Progress in stem cell research and the role of law

Ian H Kerridge and Aric Bendorf

Is it time to relax or tighten the legislation on human embryo research?

Over the past decade, human embryo research has generated both enormous scientific interest and extensive public debate. In response to this, Australia passed two Acts in 2002: the *Research Involving Human Embryos Act 2002* (Cwlth) and the *Prohibition of Human Cloning Act 2002* (Cwlth). Together, these Acts, and mirror legislation passed by all states and territories, enabled Australian scientists to undertake specific research involving human embryos, provided that they obtained a licence from the Embryo Research Licensing Committee of the National Health and Medical Research Council (NHMRC), reported regularly to this committee, and had their research approved and monitored by the appropriate institutional ethics committee. At the same time, these Acts prohibited a series of practices — including human cloning, creation of animal–human cybrids, maturation of research embryos beyond 14 days, and the buying and selling of human oocytes — and provided substantial penalties for breaches of the provisions.

Consistent with the provisions of the Acts, the legislation was reviewed in 2005–2006 by the Lockhart Committee (the Legislation Review Committee chaired by the late John Lockhart). After extensive community consultation, the Committee made 54 recommendations for amending the existing legislation. Following further public and parliamentary debate (which culminated in a conscience vote in both federal chambers), almost all of these recommendations were accepted and implemented, by the amending legislation in 2006 or administrative changes made by the NHMRC and other relevant regulatory bodies. (The current federal legislation is the Research Involving Human Embryos Act and the *Prohibition of Human Cloning for Reproduction Act 2002* [Cwlth].) As a consequence, while the major prohibitions present in the 2002 Acts remained, Australian scientists were able to create an embryo by somatic cell nuclear transfer (SCNT) for research purposes and conduct research on human embryos deemed unsuitable for implantation and on eggs in the process of fertilisation up to syngamy.

The legislation is again up for review and, as in 2005–2006, the review must consider: developments in assisted reproductive technology and embryonic stem cell (ESC) research, international developments and legislation relating to the use of human embryos in research, the effectiveness of existing legislation (including whether it has acted as a barrier to important research or clinical practice), and community standards.

Since 2006, research involving autologous and allogeneic transplantation of adult somatic stem cells has continued to advance (although the best evidence continues to be for treatment of malignant and immunological diseases) and early studies have confirmed that autotransplantation of haematopoietic and mesenchymal stem cells may have regenerative capacity in treating hepatic, pulmonary, cardiac, neurological and arthritic diseases. Over this period, human ESC research has also provided important insights into normal and pathological cellular biology, reproduction and embryogenesis, and the creation of disease models and systems for screening drugs and predicting toxicity.[1] Animal studies of ESCs have also shown promising results in the treatment of spinal injury, neurodegenerative and demyelinating disorders and retinal disease, and the first Phase 1 clinical studies involving adults with spinal injury and stroke and children with macular dystrophy have begun.[2-4] At the same time, a series of developments in related fields have also created enormous excitement.

In 2006 and 2007, teams of scientists in Japan and the United States reported that they were able to derive induced pluripotent stem (iPS) cells by inducing forced expression of specific genes in adult somatic cells.[5] These iPS cells, which resemble ESCs in terms of morphology, mitotic activity, telomerase activity and expression of stem cell genes and proteins, appeared to be an important breakthrough as they allowed generation of stem cells without the use of human embryos, did not require the use of donor oocytes, and avoided the problems of immune rejection and graft-versus-host

disease because they were autologously generated.[6] While proof-of-concept and animal studies of iPS cells in a range of degenerative disorders show great promise, recent research suggests that iPS cells may have a slightly different gene expression profile to human ESCs, have limited differentiation capacity and undergo premature ageing. Also, significant hurdles remain with regard to the efficiency and safety of iPS cells before human trials can begin.[7-9]

Recent research has also demonstrated that nuclei from "terminally differentiated" adult somatic cells can be induced ("reprogrammed") to express genes that are typical of ESCs or of other lineages, and differentiated to form other cell types, thereby enabling autotransplantation of normal tissue to areas of disease, or the generation of new organs or tissues using tissue-engineering technologies.[10-12]

Despite the fact that this research is in its infancy, the promising results of research involving iPS cells and reprogrammed adult somatic stem cells has (predictably) led some to proclaim the demise of ESC research and to call for the repeal of legislative amendments enabling human ESC research and SCNT.

This would be a mistake. Although developments in iPS cell research show promise and human ESC research has not yet been translated into medical therapies, this does not provide a reason for prohibiting ESC research. It remains unclear whether human ESCs, reprogrammed adult somatic stem cells and iPS cells will prove to be bioequivalent or to offer alternative or complementary cellular therapies.[7] In addition, as the history of medical research demonstrates, the realisation of clinical benefits from basic research can take decades. Furthermore, the stem cells derived from SCNT may also yield benefits other than medical therapies, including cell lines for drug screening and for research into early embryonic development, normal organogenesis and certain disease states. And, perhaps most importantly, the idea that advances in one field of research should mean researchers are prevented, by law, from exploring another related field of research is, in many ways, antithetical to the principles and processes of science in a liberal democratic society.

Australia's existing regulatory framework provides the most effective means for ensuring that research is important, rigorous and ethically sound in its design and conduct. Should research yield important benefits consistent with the needs and goals of the community, it will prosper. Should it prove redundant, useless or totally at odds with the values of the community, it will not. For all these reasons, and because human embryo and stem cell research enjoy high levels of public support, we should not again seek to prohibit research involving human embryos or the derivation of stem cell lines by SCNT. Whether the current legislation needs to be liberalised further to enable research into mitochondrial diseases, the creation of cybrid embryos or the payment of egg donors, is a matter for debate.

Competing interests

Ian Kerridge is a Board Member of the NSW Stem Cell Network and was a member of the Lockhart Committee in 2006.

Author details

Ian H Kerridge, MPhil, FRACP, FRCPA, Director and Associate Professor of Bioethics,[1] and Haematologist and Bone Marrow Transplant Physician[2]
Aric Bendorf, BA, MBioethics, Doctoral Research Scholar[1]
1 Centre for Values, Ethics and the Law in Medicine, University of Sydney, Sydney, NSW.
2 Westmead Hospital, Sydney, NSW.
Correspondence: ian.kerridge@sydney.edu.au

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