramming (Christine Wells)
- First robot recruited to aid study of eye diseases (Alice Pébay)
- First mini-kidneys grown from pluripotent stem cells (Melissa Little)
- Haemopedia published, an atlas of blood cells in mice (Doug Hilton)
- Blood stem cells successfully made from embryonic stem cells (Elizabeth Ng, Andrew Elefanty & Ed Stanley)
- International deal brings possible new treatments for chemotherapy patients closer (Lars Nielsen)
- New small molecule improves stem cell harvests for treatment of leukaemia patients (Susie Nilsson)
- Novel way to make beating muscle for heart research (James Hudson & Enzo Porrello)
- More than 19 clinical trials involving stem cells underway in Australia
- Melbourne to host 2018 International Society for Stem Cell Research conference

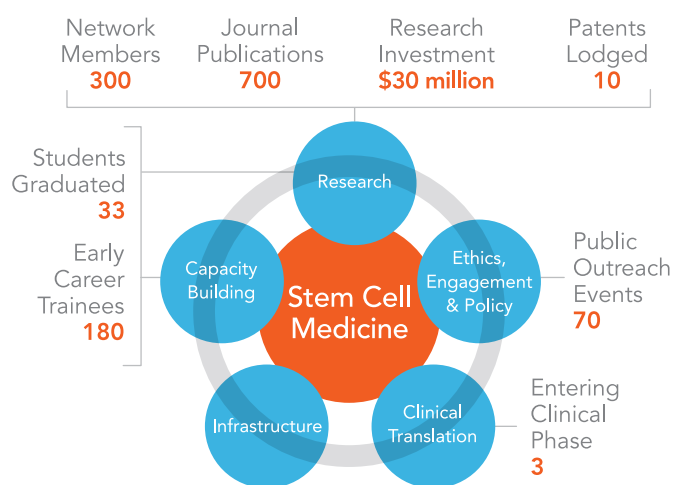
Australia at the forefront of stem cell medicine

Stem Cells Australia was established in 2011 to discover how to regulate stem cells. Nearly seven years later, the initiative is poised to harness the immense potential of these cells for new diagnostic, therapeutic and biotechnological applications.

Stem cell science has been a strength within Australian biomedical research for many decades. The Australian Government has long recognised this potential and since 2011 has provided support through the Australian Research Council's Special Research Initiatives scheme. This support has enabled Stem Cells Australia to develop a sophisticated national network of researchers and underpinning infrastructure, and has led to significant discoveries.

Key advances span new ways to improve how blood stem cells are collected for transplantation and how brain stem cells might be used to treat mood disorders, to making mini-kidneys in the laboratory to study what happens in kidney disease. Stem Cells Australia has also been critical in training the next generation of Australian researchers with over 180 early career researchers engaged across the initiative.

New support from the Australian Research Council announced in 2017 will allow Stem Cells Australia to expand and target its scientific portfolio towards medical and technological advances. Stem Cells Australia's emerging clinical network will support translation and foster the development of an Australian stem cell biotech industry for the rapid advancement of stem cell medicine. In parallel, the network will also continue to track and discuss the social and regulatory implications of this research.

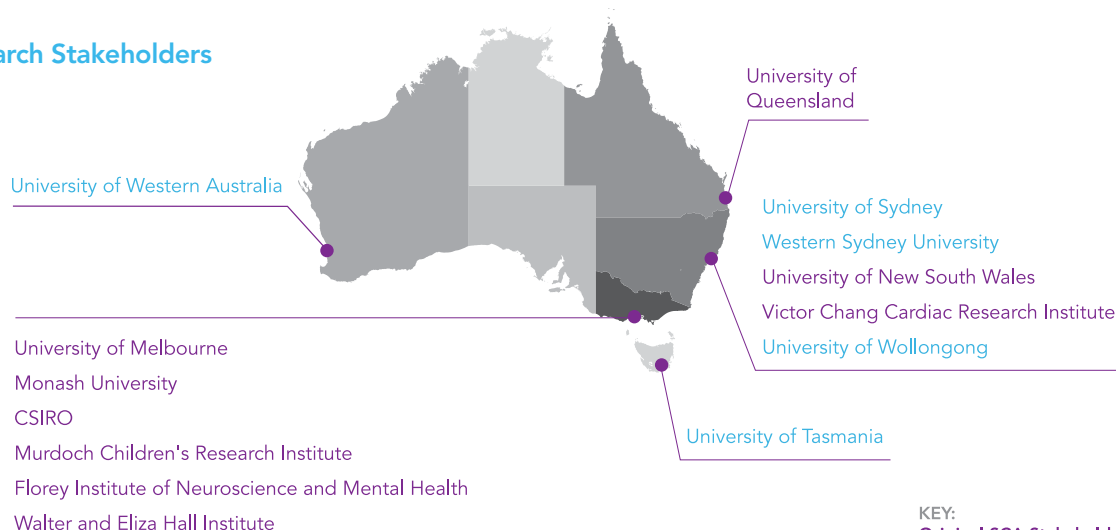


SCA Achievements (2011–2017)

Five new universities will join in 2018, extending the network to over 300 researchers across 14 leading Australian universities and medical research institutes.

