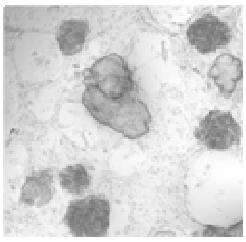
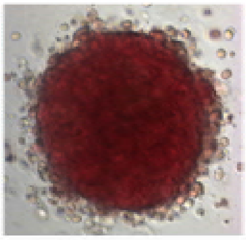
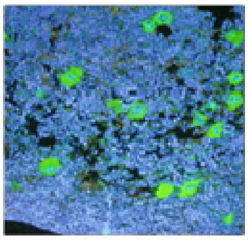
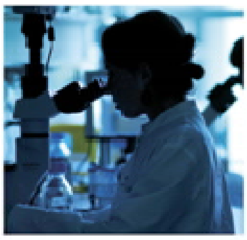

Australian Stem Cell Centre

www.stemcellentre.edu.au

Media Release

Strategy and Collaboration to Drive Australian Stem Cell Centre Research

Thursday 23 July 2009, Melbourne Australia:

The Australian Stem Cell Centre today announces funding for four collaborative research programs. These have been initiated as the centrepiece of the Centre's strategy to position stem cell research as a core discipline in Australia's biomedical research effort.

The Australian Stem Cell Centre (ASCC) is forging ahead with a new approach to supporting stem cell research which brings together the best Australian scientists. Today, the ASCC announces the expansion and reorganisation of its research portfolio into four large research programs known as 'Collaborative Streams'.

Representing excellence in Australian stem cell research, the Collaborative Streams are the centrepiece of a strategy that will guide the ASCC through the remainder of its current funding period (to June 2011) and beyond. The Centre's strategy also concentrates on facilitating the translation of research into economic benefit and public good, on the dissemination of stem cell technical expertise to build Australia's research capabilities in the field and on enhancing the public's understanding of stem cell science.

The four successful Collaborative Streams, which were selected by independent peer-review, consist of a number of research modules built around four main themes of stem cell research: embryonic stem cells, adult stem cells, induced pluripotent stem cells (iPS cells) and bioreactors for the propagation of stem cells. Each Stream is led by internationally-recognised stem cell scientists:

1. *Bioreactors and Smart Surfaces for Stem Cell Propagation*
   Professor Peter Gray, Australian Institute for Bioengineering and Nanotechnology (AIBN), University of Queensland and Associate Professor David Haylock, Australian Stem Cell Centre
2. *Reprogramming and Induction of Pluripotency*
   Associate Professor Ernst Wolvetang, AIBN, University of Queensland and Dr Andrew Laslett, Australian Stem Cell Centre
3. *Pluripotent Stem Cell Differentiation*
   Professor Andrew Elefanty, Monash University and Associate Professor Susie Nilsson, Australian Stem Cell Centre
4. *Adult Stem Cells*
   Professor Richard Harvey, Victor Chang Cardiac Research Institute and Professor Melissa Little, Institute for Molecular Biology, University of Queensland

"Our hope is that stem cells will one day be used to ameliorate and cure a wide range of human diseases. While this goal will not be fully achieved for several years and will require answers to fundamental questions about the biology and metabolism of stem cells, we believe the Collaborative Streams are the best and most efficient vehicles to attack and solve these questions" said Professor Graham Macdonald, Chair of the Australian Stem Cell Centre. He added "The Collaborative Streams involve a large proportion of Australia's stem cell research groups, providing an unprecedented opportunity to develop new collaborations. The research teams, which include scientists without a previous relationship to the Centre, will be able to call on the Centre's advanced technology services such as the provision of validated stem cell lines and training and support for junior scientists. This is an exciting development for the Centre which has been to a large extent driven by the stem cell scientific community. All of us involved with the ASCC look forward to seeing these collaborations produce significant results in the coming years and enhance our understanding of stem cells and their potential applications."

Professor Peter Gray, Director of the Australian Institute of Bioengineering and Nanotechnology at the University of Queensland and a Collaborative Stream Leader added "the establishment of the Collaborative Streams will consolidate stem cell research in this country. By working together stem cell scientists will accelerate the translation of stem cells from the lab to the clinic."

