Submission to the Senate Community Affairs Committee

Inquiry into the Legislative responses to Recommendations of the Lockhart Review

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Abbreviations

Centre	Australian Stem Cell Centre
NH&MRC	National Health & Medical Research Council
SCNT	Somatic cell nuclear transfer
IVF	*In vitro* fertilisation
ART	Assisted reproductive technology

Overview

The Australian Stem Cell Centre was established in May 2002 as the first Australian Biotechnology Centre of Excellence, with the principal goal of integrating a national multi-institutional research program involving stem cells and related technologies to ultimately develop treatments for human diseases.

The existing legislation, namely the ***Prohibition of Human Cloning Act 2002*** and the ***Research Involving Human Embryos Act 2002,*** has effectively provided a national functional framework that enabled the Centre to undertake embryonic stem cell research, alongside adult stem cell research, in a collaborative and rich research environment that is both supportive and well regulated.

The Centre believes the development and adoption of national legislation, complemented by state legislation regulating embryo research, has contributed to this country's current high standards and scientific position as leaders in quality human embryonic stem cell research. Therefore, the Centre fully supports the maintenance of national legislation to ensure the regulation and continued advancement of ethical, high quality and competitive human embryonic and adult stem cell research in Australia.

Adoption of the recommendations set out in the Legislation Review Committee Report (Lockhart Review) would not only further assist the Centre in achieving its goals and serve to attract quality scientists to Australia, but would also considerably enhance Australia's existing international competitiveness in stem cell research.

On 30 May 2002, the Prime Minister announced the successful applicant for Australia's first Biotechnology Centre of Excellence: the Centre for Stem Cells and Tissue Repair, now known as the Australian Stem Cell Centre Limited. The Prime Minister's comments[1] when making the announcement remain relevant to the Lockhart Committee's review of the legislation and the Senate Community Affairs Committee Inquiry, as they help set this whole evaluation process into a proper context. The Prime Minister noted

> "*... This centre … will ... provide the vehicle for Australia to compete in the rapidly growing area of tissue regeneration and cell therapies. A key area of research will be the potential application of both adult and embryonic stem cells in the treatment of diabetes, vascular, bone and nerve damage, kidney disease and diseases of the blood and the skin. The centre will be truly national with its headquarters in Victoria and nodes in South Australia, New South Wales, Queensland and the Australian Capital Territory, providing a valuable boost to the Australian biotechnology industry. … I hope that the centre will attract the world's best researchers to Australia, especially many of our best and brightest who are currently working overseas.*
>
> *"This is a very exciting day for Australian research, it really is. One of the goals of Backing Australia's Ability was to put Australia's name up in lights in two specific areas by establishing centres of excellence. You have to specialise, you have to carve out some organisations and units that are better than any others and you've got to give them the financial support to achieve their goals. … and I think there'll be great excitement in the Australian research community because the potential, particularly in the area of biotechnology and stem cell research, is quite literally unlimited. And I want as Prime Minister, I want Australia to be up there with more than a reasonable slice of the action."*

The legislative framework in its current form restricts the Centre's ability to participate in an important and emerging area of stem cell research. Unless the legislative framework is modified and the recommendations of the Lockhart Review implemented, the Centre will be impeded in its efforts to:

1. *fully* undertake leading research in a key identified area, namely human embryonic stem cell research;

[1] http://www.pm.gov.au/news/speeches/2002/speech1675.htm

2. retain and attract the best researchers to Australia in this area of research;

3. specialise, and make proper use of significant taxpayer funding, to explore the *full extent* of the potential in stem cell research;

4. establish important scientific collaborations with highly regarded research groups in jurisdictions that allow activities that are not currently allowed in Australia under Australian law (particularly key groups in the UK and the US); and

5. ensure that Australia is "up there with more than a reasonable slice of the action".

If the Lockhart Review recommendations are implemented by all relevant Governments, it would enable the Centre to be an active collaborator on a global scale, and enhance Australia's international reputation for ground-breaking stem cell research conducted in a legal, ethical and socially responsible manner.