We envisage a future in which Australians have access to novel stem cell medicine – for improved health and prosperity for all.

SCA's Research Stakeholders



KEY:
Original SCA Stakeholders
New SCA Stakeholders

The future of stem cell medicine will be anchored by three pillars of research and translational growth: Regenerative Medicine, Disease Modelling, and Designer Cells. Each program builds on key research outcomes generated during the initial seven years of Stem Cells Australia funding and incorporates new research partners to strengthen the portfolio's position for future success.

Strategic Research Program

THEME 1: Regenerative Medicine

Seeks to develop new therapies by either recruiting stem cells within organs to promote repair, or administering new cells and tissues made from stem cells to restore normal function after disease, illness or injury.

Neural
Eye
Heart
Kidney
Blood
Muscle

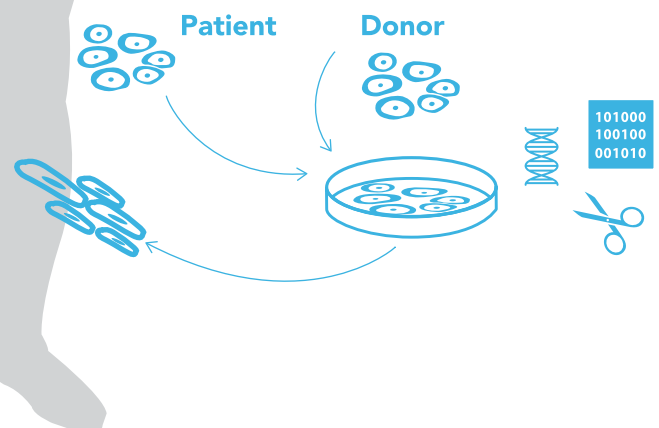
THEME 2: Disease Modelling

Delivers greater understanding of development and disease, providing a platform for testing potential new drugs. Tissues created from patient-derived stem cells will drive tailored approaches to diagnosis, disease monitoring and treatments.

Neural
Eye
Heart
Kidney
Blood

THEME 3: Designer Cells

Uses a combination of molecular tools to design and construct completely novel types of cells, built to deliver a specific function. For example, a universal cell that is engineered to be compatible for all transplant patients, or that produces therapeutic compounds only when given a specific command to do so.

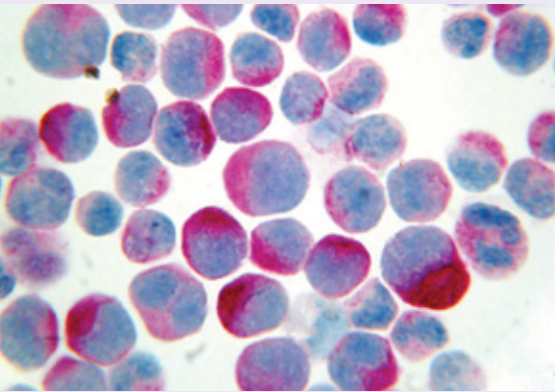


At a glance

Professor Lars Nielsen has developed a process to convert umbilical cord blood into life-saving neutrophils for chemotherapy patients.



Professor Lars Nielsen



REGENERATIVE MEDICINE

Making immune-boosting neutrophils

The need

Cancer patients who undergo chemotherapy face a number of challenges as a result of their treatment regimen: fatigue, hair loss, nausea and appetite changes, to name but a few. One of the more serious side effects, however, is neutropenia, in which the number of immune-fighting white blood cells known as neutrophils are depleted. For chemotherapy patients, neutropenia typically occurs in the weeks following a course of chemotherapy, leaving the patient vulnerable to serious or even fatal infections.

The most common treatment for chemotherapy-induced neutropenia is a drug injection that stimulates blood stem cells located in the patient's bone marrow to produce neutrophils. However, given that most intensive chemotherapy regimens also damage blood stem cells, this approach can be inefficient. New approaches to bolster the number of neutrophils for these patients are desperately needed.

The project

At the University of Queensland, Professor Lars Nielsen may have an answer. With persistence and knowledge gained from years of research, Nielsen's team has devised a method of producing therapeutically valuable neutrophils from umbilical cord blood.

Although neutrophils can be obtained from healthy donors, recruiting donors in the number required is difficult. Possible side-effects associated with the medication given to donors limits the number of times any donor can volunteer. To help a single chemotherapy patient, multiple donors may be required. To overcome these challenges the Nielsen team devised a method to isolate stem cells from umbilical cord blood, then use a bioreactor to expand the number of stem cells and coax them to develop them into neutrophils. This approach, reported in 2014, creates an end product, eNeut, that once approved for clinical use can be administered via an intravenous drip in a similar manner to other types of transfusions.

The impact

To help advance this approach into clinical trials, the process and eNeut product have been licensed by the Canadian-based commercialisation centre, CCRM. One of Nielsen's team members, Dr Nick Timmins, has relocated to Canada and it is hoped in the near future that eNeut is shown to meet the necessary standards and that valuable doses of neutrophils will be available for chemotherapy patients at facilities across the globe.