Ends

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About the ASCC

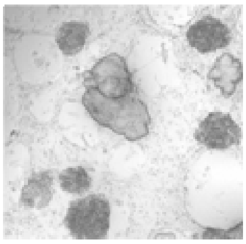
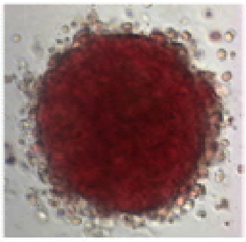
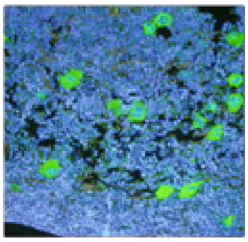
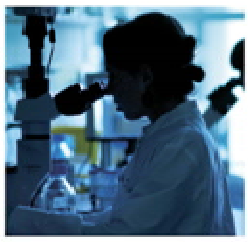
The Australian Stem Cell Centre was founded to capitalise on Australia's significant strengths in the field of stem cell research. The ASCC was selected in 2002, in a competitive bid process, as Australia's Biotechnology Centre of Excellence, an initiative of the Australian Government. The Centre provides a unique national resource for stem cell researchers to deliver outcomes that benefit the wider Australian biotechnology industry and will ultimately contribute innovative solutions to human health challenges.

The Centre was established with the financial and in-kind support of a number of institutions of which the current voting Members, who retain ultimate oversight of the Centre, are: Monash University, University of Queensland, Howard Florey Institute and University of Adelaide. The additional Stakeholder institutes are: University of Melbourne, Baker IDI, Murdoch Children's Research Institute, Victor Chang Cardiac Research Institute and Mater Medical Research Institute.

The ASCC is governed by a Board of Directors with independent scientific oversight and support from an eminent Scientific Advisory Board.

Total funding of $100 million has been awarded to the ASCC by the Australian Government and is administered by the Australian Research Council and the Department of Innovation, Industry, Science and Research. The funding is provided in instalments from 2002 to 2011. To complement Australian Government funding, the State Government of Victoria's Science Technology and Innovation program awarded the Australian Stem Cell Centre a further $11 million to support key infrastructure in Victoria.

Together the ASCC and partnering organisations support a critical mass of Australian stem cell research that is internationally competitive. The ASCC currently funds research at leading institutes and universities in Victoria, Queensland, South Australia and New South Wales with the major hubs of activity centred in Victoria and Queensland.



Australian Stem Cell Centre

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Collaborative Streams – Excellence in Australian Stem Cell Research

The Australian Stem Cell Centre (ASCC) was founded in 2002 to capitalise on Australia's significant strengths in the field of stem cell research. Together with its partnering organisations, the ASCC supports a critical mass of internationally competitive Australian stem cell research. The growth and maturation of the Australian stem cell field has created a need to consolidate the research, to maximise the outcomes from the existing research portfolio and to fund innovative research not previously supported by the ASCC. The idea of focussing research into larger collaborative groups grew out of a series of meetings with ASCC funded researchers and stakeholders. Led by researchers, four thematic groups, now called Collaborative Streams, were formed to bid competitively for ASCC research funds.

The establishment of the Collaborative Streams is an innovative way of funding stem cell research in Australia. Each Stream consists of a network of high-calibre scientists with internationally-recognised leaders who have agreed to work collaboratively to focus the Nation's expertise on key research questions.

Each stream consists of 'Modules' (individual research projects) with common goals:

1. **Bioreactors and Smart Surfaces for Stem Cell Propagation**

   For stem cells to be used to treat disease, we need to grow them in large volumes, to guarantee they are safe for use in patients and to turn them into the cell types appropriate for treatment of different diseases. Stream 1 will investigate various artificial surfaces and small molecules that recreate the natural environments in which stem cells grow and differentiate. The goal is to produce large numbers of cells in an external environment, that can be used to treat patients.

2. **Reprogramming and Induction of Pluripotency**

   The ability to reprogram normal adult cells into more primitive pluripotent cells is a significant advance in the stem cell field that can ultimately be used to better understand disease progression and potentially to develop treatments. Stream 2 brings together Australian researchers working with induced pluripotent (iPS) cells to better understand the process of reprogramming and to test their therapeutic potential in a range of diseases.