In particular, the Centre supports:

- a continued ban on human reproductive cloning;
- the continuation of a national co-ordinated approach, including legislative and licensing framework, to ensure that Australia's position in ethical human stem cell research, embryonic and adult, is enhanced;
- continued ethical access to excess ART embryos for deriving new human embryonic stem cell lines for research purposes;
- the use of somatic cell nuclear transfer (SCNT) as a means of deriving disease specific stem cells for research purposes under an ethical license regime; and
- an amendment to existing Australian Customs Regulations to allow the import and export of SCNT derived cell lines, either generally or from nominated international Centres.

Professor Stephen Livesey
Chief Executive Officer
Australian Stem Cell Centre
October 2006

Scope of Submission

The intent of this submission is for the Centre, in accordance with its obligations to the Commonwealth, to take a leadership role in the development of Australia's research expertise in the biotechnology sector and to support changes which will enable Australian researchers to remain part of, and so reap benefit from, the exciting advances in medical research that are occurring in stem cell research.

Our submission describes and discusses scientific matters relevant to the Lockhart recommendations insofar as such scientific matters pertain to stem cell research and related technologies. We have deliberately excluded from our discussion implications for research relating to assisted reproductive technology (ie ART, meaning all fertility treatments in which eggs or sperm are manipulated), save for where those factors may impinge upon the development of stem cell research.

While the Centre necessarily presents a single point of view on a number of issues, which represents a consensus, we acknowledge that this may not in every instance be exactly aligned with the views of individual stakeholders, employees or funded researchers represented by the Centre in this document. In particular, the Centre's stated position cannot be extrapolated as representative of the individual stakeholder institutions that make up the stakeholder group associated with the Centre.

Recommendations

The ASCC wholly supports the following of the Lockhart Review recommendations:

Recommendation - National Legislation

The Centre supports the continuation of a national co-ordinated approach to ensure that Australia's position in ethical human stem cell research, embryonic and adult, is not compromised.

To ensure that Australia does not to waste its resources - financial, intellectual capital, infrastructure and social even-handedness - it is vital that the State, Territory and Commonwealth Governments work together to ensure a consistent legislative framework is in place. The inherent strength of the Centre's design, in being a national and multi-nodal centre, will ultimately be sub-optimal if the Centre is not able to fully access stem cell resources and draw on and deploy the broad spectrum of research expertise available to it throughout Australia and the rest of the world.

The Centre is focussing not just on stem cells (adult and embryonic) but also on tissue repair and immune modulation. The Centre is taking a coordinated multidisciplinary approach to maximise the potential benefit from one research program to enhance the outcomes and advance research in another. This approach is a deliberate strategy of the Centre because, as was said in a recent editorial in *Nature Biotechnology* "it is too early too leap to grand conclusions about which types of cells – whether embryonic or adult stem cells – will prove more useful. It is also too early to know which approaches will work in which conditions."[2] At this stage, current scientific evidence would suggest there will probably be an ongoing role for both embryonic and adult stem cell research.

Recommendation - Reproductive Cloning

The Centre supports a ban on human reproductive cloning.

The Centre fully supports a continued ban on human reproductive cloning. There is no equivocation on the part of the Centre with respect to its view on this matter. This recommendation is supported unanimously.

[2] Nat. Biotechnol. **23**, 763 (2005)

Recommendation – Prohibition on developing and implanting embryos

The centre fully supports a prohibition on the development of a human embryo, created by any means, beyond 14 days gestation in any external culture or device.

Recommendation – Use of excess ART embryos in research

The Centre supports continued ethical access to excess ART embryos for deriving new human embryonic stem cell lines for research purposes.

Between 5 April 2002 and 5 April 2005, Australian researchers could obtain a license authorising the use of any excess ART embryos that had been created before 5 April 2002 and donated with consent to research. The 'sunset clause' was lifted by operation of section 46 of the *Research Involving Human Embryos Act 2002 (Cth)* in April 2005. Any change to the present ability of researchers to access excess ART embryos, and in particular any reinstatement of the moratorium, would seriously hinder research in Australia. Australian researchers would be required to undertake research on a diminishing pool of embryos of variable quality that have spent an ever-increasing time in a frozen state and are therefore not optimal for research purposes. Australian researchers would be required to formulate leading edge research projects with this restricted pool of aged embryos which may compromise the quality of the research itself.