Mini-kidneys in a dish

The need

More than 4,000 Australians are diagnosed with chronic kidney disease each year, a number that is increasing about 6% annually. The costs of healthcare and lost productivity exceed \$1 billion each year. No new treatments have become available in the past 60 years, making this an urgent healthcare issue.

The kidney's main function is to filter waste from the blood, making urine. Nephrons are the kidney's filtration unit, and while the kidneys can partially repair damaged nephrons, this is inadequate and ultimately leads to kidney failure. While stem cells capable of making new nephrons are present during early development, they are lost before birth. This leaves the kidneys vulnerable to long term injury. Finding ways to regenerate nephrons could provide better options for the growing number of renal failure patients.

The project

In 2015, Professor Melissa Little and her team at Murdoch Children's Research Institute produced the world's first kidney in a dish. No larger than the tip of your finger, her lab-grown mini-kidneys have the hallmarks of a regular-sized kidney, including the tiny tubes and blood vessels that form nephrons, the organ's filtering structures. This achievement, published in the prestigious journal *Nature*, was at the forefront of what is now more commonly called organoid development – referring to the process of coaxing stem cells in the lab to mimic organs.

To create the kidney organoids, Little and her team first used cell reprogramming technology, taking adult skin cells and reverting them back into a type of pluripotent stem cell. From there, they were able to direct the stem cells to begin forming kidney tissue, similar to what occurs in early development. Currently, the mini-kidneys are not functional, as they lack a constant flow of blood through the nephrons as well as a channel for any urine produced to leave the organ. However, even in their current state, the mini-kidneys are extremely valuable for research and are being used to better understand how kidneys develop and what happens in disease.

The impact

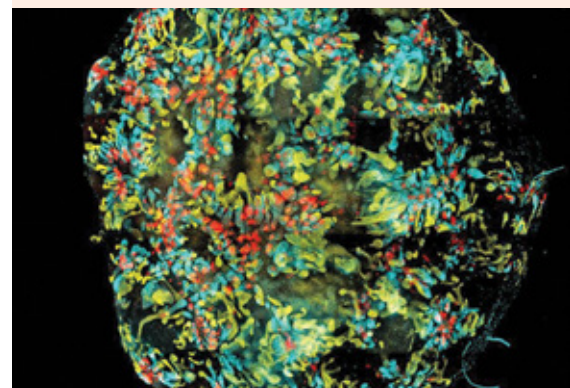
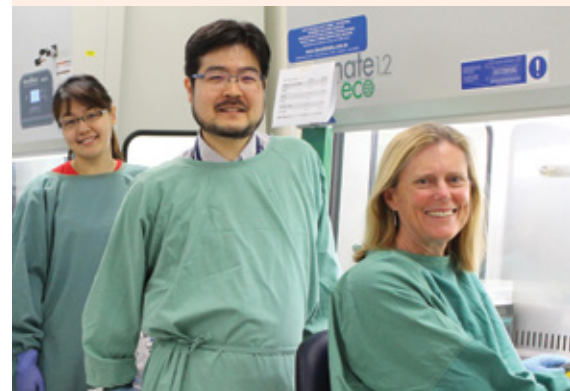
The Little lab's unique approach has already yielded important insights into kidney development and disease. Their kidney organoids are being used in the lab to screen promising new drug candidates, thereby identifying drugs that may cause kidney damage and avoiding potential side-effects for patients. The next challenge will be to produce larger more complex structures that could one day be a source of healthy cells for transplantation or entire replacement organs. To that end, in 2017, Little partnered with Organovo, a US-based company that specialises in bioprinting, to develop a more accurate 3D model of the kidney. These efforts are bringing research a step closer to a regenerative medicine solution for kidney disease.

At a glance

Professor Melissa Little is at the forefront of research to find new therapies for kidney disease, thanks to her tiny, lab-grown organoids.



Professor Melissa Little

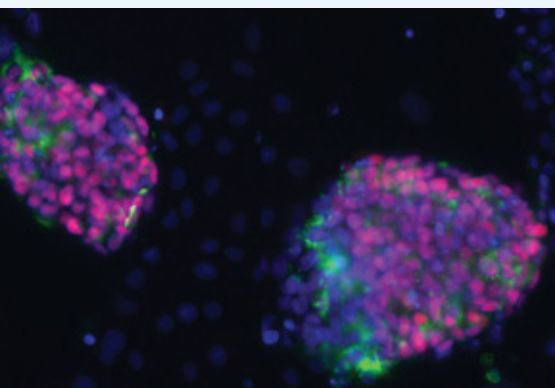
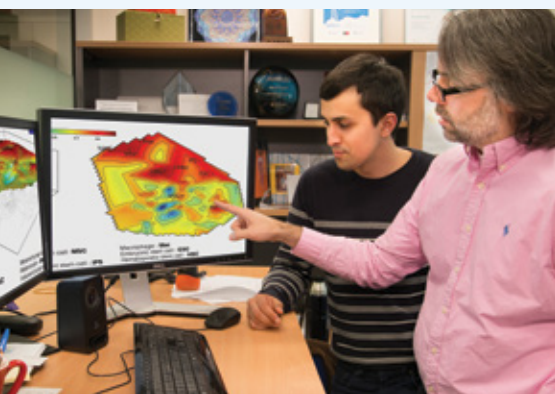


At a glance

Associate Professor Jose Polo has made the technicalities of converting one cell type into another vastly more accessible, launching a start-up company in the process.