3. **Pluripotent Stem Cell Differentiation**

   Pluripotent stem cells (human embryonic stem cells (hESC) and induced pluripotent stem (iPS) cells) have captured the public imagination because of their potential to differentiate into all the cell types in the human body. The aim of the research in Stream 3 is to dissect and understand the signals that guide stem cells along specific pathways to mature cell types including blood, heart, pancreas, lungs and kidneys. These cells will also provide valuable tools for the understanding and potential treatment of disease.

4. **Adult Stem Cells**

   Stem cells are now thought to reside in most, if not all organs of the adult body where they are involved in day to day tissue maintenance. Despite their widely differing origins, locations and capabilities, adult stem cells share many common features. The researchers collaborating in this Stream will develop a common approach to their projects, with the view that knowledge gained about stem cells in one organ may illuminate the characteristics and behaviour of stem cells in other organs.

Collaborative Stream 1 – Bioreactors and Smart Surfaces for Stem Cell Propagation

Australian Stem Cell Centre

The great promise of stem cells is that they will one day be used to replace a patient's diseased or damaged cells. It is essential that methods are developed for cells to be grown efficiently and economically in the laboratory in large enough numbers to support any cellular therapies that may become available.

S1: Bioreactors and Smart Surfaces for Stem Cell Propagation

Stream Leader:
Prof Peter Gray (AIBN, University of Queensland)
Deputy Stream Leader:
A/Prof David Haylock (ASCC)

Stream 1 Modules

M1: Assessment of Smart Surfaces for Culture of Haemopoietic Stem Cells & Megakaryocytic Cells
Module Leader: A/Prof David Haylock (ASCC)

M2: AIBN Reactor Program
Module Co-Leaders:
Prof Peter Gray, Prof Justin Cooper-White, A/Prof Ernst Wolvetang (AIBN, University of Queensland)

M3: Functional Assessment of Ex Vivo Expanded
Module Leader: Prof A/Prof Susie Nilsson (ASCC)

M4: Production of Neutrophils
Module Leader: Prof Lars Nielsen (AIBN, University of Queensland)

M5: Development of Pluripotency Reporter Lines for Facile Screening of Bioreactor Conditions
Module Leader: Dr Andrew Laslett (ASCC)

M6: Safe & Efficient Expansion of Genetically Stable hESC
Module Leader: A/Prof Ernst Wolvetang (AIBN, University of Queensland)

Stem cells of all kinds respond to specific changes in their natural environment by dividing or by changing their patterns of gene expression so that they can carry out specific functions in the body. Bioreactor technology relies on smart surfaces, complex molecules and biologicals to approximate the natural environments suitable for cellular growth and expansion. The *Bioreactor and Smart Surfaces for Stem Cell Propagation* Collaborative Stream unites six currently-funded ASCC research groups with complementary expertise ranging from biomaterials, bioengineering and haematology to pluripotent stem cell biology. This Stream, led by Professor Peter Gray, Director of the Australian Institute for Bioengineering and Nanotechnology (AIBN), University of Queensland, will design, test and validate artificial surfaces that recreate natural cell-cell and cell-surface interactions and can be mass-produced. In addition, the researchers will collaborate in the design, synthesis and testing of small molecules that can be directly added to media in the bioreactors that are used to grow particular types of stem cells and differentiated cells in large volumes.

Case Study – Bioreactors – how do we generate cells in relevant numbers for future therapies?

Stem cells hold great promise, but before they can be used in patients, several technical and practical hurdles need to be overcome. Cells will need to be grown in large numbers and in controlled conditions using culture systems designed to expand populations of stem cells with uniform properties. This will allow controlled, reproducible differentiation of stem cells into selected mature cell types such as heart cells or blood cells. In addition, cells for use in humans need to be grown in conditions free from animal products and contaminants to ensure they are safe for transplantation.

Professors Justin Cooper-White, Peter Gray and Ernst Wolvetang are working together at the AIBN to overcome these hurdles. They have combined their multidisciplinary expertise in biomaterials, microfabrication, mammalian cell culture, bioprocess development and stem cell biology to focus on developing defined bioprocesses for the expansion of stem cells and the differentiated cells derived from them. Ultimately, these bioprocesses and the associated technology will be applicable to all stem cell researchers developing potential therapeutics based on stem cell technology.