There is a strong case for the continuing effort to derive new human embryonic stem cell lines, particularly since this is a rapidly developing technology with constant improvements in the derivation and propagation of human embryonic stem cells, human feeder layers and improved media. Importantly, as well as compromising the quality of the research, many of these older existing cell lines are suitable only for certain types of research as they have been developed in vitro using animal products and may cause problems such as the raising of unwanted antibodies if used in clinical applications. In addition, many of these lines are exhibiting genetic instability, and so their potential use in therapeutic applications has been called into question.[3]

Although many more cell lines have been reported in the literature since 2002, many of these are not well described and most are not in widespread circulation. Many existing cell lines have significant limitations, including derivation under sub-optimal conditions and commercial restrictions that may restrict their use in certain projects. There is an inadequate understanding of how the properties of various existing cell lines derived and propagated under a variety of conditions compare with one another. There may well be certain desirable or less desirable features associated with particular cell lines which are a function of the particular growth conditions (which may/may not have been properly documented). To remedy some of these limitations on a global scale, there is an established co-ordinated analysis underway via the International Stem Cell Initiative to evaluate and standardise all human embryonic stem cell lines.

While controls and standardisation can be applied to the derivation of embryonic stem cell lines going forward, it is clearly impossible to correct the inadequacies of processes previously used to develop embryonic cell lines and accordingly, reliance exclusively on these old cell lines for research purposes must necessarily be similarly inadequate.

A further issue is to ensure that IVF couples will continue to have the option of donating to research the unused embryos that would otherwise be destroyed in the IVF process. It is important to note that the scientists interviewed for this submission are not arguing for indefinite or unlimited access to embryos for research for any purpose. Fundamentally, they and the Centre believe that donors should be given an informed opportunity to consider a variety of options with respect to their excess embryos:

1. donation to another couple for the purpose of achieving a pregnancy;

2. donation to dedicated embryo research for the improvement of IVF techniques or training;

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[3] Nature Genetics paper from the Johns Hopkins group: Anirban Maitra et al. Genomic alterations in cultured human embryonic stem cells; Published online: 4 September 2005; | doi:10.1038/ng1631

3. donation to embryonic stem cell research; or

4. destruction of their spare embryos according to their wishes.

At present it appears that a reasonable number of Australian donors are prepared to commit their excess embryos to research which has, to date, provided an adequate pool of embryos available to research projects under license.

Recommendation – Use of fresh ART embryos

The Centre supports the recommendation that fresh ART embryos that are diagnosed by preimplantation genetic diagnosis (according to the ART guidelines) as being unsuitable for implantation should be permitted to be used, under licence, for research, training and improvements in clinical practice.

Currently, scientists are unable to obtain IVF created embryos (created for the purpose of reproduction) affected by an inherited genetic disease, deemed unsuitable for implantation. IVF clinics, under current legislation, must destroy, rather than donate to research, all embryos that have been identified as having genetic defects or disease. The potential benefits for the study of disease by developing disease-affected stem cell lines, with appropriate consent from the donors, could have many uses from understanding the genetic triggers and processes during the onset of disease to using the cells for the development of new drugs and treatments for such diseases.

Recommendation – Use of human embryos created by somatic cell nuclear transfer

The Centre supports a provision to allow the use of somatic cell nuclear transfer (SCNT) as a means of deriving new disease specific stem cell lines.

The Centre prefers the use of human eggs over animal eggs for SCNT experiments.

SCNT should be viewed as an important tool for reprogramming an adult cell genome in an experimental environment and not as a procedure related to reproductive biology to achieve a live birth.

Understanding the reprogramming of an adult cell nucleus to achieve a more flexible or plastic state would have far-reaching beneficial implications for biology and medicine. Ultimately, SCNT may deliver an understanding of those unidentified factors within an egg cell that can reprogram the behaviour of a mature cell, these findings might eventually obviate the need to use eggs or produce embryos at all, because it could be applied directly to the reprogramming of adult cells. In addition, understanding reprogramming would also increase our knowledge of adult tissue stem cell plasticity (the conversion of one type of tissue stem cell into cells of another tissue). This important area of SCNT is currently entirely closed to Australian researchers.