Associate Professor Jose Polo



DESIGNER CELLS

Understanding and controlling cell reprogramming

The need

The Nobel-winning discovery of induced pluripotent stem (iPS) cells – in which an adult cell, such as a skin cell, can be reprogrammed back into a stem cell – opened up a wealth of opportunities to better understand and treat disease. Suddenly, it was possible to recreate specific diseases in a dish, mirroring what was happening in the patient's body. It also fuelled the idea of converting any cell type directly into any other cell type using reprogramming technology. However, the challenge in reprogramming is understanding exactly how the process works. Solving this problem is key to creating cell-based therapies that are both affordable and feasible within the current healthcare system.

The project

The original reprogramming recipe created by Nobel Laureate Shinya Yamanaka in 2006 relied on use of four genes. When added to a skin cell, this combination of genes pushed the cell back to a pluripotent state capable of then being coaxed to form any other cell of the body. But the results were not always stellar – only 1% of cells were successfully reprogrammed and the resulting iPS cells were not always stable.

Associate Professor Jose Polo of Monash University and his team have helped address this limitation through three landmark studies. The first, published in *Cell* in 2012, effectively provided a road map to explain the sequence of events triggered inside the cells that leads to both successful, and unsuccessful reprogramming efforts. With this guide to the reprogramming process, Polo's team then joined forces with an international group to develop and validate a computational tool, called Mogrify, that could model how to control the conversion of an adult cell into any other type of cell. The results, published in 2016, have the potential to greatly accelerate reprogramming research including bypassing the iPS stage altogether. Most recently the Polo team have further explored the "pluripotent state" in work published in *Nature Methods*. Drawing from the team's understanding of the molecular make-up of cells, they characterised the continuum in which iPS cells exist, and from this can better identify pathways to create mature cells of the desired type.

The impact

Understanding reprogramming and ways to accelerate this process has direct implications for advancing research discovery and reducing its cost. The Polo group's work has also become the basis of a UK and Australian start-up company, Cell Mogrify, which seeks to commercialise its reprogramming technology. Making this technology more accessible is also likely to assist medical professionals and researchers who seek to grow patient-specific, disease-based tissues to test and select potential drugs or drug combinations prior to treatment. It has the potential to usher in precision medicine in a real way.

Regenerating brain cells

The need

Brain disorders that affect mood, memory and cognition, long thought to be due to chemical imbalance, are now recognised as having a cellular origin. Extensive research is beginning to reveal how impairments to the production of neurons from stem cells in the brain can trigger a wide range of illnesses, including anxiety, depression, dementia and trauma-based disorders. Collectively, these disorders come with high impact for affected individuals and their families as well as staggering healthcare costs and lost productivity. There are many lingering questions about how new nerve cells can regulate brain function. Finding the answers could lead to new treatments and benefit millions of Australians.

The projects

Unravelling the complexities of the brain has been a lifelong pursuit for Professor Perry Bartlett. Back in 1982, he predicted the presence of stem cells in the brain, a promise he delivered in a world first a decade later. His discovery overturned a previously-held belief that the brain was a static organ, incapable of regeneration or repair.

The age of the plastic brain had begun. But, it turns out the brain has more than one kind of stem cell. In 2015, Bartlett and Dr Dhanisha Jhaveri – once a postdoctoral fellow of Bartlett's at the University of Queensland who has since established an independent lab – identified two distinct populations of stem cells within the hippocampus, the region of the brain responsible for mood, memory and spatial awareness. In 2017, Jhaveri identified a third population in the amygdala, an adjacent region of the brain. The findings help explain why this region of the brain is capable of managing several different functions. Determining strategies to encourage these cells to repair damage, or stay active as we age, is the long-term goal of these researchers.

Bartlett's team have also shown that the brain's immune cells, microglia, respond to exercise by stimulating production of new neural cells. This link between exercise and improved memory in mice is an extremely promising finding.

The impact

A clinical trial, based on the Bartlett team's finding, is now underway. It will follow 300 people aged between 65 and 85 to determine the optimal amount, intensity and type of exercise required to stimulate cognitive improvements in the brain. Additionally, identification of molecules that control the different neural stem cells, as well as the microglia, offer a new path for developing and testing drugs for the treatment of dementia and mood-related disorders.

At a glance

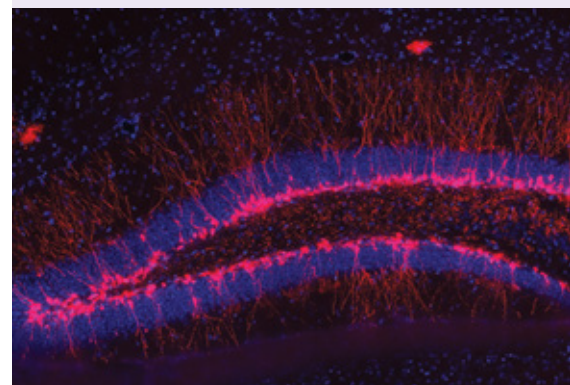
Stem cells found in regions of the brain could offer possible treatments for age- and mood-related disorders.