Collaborative Stream 2 – Reprogramming and Induction of Pluripotency

Reprogramming, of an adult cell to a pluripotent stem cell – referred to as an induced pluripotent stem (iPS) cell - has been one of the most significant advances of the past ten years. First described using adult mouse cells in 2006, iPS technology was quickly adapted for use in human stem cells. iPS cell technology provides scientists with a new method to investigate reprogramming, cell maintenance and differentiation. Ultimately, iPS cell technology will also be used to better understand disease and to develop possible treatments.

S2: Reprogramming & Induction of Pluripotency
Stream Leader:
A/Prof Ernst Wolvetang (AIBN, University of Queensland)
Deputy Stream Leader:
Dr Andrew Laslett (ASCC)

A number of Australian researchers, including those funded by ASCC, have already established iPS technology within their laboratories. The *Reprogramming and Induction of Pluripotency* Collaborative Stream will bring these researchers together to drive the development of iPS-cell based disease models and drug screening platforms. Led by Associate Professor Ernst Wolvetang who is based at the AIBN, University of Queensland, the researchers will investigate the molecular mechanisms involved in reprogramming and will apply these skills to the investigation of disease models – for example schizophrenia and dental disease.

The collaboration consists of eight modules, groups who will form a close liaison with the ASCC's core facilities, which will bank, analyse and distribute the iPS cells generated within the collaboration for use by researchers around Australia.

Stream 2 Modules

M1: Novel Methods of Reprogramming
Module Leader: A/Prof Ernst Wolvetang
(AIBN, University of Queensland)

M2: Novel Approaches for the Generation of Clinically Relevant iPS Cell Lines
Module Leader: Dr Paul Verma
(Monash Institute of Medical Research)

M3: Are Human iPS Cells Equivalent to hESC?
Module Leader: Dr Andrew Laslett (ASCC)

M4: Transcriptomic & Epigenomic Analysis of Pluripotency & iPS Utility
Module Leader: Prof Sean Grimmond
(IBM, University of Queensland)

M5: iPS Cells as Models of Complex Brain Disorders
Module Leader: Prof Alan Mackay-Sim
NCAS, Griffith University)

M6: Reprogramming Adult Cardiac Stem Cells to Pluripotent iPS-like Cells In Vitro Without Genetic Modification
Module Leader: Prof Richard Harvey (VCCRI)

M7: Primitive iPS-derived MSC for Bone Repair
Module Leader: Prof Nick Fisk
(University of Queensland Centre)

M8: Characterisation & Utilisation of iPS Cells for Dental Regeneration
Module Co-Leaders: Prof Mark Bartold (Colgate Australian Clinical Dental Research Centre, University of Adelaide) &
Prof Stan Gronthos (Hanson Institute)

Case Study – How collaboration using iPS cells will help us better understand schizophrenia

Professor Alan Mackay-Sim, Director of the National Centre for Adult Stem Cell Research at Griffith University has a long-standing research interest in neurological diseases. In this new collaboration he will work with Associate Professor Ernst Wolvetang in Queensland to generate iPS cells from patients with schizophrenia.

Schizophrenia, a medical condition affecting the normal functioning of the brain, arises from complex interplays between genes and the environment with multiple genes of small effect acting together.

The schizophrenia iPS cells will be compared with control cells, ultimately aiming to elucidate the differences in the many genes thought responsible for this disease. Increased understanding of these differences may help to develop better treatments for individuals with the disease.

Case Study – Investigating the use of iPS Cells to treat gum disease

Professor Mark Bartold of the University of Adelaide and Dr Stan Gronthos of the Hanson Institute, are leaders in the analysis of dental stem cells. Their current work is focused on sheep and pigs, whose teeth, like those of humans, suffer from periodontitis - inflammatory diseases of the bone, gums and tissues that can result in tooth loss.