SCNT offers a unique approach to the study of genetic disorders in humans. The availability of such cell lines would enable the study of the cellular basis of disease susceptibility, an understanding of the evolution or trigger for the emergence of a genetic disease in the very early human and the testing of hypotheses concerning the involvement of specific genes for patients suffering from a number of serious diseases.

Stem cell lines can be created by using SCNT technology from individuals with a known genetic predisposition to a particular disease. In particular, stem cell lines can be created for diseases that are unable to be detected by pre-implantation genetic diagnosis. These cell lines would be models for investigation of the cell biology and genetic basis of the given disease or disorder they would also be highly useful for testing and developing new drugs and treatments. Research into the reprogramming of human cells will yield new information into the human condition that is not available from the study of animal cells.

Without the ability to perform SCNT, elite researchers remaining in Australia will always be behind the lead of the top researchers in the United States, United Kingdom and other countries where SCNT is lawful. –Inevitably, without the ability to perform SCNT and collaborate on SCNT projects, the strategy and

outlook for the Centre will also be hindered. A number of key senior scientists have this year left Australia for the United States where SCNT is permitted and considerable funds are available. The length of time the legislative review has taken to date and the uncertainty in the outcome is a significant deterrent to the Centre being able to attract leading scientists, from this field, to come to Australia. It is also a significant risk to the stability of the Australian scientists working in this field at present. Our attempts to fulfil and exceed the expectations of the broad Australian community and our vision of contributing and supporting the great strength within the Australian stem cell science community will certainly be restricted if SCNT is not permitted.

Use of Eggs for SCNT.

The ASCC prefers the use of human eggs to animal eggs in SCNT experiments that involve a human nuclei (somatic cell). The Centre believes there is limited merit in inserting human nuclei into an animal egg. In addition, due to the scarcity of human eggs, the Centre believes that, ideally, preparatory training for scientists in the technique of SCNT should occur using animal eggs with animal nuclei until such time that a very high standard of technical capability has been achieved.

Recommendation – Egg Donation

The Centre supports the current principles of consent and prohibition of sale of human gametes.

The Centre advocates the responsible use of human eggs for research minimising wherever possible the amount of eggs required. There are several ethical ways of obtaining human eggs for SCNT experiments including: patient donation (single donor of egg and somatic cell), stimulating egg growth from biopsied and donated ovarian tissue, eggs harvested during the IVF process and supernumerary to the completed IVF process and altruistic donation.

Recommendation – Trade and international exchange of human reproductive materials and stem cells

The Centre supports an amendment to existing Australian Customs Regulations to allow the import and export of SCNT derived cell lines.

The Centre supports an amendment to the Customs (Prohibited Imports) Regulations 1956 to allow Australian researchers access to stem cells and stem cell lines derived from SCNT embryos developed overseas. If SCNT becomes lawful in Australia as a result of this inquiry, co-extensive amendments must be made to allow importation of SCNT-derived cell lines in order for researchers in Australia to effectively use this technology and collaborate with other international scientific groups. This would also ensure no duplication of unnecessary stem cell lines, effectively minimising the number of nuclear transfer embryos created and the number of human eggs used to create those cell lines.

The amendments become even more critical to the survival of Australian stem cell research if, the Committee is of the view that Australian researchers may use SCNT-derived cell lines but should not be entitled to undertake SCNT experiments in Australia.

Recommendation – National stem cell bank

The Centre supports a feasibility study to determine the structure by which a national stem cell bank may be established.

The formal implementation of an Australian stem cell bank would enhance Australia's reputation as a leading producer of high quality cell lines. A national stem cell bank would have many positive features including:

1. ensuring regulatory and ethical compliance of all cell lines deposited;

2. standardizing the quality of all cell lines;

3. providing consistent complementary information and service advice with all cell lines;

4. conserving embryos; the Bank would reduce duplication of research to produce specific cell lines;

5. being a national (and eventually international) resource by requiring compulsory deposition of all Australian derived cell lines;

6. providing an independent assessment of the quality and standard of cell lines;

7. being a database of historical records of production and distribution of all cell lines;

8. monitoring the import and export of cell lines; and

9. providing a central body for the independent reporting requirement to licensing bodies.