Professor Perry Bartlett



Dr Dhanisha Jhaveri



At a glance

New insights delivered by two Australian research teams puts heart research on the fast track to the clinic.

REGENERATIVE MEDICINE

Pathways to heart repair

The need

Heart trauma and disease are a leading cause of disability and death in children and adults, affecting one in every six Australians. Next to cancer, it has the highest burden in terms of treatment cost and lost income to patients and their families and caregivers. Most current treatments focus on reducing the risk or impact of heart conditions. This is largely due to the fact that heart muscle cells, also called cardiomyocytes, do not readily divide to replace damaged tissue. New regenerative medicine approaches are required to stimulate the heart's cells to form healthy new heart tissue, and will offer hope of a better quality of life for those affected by heart disease.

The projects

Finding ways to motivate the heart to regenerate requires a deep understanding of the intrinsic cues that control normal heart growth and repair. Professors Robert Graham and Richard Harvey, based at the Victor Chang Cardiac Research Institute and the University of New South Wales, have made substantial contributions to this quest.

In 2014, Graham's research team overturned a long-standing belief that heart cells do not divide after birth. They meticulously followed the development and division of heart cells in mice and found that the number of heart cells increased rapidly, by 40%, during pre-adolescence and that this spike in growth was linked to the presence of thyroid hormone.

Nearby, Harvey's team was making its own discoveries. In a 2015, they showed that a single protein that binds the hormone neuregulin could supercharge the repair pathways of the adult heart, causing a ~5-fold increase in cardiomyocyte division. This pathway may work hand-in-hand with how heart stem cells are regulated, a theme they are now investigating. In the same year, Harvey also identified a new network of proteins that interact with the gene NKX2-5, one of the master-regulators of heart development. Through genome-wide and computational approaches, Harvey's team revealed how this network goes awry to cause congenital heart disease.

The impact

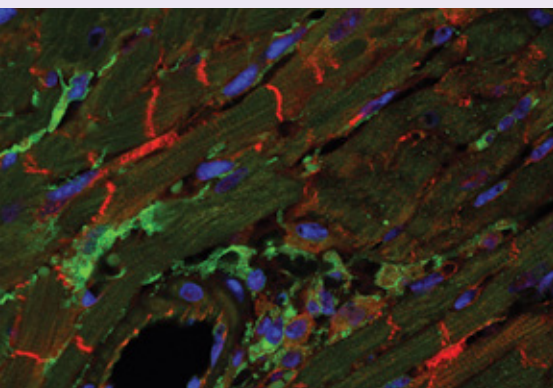
The research from these labs could fast-track new and desperately needed heart therapies. Based on the work of the Graham lab, research is underway to see if thyroid hormone could be harnessed to help repair damage in adult hearts. Similarly, research from the Harvey lab opens new avenues to determine whether existing or new drugs could stimulate adult heart muscle to divide. Through understanding how heart development is regulated, the Harvey team is also one step closer to identifying the point during development in which congenital abnormalities occur. Both of these labs have built a strong, international network of colleagues, ensuring that their findings directly contribute to global efforts to improve cardiovascular health.



Professor Robert Graham



Professor Richard Harvey and team



Seeing eye disease clearly with robotics

The need

Nearly half a million Australians live with a form of vision impairment or blindness. By far, most of these cases – 80% or more – are treatable with prescription eyewear or surgery. However, within the remaining cases lurk several debilitating forms of eye disease, many rooted in genetic abnormalities that lead to blindness. With no interventions or cures, Australians with hereditary eye conditions that result in blindness face significantly a decreased quality of life, mobility and ability to contribute to the community.

The projects

Two researchers at the Centre for Eye Research Australia (CERA) are hot on the trail of innovative therapies for treating vision loss and even curing blindness thanks to recent advances – and investments – in stem cell and gene-editing technologies.

Associate Professor Alice Pébay, also of the University of Melbourne, and Associate Professor Alex Hewitt, also with the University of Tasmania, are reprogramming patients' skin cells into induced pluripotent stem cells, then growing them into cells affected in various eye diseases. These cells can be used to study eye diseases by modelling how certain diseases occur, and then using these cells to identify and to test novel interventions to treat vision impairment and blindness.

Ground-breaking robotic cell culture technologies at CERA's Automated Stem Cell Facility allow the research teams to grow and sustain millions of cells collected from a large number of donors. The robotic system enables maintenance and expansion of the cells, allowing the researchers to work on a greater number of conditions to obtain a more accurate image of how disease develops and the potential for drug-based therapies for blindness. For example, they have been able to develop a deeper insight into three different diseases that affect the retina, that until now have been poorly understood. In a 2017 paper, the Pébay and Hewitt labs demonstrated use of the gene-editing platform known as CRISPR to successfully edit genetic errors that cause inherited eye disease. They have also worked with collaborators to explore a type of mitochondrial disease that affects the optic nerve.

