

Human embryonic stem cells leap the barrier

David G Penington and Graham F Mitchell

Our democratic processes have moved on — so must our science

In April 2007, Victoria became the first Australian state to enact legislation (the Infertility Treatment Amendment Bill 2007) that followed the passage by federal Parliament in December 2006 of the *Prohibition of Human Cloning for Reproduction and the Regulation of Human Embryo Research Amendment Act 2006* (Cwlth). This Act gave effect to most of the recommendations of the Legislation Review Committee, chaired by the late John S Lockhart, which reported in December 2005. The Lockhart Committee engaged in wide community consultation and considered expert advice from many sources before making its recommendations on what was inevitably an issue arousing passionate public debate. Similar intense debate had crossed party lines in both federal and Victorian Parliaments, but with a “conscience vote” in both houses in each instance (allowing members to vote as they personally wished rather than along set political party lines), legislation was passed containing major provisions for strict regulation of all aspects of research involving human embryonic material and the strict prohibition of human cloning for reproductive purposes — with draconian penalties for transgression. Many other prohibitions set out in the previous *Research Involving Human Embryos Act 2002* (Cwlth) have been firmly retained.

Similar legislation has now passed both houses of the New South Wales Parliament, following vigorous public controversy over the respective roles of the legislature and of the Catholic church on the issue. Corresponding legislation is expected to be considered in other states and territories, as Australia moves to permit further progress in this critical and fast-moving area of scientific development. Legislative protection from both federal and state governments allows greater freedom in the quest to understand disease mechanisms by studying stem cells containing abnormalities underlying genetic disorders, and the development of new approaches to treatment of hitherto unyielding diseases. The new science of regenerative medicine can move ahead in Australia, with the research and technological developments now permitted having great implications for human medicine. A new international system for collaboration in this important field is also emerging.¹

Human embryonic stem cell lines were first created in 1998 from blastocysts;² the techniques used were based on at least a decade of research on mouse embryonic stem cells. The key characteristic of embryonic stem cells, not shared with adult stem cells, is their capacity for long-term or immortalised culture, permitting extended research and growth of the large number of cells necessary for human implantation. The process of somatic cell nuclear transfer allows human embryonic stem cells to contain the nucleus of the recipient cell, so an individual’s immunological constitution will be conferred to the stem cell and its progeny.

Technological developments to date have included:

- Better methods for growth and maintenance of human embryonic stem cells in vitro, including Good Manufacturing Practice (GMP) compliance and industrial scale production;

- Better methods to more reliably drive embryonic stem cells along particular cell and tissue pathways;
- Differentiated embryonic stem cell progeny have been used for drug screening and toxicology testing;
- Demonstration of the medically relevant capabilities of human embryonic stem cells in animal models; and
- Isolation of new embryonic stem cell lines and creation of collaborative cell banks and networks. Regulatory compliance still presents challenges, as expected of any living-cell therapy.

The potential applications to human disease are many, as shown by real advances made recently with human diseases in animal models. Studies transplanting cells derived from human and monkey embryonic stem cells into animal models have shown correction or partial correction of Parkinson’s disease.^{3,4} Growth of cardiac myocytes derived from human embryonic stem cells has been demonstrated in pigs, with correction of electromechanical function;⁵ human embryonic stem cell-derived oligodendrocytes have improved spinal cord injuries in rats;^{6,7} and human embryonic stem cell-derived islet cells have functioned in animals with diabetes.⁸

However, regenerative medicine in human subjects using transplanted stem cells or their progeny faces three serious technical hurdles:

- Transplant rejection (and the monitoring of this);
- Efficient guidance of embryonic stem cells down correct pathways of differentiation using growth factors; and
- Ensuring cells of such great proliferative potential do not, on rare occasions, develop into cancers.

Strongly held views in the community on all aspects of research involving human embryonic stem cells must be acknowledged. Similarly, unrealistically high hopes for rapid advances in developing new treatments for distressing and debilitating diseases fail to grasp the long lead times that inevitably apply; medical practitioners will probably be asked for their advice on such matters.

Our democratic processes have moved on — so must our science. It is important to recognise that there will continue to be strict regulatory oversight of all research involving human embryonic stem cells, and regular reviews of progress will be important.

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