The Australian Stem Cell Centre, in 2002 joined with a complementary Major National Research Facility (MNRF). The MNRF facility, initially focused on tissue repair and cell therapies, is based in Melbourne, and has received support funding from both the Victorian and Australian Governments. The Australian Stem Cell Centre, supported by the MNRF, is the logical organisation to oversee a national stem cell bank as it has an existing cell storage facility and trained staff. Presently the MNRF facility offers Mel 1 and Mel 2 embryonic cell lines (developed by Stem Cell Sciences in collaboration with the Centre) for distribution to researchers free of encumbrances. Mel 3 and Mel 4 are almost ready for distribution with a further two lines in development under an NH&MRC licence.

To further develop the Major National Research Facility's capacity to also become a national stem cell bank for the region would require additional funding and infrastructure. The Major National Research Facility has an existing Access Committee, with an independent chairman, that determines policies and structure regarding access by scientific groups around the country to use the facilities in Melbourne.

The development of a national stem cell bank, when coupled with the implementation of the other Lockhart recommendations – principally, allowing SCNT technology in Australia and also amending Customs Regulations – would offer an significant practical benefit for Australia and would greatly enhance Australia's reputation as a leader in stem cell research and development. It may be possible to use SCNT for the creation of banks of stem cell lines possessing specific genes (the so-called 'histocompatibility loci') that determine the compatibility of tissues. A bank of such stem cell lines specific for each locus could provide an effective tissue cell match for a significant proportion of the population.

Recommendation – Public Education

Public education is fundamental in helping the public understand and engage in emerging and complex issues in biotechnology and, in particular, stem cell technology.

One of the principal educational functions of the Australian Stem Cell Centre (ASCC) is to inform public debate and encourage a deeper understanding and knowledge of the progress of research and development in this field.

This has been especially important over the last year, as the applicability of advances in human embryonic stem cell research, continued questions about the potential use of different cell types, and considerations of the ability to perform certain aspects of research in Australia are each under consideration.

In fostering public discussion, the ASCC acknowledges and respects that there are different views in society on the ethics of certain forms of stem cell research. For some, the promise of stem cell research is counter balanced by ethical and religious objections to embryo and embryonic stem cell research.

The ASCC encourages and facilitates discussion and information exchange to form an educated debate, not only to improve the community's understanding of stem cell research and its realistic applications, but to promote an awareness of the spectrum of views.

Further Review of the Legislation

The Centre supports continuous review of the legislation.

The Centre believes it is paramount that legislation keeps pace with scientific advances and to ensure the field is appropriately regulated and to allow the ongoing advancement of knowledge and the application to discoveries to therapeutic outcomes.

As this field of research is developing so rapidly, the Centre is supportive of the proposal to review the amended act following the third anniversary of its Royal Assent. Any review must be independent and performed in consultation with the Council of Australian Governments.

Research Developments

Recent advances in knowledge from stem cell research have exceeded expectations in some areas of research and been disappointingly slow in others. It is important to consider that progress in scientific research is incremental and may take many years and the participation of many researchers through collaboration (nationally and internationally). Often progress is made in areas that are highly important but not always apparent or understandable to the general public such as improved research techniques or growth variables. The development of knowledge regarding the potential of adult stem cells and embryonic stem cells is evident by the wide number of excellent articles published in prestigious journals. The rate of publication is intense; one journal site alone, Nature.com, in 2006 alone to date, published 435 articles on somatic cell nuclear transfer and 1896 on stem cells. If we multiply this across the many scientific publications the intensity and scope of the research is enormous. Several new journals dedicated to stem cell research have also become recently available, including: *Stem Cells and Development*; *Cloning and Stem Cells*; *Stem Cells*; *Regenerative Medicine* and *E-biomed*: the *Journal of Regenerative Medicine; Stem Cell Review.*

The table below outlines the progression of this young but rapidly progressing science.