The impact

Pébay's and Hewitt's investigations are game-changers for eye health. Beyond the potential for creating new cell-based and pharmaceutical treatments for vision impairment, their work may also be paving the way for greater public understanding of developments in the field. The science of altering genetic codes to change health and other outcomes is not without controversy, but a recent global survey conducted by the team suggested two-thirds of people support genetic interventions for debilitating or potentially lethal diseases. That level of public support, combined with significant public- and private-sector investment, puts Pébay's and Hewitt's research on track for success – one that will have lasting benefits for thousands of Australians.

At a glance

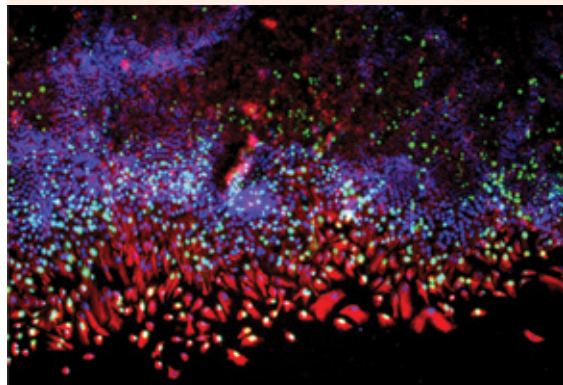
Induced pluripotent stem cells combined with state-of-the-art robotics offers new insights into eye disease.



Associate Professor Alice Pébay



Associate Professor Alex Hewitt

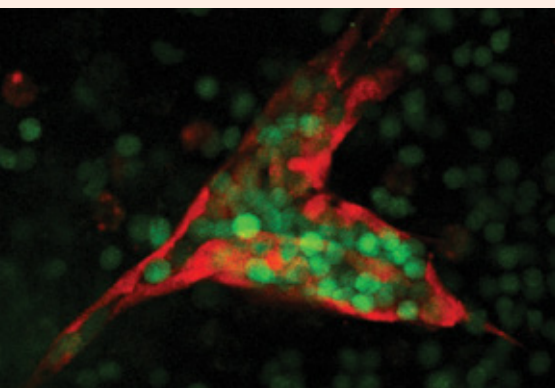


At a glance

A powerhouse trio of laboratories is refining the way of making blood and heart cells, bringing future therapies closer to reality.



Dr Elizabeth Ng and Professor Andrew Elefanty



DISEASE MODELLING

Making the right cells from stem cells

The need

Pluripotent stem cells are an invaluable source of cells for research and for the development of new therapies for a range of diseases. Since pluripotent stem cells have the potential to make any cell in the body, a critical challenge is developing methods to coax stem cells to form the desired cell type, while ensuring they do not form unwanted cells. Perfecting these methods is necessary to enable pre-clinical research to advance into clinical trials, and eventually, new treatments.

The projects

The laboratories of Professor Andrew Elefanty, Professor Ed Stanley and Dr David Elliott are among the world's leaders in the art of making pluripotent stem cells turn into the cells that make up the blood, heart and their supporting tissues. The three teams are all based at the Murdoch Children's Research Institute, a co-location that facilitates the exchange of ideas and knowledge. The longstanding collaborations between these groups has helped advance critical research, underpinning the future use of stem cells for both clinical and biotechnological applications. So it's no surprise that these teams have also achieved significant breakthroughs in recent years.

In an international collaboration in 2011, Dr Elliott's team helped identify a new way to more easily obtain and purify heart muscle cells from stem cells, directly aiding efforts to study heart disease and develop new drug and cell therapies. More recently, his lab identified mutations in a gene called *ALPK3* that prevents heart cells from correctly communicating with each other, resulting in a disease known as hypertrophic cardiomyopathy.

Building on years of research, the Stanley and Elefanty labs reported the successful conversion of human pluripotent stem cells to blood cells that closely resemble the first blood stem cells that are found during early human development. These cells provide researchers with an important new method for studying the development of blood disorders such as thalassemia and leukaemia.

The impact

Based on their extensive research achievements, the efforts of this trio of labs has far reaching impact. These range from the introduction of new genetic screens to identify and better support children and families at risk of developing hypertrophic cardiomyopathy, to advancing global efforts to develop suitable replacement heart cells for human transplantation. The capacity to develop laboratory-grown blood cells opens up the possibility of creating red and white blood cells for transfusion purposes, as well as regenerating bone marrow for patients with leukaemia and other blood diseases who lack a suitable matched donor. It is also anticipated that cells produced in the lab could be personalised for each individual, reducing the risks of graft rejection or graft-versus-host disease.

Expanding horizons for stem cell transplants

The need

Hematopoietic stem cells (HSCs) are responsible for making all the types of cell in our blood. HSC transplants – where stem cells are harvested from donor bone marrow – have been widely used to treat aggressive forms of blood cancer such as leukaemia for more than 30 years. Today, nearly 70,000 such transplants are conducted annually worldwide, and 1,000 each year in Australia alone.

Donating HSCs is not without challenges. Currently, donors are given a drug to stimulate the release of stem cells from bone marrow into the blood for harvesting. The process involves multiple injections over several days and may not always produce a sufficient number of stem cells. It also presents a risk of side effects ranging from bone pain to enlargement and rupturing of the spleen. There is an urgent need to develop faster and safer methods for harvesting HSCs to encourage more people to become stem cell donors, thereby significantly improving the outcomes for cancer patients.