Working with Dr Andrew Laslett at the Australian Stem Cell Centre in Melbourne, the Adelaide group will investigate the development of iPS cells from oral cells and investigate their usefulness for tissue regeneration around teeth and dental implants in sheep and pigs. These animal models, the researchers believe, are a stepping stone to one day translating the research into humans.

Collaborative Stream 3 – Pluripotent Stem Cell Differentiation

S3: Pluripotent Stem Cell Differentiation Program
Stream Leader: Prof Andrew Elefanty (MISCL)
Deputy Stream Leader: A/Prof Susie Nilsson (ASCC)

Human embryonic stem (hES) cells and iPS cells (see Collaborative Stream 2) are highly prized by researchers because they are pluripotent, that is, they have the ability to turn into any cell type in the body. However it remains a major scientific challenge to reliably direct these pluripotent stem cells to differentiate into specific cell types such as blood, heart or pancreas. Once these hurdles are overcome, it will be possible to create the large numbers of mature human cells needed for research into normal development, disease progression and, in the longer term, for clinical use as cell therapies.

The *Pluripotent Stem Cell Differentiation* collaboration brings together eight modules, including one previously unfunded by the ASCC, with extensive expertise in researching pluripotent stem cells and in guiding these cells to become specific cell types.

Led by Professor Andrew Elefanty, Joint Laboratory Head of the Embryonic Stem Cell Differentiation Laboratory of the Monash Immunology and Stem Cell Laboratories (MISCL), the immediate goals of this Collaborative Stream are to:

- efficiently generate human progenitor and mature cells to study both normal development and disease;
- generate reporter lines to facilitate this first goal and also for use in screening programs to identify small molecules replacements for expensive growth factors;
- provide mature cells of value to researchers and the pharmaceutical industry for testing drug efficacy and toxicity.

The long-term goal of the Stream is to generate large numbers of safe, mature cells for transplantation therapy.

Stream 3 Modules

M1: Haematopoietic Differentiation & Expansion of Human Pluripotent Stem Cells
Module Leader: Prof Andrew Elefanty (MISCL)

M2: Genetic Modification of Pluripotent Stem Cells
Module Leader: Prof Ed Stanley (MISCL)

M3: Characterisation of Pancreatic, Respiratory & Thymic Epithelium Derived from the In Vitro Differentiation of Pluripotent Stem Cells
Module Leader: Prof Ed Stanley (MISCL)

M4: Refining the Pluripotent Stem Cell Phenotype
Module Leader: Dr Andrew Laslett (ASCC)

M5: Regenerative Therapies for Renal Repair
Module Leader: Prof Melissa Little (IMB, University of Queensland)

M6: Functional Assessment of HSC & HPC Derived from Directed Differentiation of hESC & iPS Cells
Module Leader: A/Prof Susie Nilsson (ASCC)

M7: Characterisation & Propagation of hES &/or iPS Cell Derived Haemopoietic Precursors
Module Leader: A/Prof David Haylock (ASCC)

M8: Stem Cell Derived Cardiomyocytes: Tools for Investigating Cardiac Disease
Module Leader: Dr David Elliott (MISCL)

Case Study – Investigating the safety and potential of blood cells made from pluripotent cells
Associate Professor David Haylock of the ASCC has long been interested in the development of innovative cell therapies based on haematopoietic, or blood forming, stem cells. In this new collaboration, Associate Professor Haylock will apply his expertise in haematopoietic stem cells (HSCs) from adult sources such as bone marrow and cord blood, to understand whether haematopoietic cells made from embryonic stem cells and iPS cells are similar to their adult counterparts. He will collaborate with embryonic and haematopoietic stem cell experts to determine the genetic stability, safety and ability of haematopoietic stem cells generated in the laboratory and to grow these cells in large numbers with the ultimate view to using them in patients.

Case Study – Pluripotent stem cells as tools for research and biotechnology
Professor Ed Stanley is an expert in making stem cells glow in the dark. By genetically modifying human pluripotent stem cells so they fluoresce when certain genes are switched on or off, researchers are able to quickly see if stem cells have turned on the genetic differentiation pathways that lead to the generation of blood, pancreatic or cardiac cells. Recently, Professor Stanley and his collaborators have been able to modify ES cells to glow green when they turn into beating heart cells. This 'reporter-line' technology is a key tool to understanding how stem cells differentiate into other cell types.