Time line of key developments in Embryonic Stem Cell Research

Date	Milestone
1981	**Derivation of Mouse Embryonic Stem Cells** Mouse embryonic stem cells (ES cells) are derived directly from the mouse blastocyst in culture by two groups.[4]
1997	**Cloning of Dolly the Sheep** Embryologist Ian Wilmut and his colleagues at Scotland's Roslin Institute report in *Nature* that his group had cloned a lamb using a cell nucleus taken from an adult ewe's udder. Dolly quickly became the worlds most first and most famous cloned mammal.[5]
1998	**Derivation of first human ES and embryonic germ cell lines.** Biologist James Thomson and his team at the University of Wisconsin, Madison, report in *Science* that they have isolated stem cells from human embryos and coaxed them to grow in five "immortal" cell lines.[6]
2001	**Derivation of Mouse ES Cells from Blastocysts created by Somatic Cell Nuclear Transfer.** Megan Munsie and the team at Monash University in Melbourne, Australia derived the first Mouse ES cells from blastocysts that are produced by transfer of somatic nuclei into enucleated oocytes (somatic cell nuclear transfer).[7]

[4] Evans, M. J. & Kaufman, M. H. Establishment in culture of pluripotential cells from mouse embryos. Nature 292, 154–156 (1981).

Martin, G. R**.** Isolation of a pluripotent cell line from early mouse embryos cultured in medium conditioned by teratocarcinoma stem cells**.** Proc. Natl Acad. Sci. USA 78, 7634–7638 (1981).

[5] Wilmut I, Schnieke AE, McWhir J, Kind AJ, Campbell KH. Viable offspring derived from fetal and adult mammalian cells. Nature. 1997 Feb 27;385(6619):810-3.

[6] Thomson, J. A. *et al*. Embryonic stem cell lines derived from human blastocysts. Science 282, 1145–1147 (1998).

2003	**Potential of ES Cells to Treat Parkinson's Disease** In 2003, a group from New York demonstrated that the Parkinson's mouse model phenotype was alleviated of its symptoms for 8 weeks when transplanted with ES cell differentiated dopamine neurons[8]. Following this study another group performed, a similar cell transplantation in the Parkinson's phenotype monkey model. In a chemical analysis 14 weeks after transplantation the presence and survival of dopamine neurons and dopamine transporter cells was confirmed[9].
2004	**SCNT Licences Granted in the UK** SCNT is performed at three locations across the UK: Newcastle, Edinburgh and London. Licences Granted by the Human Fertilisation and Embryology Authority in the UK: ▪ 11 August 2004 – the HFEA granted the first licence for SCNT to the Newcastle Centre for Life. ▪ 8 February 2005 – licence granted to Professor Ian Wilmut in Edinburgh and a team of collaborators at Kings College London to perform SCNT to investigate Motor Neuron Disease.
2006	**SCNT Licence Granted to Harvard University** Harvard University researchers have been given the go-ahead to use cloning to create disease-specific lines of human embryonic stem cells. Scientists plan to use SCNT to study diabetes and blood and neurodegenerative diseases. **No fewer than five institutions and eight Institutional Review Boards approved the proposals.** Private funding will support the work, which cannot be paid for with federal dollars. Researchers plan to use excess eggs from fertility clinics as well as fresh eggs from unpaid compassionate donors. Douglas Melton and Kevin Eggan of the Harvard Stem Cell Institute plan to create stem cell lines that will enable them to study diabetes in a dish. Eggan also plans to use the technique to study neurodegenerative diseases such as amyotrophic lateral sclerosis. George Daley of Children's Hospital Boston is aiming for customized cell lines using skin biopsies from patients with sickle cell anaemia and other blood diseases.

Please see Appendix A for a more comprehensive list of major journal articles on stem cells and somatic cell nuclear transfer.