The project

Professor Susie Nilsson and her research team at the Commonwealth Scientific and Industrial Research Organisation have high hopes for improving HSC collection. Also working as part of the Australian Regenerative Medicine Institute at Monash University, the team recently showed that a new molecule, BOP, has great promise. When used in animal studies, BOP combined with the routine drug treatment resulted in HSCs from the bone marrow being mobilised into the bloodstream within an hour, rather than the current standard of 5–6 days.

The impact

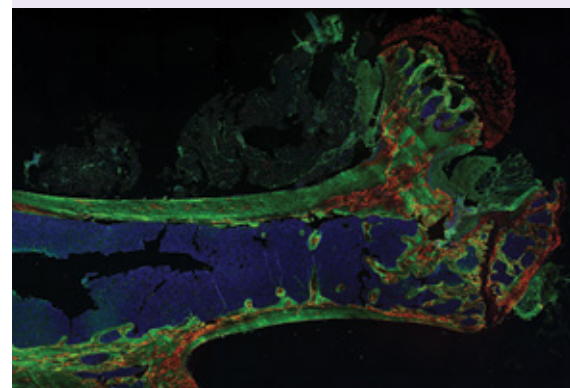
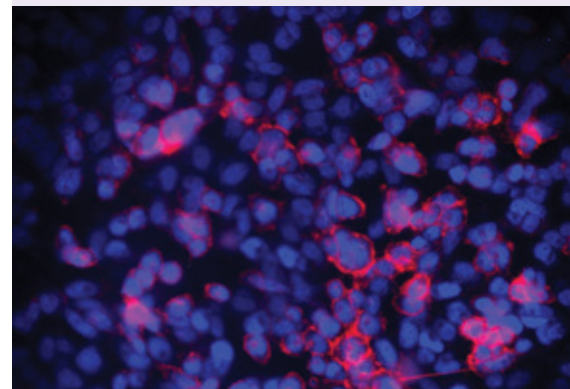
The Nilsson team's findings made headlines worldwide when results were published in the journal *Nature Communications* in 2016. Their new approach may revolutionise the way leukaemia and other serious diseases are treated using HSC transplants, in terms of improved outcomes for patients but also donor satisfaction and safety. The team will now test their approach in humans in a phase 1 clinical trial. Reducing the risk of serious side-effects and shortening the process from days to an hour, could one day make donating stem cells simply a matter of going with the flow.

At a glance

A new blood stimulation procedure may provide a faster, pain-free way for stem cell donors to help save lives of cancer patients.



Professor Susie Nilsson



At a glance

By pairing biology with engineering, two research groups are developing innovative ways to understand what happens in diseases associated with brain function.

DISEASE MODELLING

Miniaturised stem cell laboratories

The need

There are more than 400 neurological conditions that can affect the human brain during development or in adulthood. They can be common, such as Alzheimer's (affecting approximately 300,000 Australians) or extremely rare, such as Ataxia Telangiectasia (affects 1 in 50,000 births). These many, variable conditions have one thing in common: they have few treatment options and no cure. Their cumulative impact on society, in terms of lost quality of life, reduced income and costs to the healthcare system are immeasurable – and on the rise given an ageing population. There is an urgent need to improve our understanding of these diseases and identify treatments. Stem cells can help.

The projects

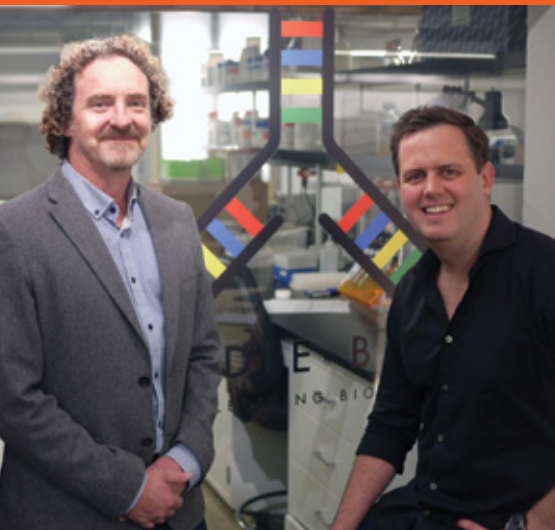
At the University of Queensland, Professors Ernst Wolvetang and Justin Cooper-White are applying biological and engineering approaches to address this issue.

In the Wolvetang lab, millions of brain cells are growing in the lab. Some are being used to examine what happens in conditions such as Down's syndrome or motor neurone disease. Others are used to understand the ageing process. Each batch of cells has been made using induced pluripotent stem (iPS) cell technology, where a patient's cell is made into stem cells and then turned into neurons that display the characteristic of the patient's condition. Currently, the Wolvetang group is developing 3D brain organoids, structures that mimic the developing brain, to study how these cells interact.

