EDITORIAL

The Wonder of Stem Cells and their Clinical Applications

Stem cells have been hailed as a wonder solution for tissue repair in many situations and have been used clinically for years to replace bone-marrow derived blood cells. Embryonic stem cells (ESC) have attracted additional attention for *in vitro* reproductive interventions and uses such as somatic nuclear transfer. A more controversial aspect is the use of ESC for cloning entire individuals; this was first demonstrated for mammals in 1996 with Dolly the sheep and has subsequently been achieved for many species, but is less likely to eventuate for humans.

Cell transplantation has been intensively studied for many years using precursor cells from a huge array of tissues. Key problems relate to survival of the transplanted cells: the rapid initial death of cells after transplantation and longer-term immunological rejection by the host immune system. In addition, the local tissue environment can determine the ultimate fate of the donor cells, although the impact of complex interactions between the local tissue environment and the extracellular matrix *in vivo* has barely been addressed to date.

The ideal source of stem cells for transplantation (often in combination with gene correction) is autologous i.e. from the same patient, to avoid problems of immune rejection. This is the dream scenario and, indeed, mesenchymal stem cells show much promise as a source of autologous multipotential adult stem cells for transplantation. While there is a strong case for adult derived stem cells and even for stored cord blood cells, there are complications with ESC. First, they cannot be autologous (for transplantation purposes) and therefore are likely to be rejected in the absence of immunosuppression. However, there are claims that allogeneic (from an individual with a different set of genes) ESC are exempt from immunorejection and there is also the exciting possibility of using dendritic cells, derived from ESC, to induce host tolerance to donor cells. Second, the high proliferative rate of ESC is normally precisely controlled by constant changes in the local environment during development. The possibility arises that placing ESC into a mature tissue environment may lead to cancers and clearly this needs to be carefully addressed. Third, there is the issue of ethics, although the use of cell lines tends to get around the ethical dilemmas associated with the harvesting of such cells from human embryos. While much vital information can be gleaned from the study of human ESC in tissue culture, their practical application for clinical transplantation therapies needs careful evaluation and appears relatively remote.

Many laboratories around Australia are engaged in stem cell research and some of this exciting work is covered in this Showcase on Research. The roles and potential clinical applications of adult-derived stem cells are described for four tissues: Tracey Lee-Pullen and I provide an update on putative stem cells for skeletal muscle; the transplantation of bone-marrow derived mesenchymal stem cells to repair cartilage and bone is discussed by Rosa McCarty, Davis Leavesley and Paul Simmons; the repair of liver by stem cells and progenitor cells is championed by Vance Matthews and George Yeoh; and finally, Pritinder Kaur and Fiona Wood discuss stem cells in the skin for reconstruction of epidermis and dermis especially for clinical treatment of burns – it is timely that Fiona has been named Australian of the Year 2005 for her fine work in this field.

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Cover Illustration

Gene replacement by muscle derived stem cells. Cells in primary cultures of mouse skeletal muscle, that are reluctant to attach, have been called muscle derived stem cells. When these late pre-plate donor cells (from normal male mice) are injected into muscles of female dystrophic mdx mice (that lack dystrophin) the extent of replacement of dystrophin protein by the donor cells is visualised by immunostaining: dystrophin (made by the donor nuclei) is shown in red outlining the cell membrane of large and small (newly formed) myofibres cut in cross-section, with nuclei stained blue. For successful cell therapy it is essential to demonstrate the expression of the required muscle specific genes, in addition to the presence of donor nuclei.

Stem Cells

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In the next issue...

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