International Stem Cell Cooperation and Collaboration

The International Society for Stem Cell Research (ISSCR), a research society of stem cell scientists from around the world (www.isscr.org), continues to grow with nearly 2500 members internationally. The prestigious ISSCR Board includes a number of Australian representatives and the President of the ISSCR for 2006/07 is eminent Australian researcher Professor Paul Simmons. The Australian Stem Cell Centre

[7] Munsie MJ, Michalska AE, O'Brien CM et al. Isolation of pluripotent embryonic stem cells from reprogrammed adult mouse somatic cell nuclei. Curr Biol 2000;10:989–992

[8] Barberi T, Klivenyi P, Calingasan NY et al. Neural subtype specification of fertilization and nuclear transfer embryonic stem cells and application in parkinsonian mice. Nat Biotechnol 2003;21:1200–1207.

[9] Takagi Y, Takahashi J, Saiki H et al. Dopaminergic neurons generated from monkey embryonic stem cells function in a Parkinson primate model. J Clin Invest 2005;115:102–109

has sponsored and secured a bid to host the 2007 ISSCR meeting to be held in Cairns; the first time it will be hosted outside North America.

The International Stem Cell Forum (www.stemcellforum.org.uk) was established in January 2003. The aim was to bring together international funding agencies that were united in the belief that bilateral collaboration and information-sharing, thereby accelerating scientific progress and global practices in stem cell research. The Australian NH&MRC is a member of the Forum.

On November 6, 2004 the International Stem Cell Forum held its fourth meeting in Montréal, and at the same time Canada's Stem Cell Network hosted a meeting of representatives of some of the existing stem cell Centers or Networks to share information and discuss multinational collaborations between the national groups. The outcome of the "Networks" meeting in Montréal was a recommendation to create an international coordinating group that will be committed to international cooperation and collaboration, extending the concept of national research networks to the international level. That group has now become known as the International Consortium of Stem Cell Networks (ICSCN).

In 2005 the Victorian State Government, recognising the importance of international collaboration and relations, made available $200,000 funding to a Secretariat to underpin and coordinate the ICSCN. That Secretariat is located at the Australian Stem Cell Centre. The Consortium is co-chaired by the Chief Executive Officer of the ASCC and the Scientific Director of the Canadian Stem Cell Network.

ICSCN Mandate

The International Consortium of Stem Cell Networks is a 'network of networks' that aims to unify international efforts to accelerate opportunities to make stem cell therapy a reality for a broad range of debilitating diseases, by:

- providing a forum for scientific and other discussion
- providing a forum for exchange of best practice and development of international equivalents of national initiatives
- organising and promoting international workshops and symposia
- encouraging and facilitating the exchange of researchers between network members
- facilitating communications to help in the coordination of research and translation between different countries

Current members of the ICSCN include: Australian Stem Cell Centre, Bereshith (Israel Consortium), California Institute for Regenerative Medicine, International Society for Stem Cell Research , RIKEN Center for Developmental Biology, Japan, Scottish Stem Cell Network , Spanish Stem Cell Bank , Stem Cell Network North Rhine Westphalia , Stem Cell Network, Canada, The Institute of Stem Cell Biology and Regenerative Medicine (North East England), Network in Regenerative Medicine, Berlin , National Institutes of Health , Norwegian Centre for Stem Cell Research , Stem Cell Research Forum of India.

The Australian Stem Cell Centre

The Australian Stem Cell Centre was established four years ago, at around the same time that the current legislation was enacted. The progress made by the Centre in developing a broad national approach toward the progress of stem cell research and regenerative medicine has been very successful. The four major platform technologies have numerous associated statements of work from scientific groups from around the country that are rigorously and systematically monitored and refined to achieve the most useful and valuable results. The Australian Stem Cell Centre is unquestionably one of the most ambitious and progressive partnerships between the Commonwealth, the scientific community and academia. The Centre believes one of the key future critical success factors in this research field is the investment in building highly trained human capital and intellectual assets. Currently the Centre is supporting over 18 PhD students across Australia.

Commercially, since its inception, the Centre has filed an impressive number of patents and created a valuable portfolio of intellectual property derived from the world-class scientific research undertaken by researchers funded by the Centre. We believe this portfolio will deliver significant benefits to all stakeholders, which ultimately includes the Australian community as well as individuals suffering from disease around the world.