Collaborative Stream 4 – Adult Stem Cell Program

Bone marrow contains large numbers of haematopoietic or blood-forming stem cells which were first used clinically in bone marrow transplants in the 1950s and 1960s. Subsequently, the discovery of adult stem cells in other organs suggests that stem cells exist in all tissues of the body.

S4: Adult Stem Cell

Stream Leader:
Prof Richard Harvey (VCCRI)
Deputy Stream Leader:
Prof Melissa Little (IMB, University of Queensland)

Adult stem cells are involved in the day-to-day maintenance of organs and tissues as well as repair of disease and injury. When required, adult stem cells emerge from their dormant state, divide, and differentiate into the appropriate cell types, which repopulate the organ. Adult haematopoietic stem cells from patients can be isolated in the laboratory and used in clinical procedures. Such an example is the delivery of healthy hematopoietic cells into a patient whose own bone marrow is either dysfunctional or has been destroyed by treatment for leukaemia or other types of cancer.

The *Adult Stem Cell* Collaborative Stream brings together world class adult stem researchers in Australia, who will share their knowledge and expertise in the biology of stem cells from a variety of organs - kidney, blood, thymus, heart, lung and brain. The Stream will also analyse the properties and roles of stem cells in disease, particularly cancer, where recent research has shown a possible role for stem cells in tumour formation.

The *Adult Stem Cell* collaboration is led by Professor Richard Harvey, Deputy Director of the Victor Chang Cardiac Research Institute in Sydney, and consists of ten modules of which half are currently ASCC funded projects.

Stream 4 Modules

Stream 4 Modules
M1: Endogenous Cardiac Stem Cells *Module Leader:* Prof Richard Harvey (VCCRI)
M2: Determining the Location, Origin & Normal Function of Endogenous Renal MSCs & their Relative Capacity to Elicit Renal Repair *Module Leader:* Prof Melissa Little (IMB, University of Queensland)
M3: Endogenous Neural Stem Cells: Function & Regulation *Module Leader:* Prof Perry Bartlett (Queensland Brain Institute)
M4: Adult Lung Stem Cells *Module Leader:* Prof Ivan Bertoncello (ASCC)
M5: Adult Thymic Stem Cells *Module Co-Leaders:* Prof Richard Boyd (MISCL) & Dr Anne Chidgey (MISCL)
M6: Models of Human Breast Epithelial Stem Cell Function *Module Co-Leaders:* A/Professor's Jane Visvader & Geoff Lindeman (WEHI)
M7: Haemopoietic Stem Cells & Their Niche *Module Leader:* A/Prof Susie Nilsson (ASCC)
M8: Molecular Control of de novo Haemopoietic Stem Cell Generation *Module Leader:* Prof Doug Hilton (WEHI)
M9: Transcriptional Regulation of Haemopoietic Stem Cells *Module Leader:* Drs Tim Thomas & Anna Voss (WEHI)
M10: Database of Adult Stem Cell Transcription *Module Leader:* Prof Doug Hilton (WEHI) & Dr Christine Wells, Griffith University

Case Study – Stem cells in the heart

Heart attack, stroke and related diseases are the leading cause of death in the western world, with 300,000 Australians suffering from heart failure alone. The current optimal therapy for heart failure is heart transplantation, however donors are scarce.

The possibility of alternative therapies is driving the research of Professor Richard Harvey at the Victor Chang Cardiac Research Institute in Sydney. His team is working towards a better understanding of the stem cells that reside in the heart and how we might one day use these cells to help prevent or repair damage.

Case Study – Using adult stem cells to understand breast cancer and other cancers

The epithelium is the membranous tissue that covers most internal and external surfaces of the body and its organs. Epithelial cancers such as breast, lung, colorectal and prostate account for 80% of human cancers. Breast cancer is of particular interest to Associate Professor's Jane Visvader and Geoff Lindeman of the Walter and Eliza Hall Institute in Melbourne. Their research is focused on cancerous stem cells in the breast, with the long-term goal of identifying tumour markers that could be used for more accurate diagnosis and prognosis, and for development of potential therapies for breast and other cancers.