As an engineer, Cooper-White's research is aimed at solving problems associated with how stem cells are grown and used in the lab. By looking at the micro-environment that regulates stem cell behaviour, his team devises scaffolds and automated or robotic systems to improve stem cell performance in the lab. As outlined in a 2016 paper, his micro-bioreactor technology contains 8,100 culture chambers in a space about the size of a credit card, making it possible to optimise culture conditions or screen drugs with extreme time and cost efficiency.

The impact

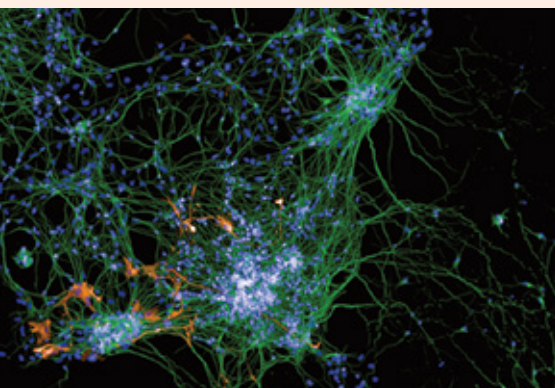
In combination, these approaches open up an array of possibilities for understanding brain disease and ageing, as well as testing for drug effectiveness or likelihood of harm. The Wolvetang lab is currently screening molecules that may inhibit the progression of Alzheimer's disease in collaboration with the company InterK Peptide Therapeutics. Cooper-White and team member Dr Drew Titmarsh used this technology as the basis of a start-up, Scaled Biolabs, that in June 2017 was awarded a US \$700,000 discovery grant from CIRM, California's stem cell agency. In 2016, Wolvetang and Cooper-White teamed up with colleagues at the University of Queensland to form StemCARE, a centre focused on studying the ageing process and on engineering innovative clinical solutions in support of healthy ageing.



Professor Justin Cooper-White and Dr Drew Titmarsh



Professor Ernst Wolvetang and team



Towards stem cell therapies for Parkinson's

The need

Science is only beginning to tease out the many mysteries the brain holds regarding its function and the impact of disease or injury. As one of the most prevalent forms of brain disease, affecting approximately 700,000 Australians, Parkinson's Disease has been the subject of considerable study. We now know that Parkinson's is caused by a loss of dopamine-producing neurons, and while this loss occurs throughout the brain it is in the region called substantia nigra where the loss is most devastating. Because the disease is linked to a single type of cell, a stem-cell-based therapy to replace or repair cells in the damaged region is feasible. Early clinical studies have identified some of the obstacles – such as the best type of cells to transplant – but more needs to be done before a clinical treatment is a reality.

The projects

The research labs of Associate Professor Clare Parish and Dr Lachlan Thompson at The Florey have long been at the forefront of discovery in brain repair, particularly for Parkinson's. At the time Stem Cells Australia was founded in 2011, the pair had already been working together to solve some of the problems associated with growing replacement cells in amounts that would be necessary for eventual therapy.

More recently, the Parish and Thompson labs have focused on finding ways to ensure safe and effective incorporation of these cells into human patients. Up to now, one of the key challenges has been cell survival as the brain is a hostile place and transplanted cells often don't survive long enough to properly engraft. Bioengineering – creating scaffolds and hydrogels to support the transplanted replacement cells – offers an attractive solution. Scaffolds can provide cells with an architecture that is more closely aligned with how cells would normally exist, while hydrogels can provide both a buffer from attack and can be infused with proteins or other factors to ensure longer cell survival. Over the past few years, the Parish and Thompson research teams have published several articles outlining their advances using this strategy.

In addition, the teams have continued to refine the processes of generating neurons from pluripotent stem cells and have shown in animal studies that their cells are able to survive and forge critical brain connections.

The impact

Cumulatively, the Parish and Thompson labs have made a series of rapid advances, bringing the goal of a cell-based therapy for Parkinson's a notch closer to reality, something the pair holds as their primary focus. Of equal importance, their findings, in terms of how to effectively grow neurons and how to deliver them into the injured brain, will have broader impact on research for a range of neurodegenerative conditions such as Alzheimer's and Huntington's, as well as brain damage caused by stroke and other injuries.

At a glance

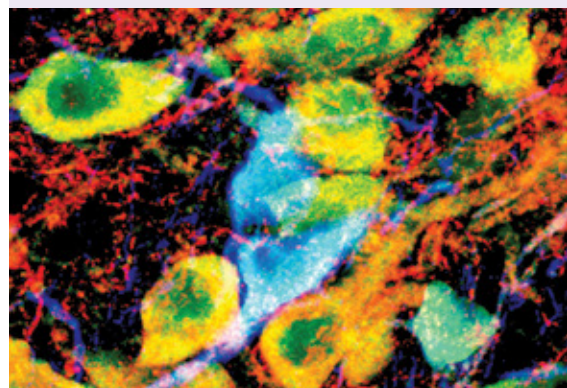
A bioengineering approach that supports survival of cells transplanted into the brain offers new hope of a treatment for Parkinson's and other brain diseases.




Associate Professor Clare Parish



Dr Lachlan Thompson





From better treatments for blood cancers, or understanding how the brain and heart grows and heals, to making cells in the lab to study and treat disease, Australian researchers are global leaders in advancing stem cell medicine for a healthier future.