Appendix A

Key Publications 2003 to 2006

Key publications on transplantation of human embryonic stem cells into preclinical animal models of human disease and injury are:

Ben-Hur T, et al. 2004. Transplantation of human embryonic stem cell-derived neural progenitors improves behavioral deficit in Parkinsonian rats. Stem Cells 22(7):1246-1255.

Kehat I, et al. 2004. Electromechanical integration of cardiomyocytes derived from human embryonic stem cells. Nat Biotechnol 22(10):1282-1289.

Keirstead HS, et al. 2005. Human embryonic stem cell-derived oligodendrocyte progenitor cell transplants remyelinate and restore locomotion after spinal cord injury. J Neurosci 25(19):4694-4705.

Banin E, et al. 2006. Retinal incorporation and differentiation of neural precursors derived from human embryonic stem cells. Stem Cells 24(2):246-257.

The key publications on the use of nuclear transfer (NT) involving adult (somatic) cells are:

Li-Ying Sung, et al. 2006. Differentiated cells are more efficient than adult stem cells for cloning by somatic cell nuclear transfer. Nature Genetics Online, @ www.nature.com/naturegenetics.

Takagi Y, et al. 2005. Dopaminergic neurons generated from monkey embryonic stem cells function in a Parkinson primate model. J Clin Invest 115(1):102-109.

Blelloch RH, et al. 2004. Nuclear cloning of embryonal carcinoma cells. Proc Natl Acad Sci U S A 101(39):13985-13990.

Doss MX, et al. 2004. Embryonic stem cells: a promising tool for cell replacement therapy. J Cell Mol Med 8(4):465-473.

Hochedlinger K, et al. 2004. Reprogramming of a melanoma genome by nuclear transplantation. Genes Dev 18(15):1875-1885.

Hochedlinger K and Jaenisch R. 2006. Nuclear reprogramming and pluripotency. Nature 441(7097):1061-1067.

Hochedlinger K and Jaenisch R. 2003. Nuclear transplantation, embryonic stem cells, and the potential for cell therapy. N Engl J Med 349(3):275-286.

Lanza R, et al. 2004. Regeneration of the infarcted heart with stem cells derived by nuclear transplantation. Circ Res 94(6):820-827.

Lerou PH and Daley GQ. 2005. Therapeutic potential of embryonic stem cells. Blood Rev 19(6):321-331.

Other key papers regarding SCNT

2006

Blelloch R, Wang Z, Meissner A, Pollard S, Smith A, Jaenisch R. Reprogramming efficiency following somatic cell nuclear transfer is influenced by the differentiation and methylation state of the donor nucleus. Stem Cells. 2006 Oct;24(9):2007-13. Epub 2006 May 18.

Wakayama S, Jakt ML, Suzuki M, Araki R, Hikichi T, Kishigami S, Ohta H, Van Thuan N, Mizutani E, Sakaide Y, Senda S, Tanaka S, Okada M, Miyake M, Abe M, Nishikawa S, Shiota K, Wakayama T. Equivalency of nuclear transfer-derived embryonic stem cells to those derived from fertilized mouse blastocysts. Stem Cells. 2006 Oct;24(9):2023-33. Epub 2006 May 11.

Rodolfa KT, Eggan K. A Transcriptional Logic for Nuclear Reprogramming. Cell. 2006 Aug 25;126(4):652-655.

Hall VJ, Stojkovic P, Stojkovic M. Using therapeutic cloning to fight human disease: a conundrum or reality? Stem Cells. 2006 Jul;24(7):1628-37. Epub 2006 Mar 23.

Zhao ZJ, Ouyang YC, Nan CL, Lei ZL, Song XF, Sun QY, Chen DY. Rabbit oocyte cytoplasm supports development of nuclear transfer embryos derived from the somatic cells of the camel and Tibetan antelope. J Reprod Dev. 2006 Jun;52(3):449-59. Epub 2006 Mar 31.

Yan LY, Shi LH, Sheng HZ, Liu SZ, Huang JC, Zhu ZY, OuYang YC, Lei ZL, Song XF, Sun QY, Chen DY. Dynamic changes in NuMA and microtubules in monkey-rabbit nuclear transfer embryos. Front Biosci. 2006 May 1;11:1892-900.

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