Advances and challenges in the therapeutic use of stem cells

The consensus is that there is far more to be done in understanding the potential of stem cells. Adult stem cells are found in very limited quantities in a relative few places, and the process of identification and culture can be painstaking. There are also concerns that the relative old age of adult stem cells means that they have greater potential for disease or dangerous genetic mutation.

Stem cells have also been found in umbilical cord, amniotic fluid and deciduous (milk) teeth. More research is needed to find out their full potential for differentiation, but these may prove to be a richer supply of adult stem cells that are younger, more vigorous, and easier to culture in stem cell lines.

**Stem cell lines**

Stem cell lines are populations of cells that have grown from an original stem cell. These populations provide stem cells for research. They reproduce themselves for long periods of time under controlled laboratory conditions that mimic the mammalian body environment. They are, in theory, immortal because the cells will continue to divide and replenish supply.

**Current therapy**

Adult haematopoietic stem cells – the cells from which blood tissue cells grow – are the best understood of human stem cells and have been used in therapeutic applications for some time. A typical example is the use of peripheral blood stem cell transplant used in the treatment of cancers, such as lymphoma, for well over a decade. Stem cell transplant means that high dose myeloablative therapy can be given to treat lymphomas that do not respond to regular treatment, that relapse following initial...
therapy or that have a high tendency to relapse. Stem cells are harvested from the peripheral blood, following treatment with stimulant growth factors, and stored for retransfusion after high dose therapy. Through a process of ‘stem cell homing’ the reinfused cells find their way from the blood stream to the bone marrow and begin the process of replenishing myeloid tissue and blood cells. It is suspected that haematopoetic stem cells have the potential to transdifferentiate – to grow into cells other than bone marrow and blood. This is also referred to as plasticity. Clinical trials designed to explore this potential have used infusions of stem cells in a variety of disease settings.

For example, several studies have used bone marrow stem cells to restore the heart muscle following myocardial infarction. Such applications remain experimental but could lead to more diverse use of adult stem cells in the future.

The future

The most widely publicised application of stem cell research is the growth of replacement tissues. Of particular interest have been tissues that, until relatively recently, have been considered difficult or impossible to replace once damaged – tissues such as heart, liver, brain and spinal cord. According to the International Society for Stem Cell Research (ISSCR): ‘Any disease in which there is tissue degeneration can be a potential candidate for stem cell therapies, including Parkinson’s and Alzheimer’s diseases, spinal cord injury, heart disease, type 1 diabetes, osteoarthritis, rheumatoid arthritis, muscular dystrophies and liver diseases’ (2005). Table 1 offers a few examples of the kind of research taking place.

Stem cell research is not only about replacement cells. Study into stem cells is also undertaken in order to understand cellular development and gain further understanding of disease processes. These applications may lead to prevention of birth defects, slowing of progression of disease and better treatment of debilitating illnesses.

An example of this kind of stem cell research is in motor neurone disease (MND). Scientists at the Roslin Institute in Edinburgh have generated stem cell lines using DNA from patients with MND. They can closely observe the behaviour and chemical profile of these cells, identifying the factors that contribute to cell death and testing new medicines (Hopkins Tanne, 2005a).

Research into stem cell behaviour might also enhance capacity to heal, for example, utilising the brain’s own supply of stem cells to repair neurological damage as a result of stroke, trauma or multiple sclerosis. However, this advance requires a greater understanding of what triggers the repair process (Hopkins Tanne, 2005b).

The challenge ahead

The challenges of the immediate future – the scientific, the ethical and the political – seem monumental. Individuals including Professor Sir Robert Winston have asked whether the potential of stem cell research has been overstated, and the difficulties understated (Amos, 2005).

The most pressing scientific challenges can be summarised as follows:

- More needs to be learnt about adult stem cells – their real potential for transdifferentiation, and how adult stem cells can be better identified and cultured;
- Researchers need greater understanding of the process of cell differentiation – what factors influence it, and how it might be influenced in a controlled and managed way;
- The process of differentiation of embryonic stem cells is potentially hazardous – stem cell lines may acquire harmful genetic mutations, or viruses, over time – there is a demonstrated risk of tumour formation as a result of uncontrolled rapid growth of undifferentiated cells;
- The function of new tissues must be maintained within, and adequately integrated with, the patient’s body. For example, heart muscle cells that beat in the laboratory must beat in time with the patient’s own heart muscle cells;
- The problem of tissue rejection must be overcome, as the patient’s immune system will reject transplanted cells.

The ethical issues

An important issue for stem cell research is where the original cells come from, and both embryonic and adult stem cells have their limitations. Embryonic stem cells come from embryos created for in-vitro fertilisation treatment. After a cycle of IVF, some embryos are left surplus to requirements. The couple can then consent to donate the embryos for research purposes. The extraction of stem cells means that the embryo dies. This means that embryonic stem cell research is troubling to many people on moral and ethical grounds.

Scientific progress is made infinitely more complex in light of the bioethical context of stem cell research. Put simply, do the potential ends justify the means? Two of the most sensitive aspects of stem cell research are the use of cloning and the question of the human status of the embryo.

Cloning

A potential solution to the problem of tissue rejection is the use of cloning technology. Somatic cell nuclear transfer is a process in which the nucleus from one of the recipient’s cells, such as a skin cell, is used to replace the nucleus of an egg. Using an artificially induced process of parthenogenesis
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