

Ethical legal and social issues in stem cell research and therapy

A briefing paper from Cambridge Genetics Knowledge Park

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Summary version

The full version of this paper is available at www.cgkp.org.uk and www.eescn.org.uk

1. Introduction

1.1 Scientific background

Stem cell researchers hope that it might be possible to use stem cells, or specialised cell types derived from them, to repair organs and tissues damaged by injury or by degenerative or autoimmune diseases. Other applications for stem cells are also being investigated, for example as sources of differentiated cell types for drug screening and toxicity testing, or as vehicles for drug delivery. Research on stem cells also promises to yield new insight into the molecular control of cell differentiation.

Research programmes are underway using both pluripotent embryonic stem (ES) cells and various types of non-embryonic stem cells. There is no significant controversy surrounding research on adult stem cells. ES cell research has, however, aroused vigorous debate. Particular controversy surrounds the creation of embryos for research, either by fertilisation or by cell nuclear replacement, which uses cloning technology to obtain stem cells genetically (and immunologically) identical to an existing person.

Less public attention has been paid to the regulatory issues surrounding the therapeutic use of stem cells and derived cellular products. In this context, stem cell therapy represents a subset of the wider field of cell and tissue therapy, which is subject to an increasingly complex system of legislation and regulation.

1.2 Aims of the paper

- To present a critical summary of the major debates and policy responses relating to ES cell *research*
- To provide an analysis of the key ethical and regulatory implications for stem cell *therapy*

Our report focuses on the current position in the United Kingdom. We have called our analysis a 'briefing paper'. By this we mean that, while we have attempted to highlight a broad range of issues in the fields of ethics, law and social science, there may be additional topics that would need to be addressed in a fully comprehensive survey.

2. Embryonic stem cell research

2.1 The moral status of the embryo

Embryos have to be destroyed when ES cells are derived. Views on whether it is right to do this vary widely. Some of the key issues include whether the early embryo should be regarded as a 'person' with full moral rights, and whether it is acceptable to use embryos that would otherwise die or be destroyed. A liberal ethical position that has been adopted in UK policy is that the embryo does not have the full moral status of a person but that we should 'respect' embryos.



This 'respect' may take the form of using embryos only for research aimed at alleviating the suffering of people suffering from serious diseases.

The creation of embryos for research purposes has been criticised on the grounds that such research treats embryos as mere commodities, entails risks for oocyte donors, and is not justifiable if surplus embryos are already available. Concerns have also been expressed that cell nuclear replacement research could be a 'slippery slope' leading to the reproductive cloning of human beings.

2.2 Regulation of embryo research and embryonic stem cell research in the UK

In the UK, ES cell research was legally enabled in 2001 when Regulations under the 1990 Human Fertilisation and Embryology (HFE) Act extended the permitted purposes for embryo research to include research that is 'necessary or desirable' for understanding the development of embryos, or understanding or treating serious disease. The creation of embryos for research is legal, as is cell nuclear replacement research. All embryo research must be licensed by the statutory Human Fertilisation and Embryology Authority (HFEA). Reproductive cloning is banned by statute.

A national Stem Cell Bank manages stem cell resources under an ethical framework. The HFEA has made compliance with the Stem Cell Bank's Code of Practice a condition of a licence for ES cell research, and requires a sample of all ES cell lines to be deposited with the Bank. Strictly speaking, however, it is questionable whether the HFEA has legal power to make the Stem Cell Bank Code binding on those who apply for its licences.

There are some ambiguities in the current governance of embryo research. For example, the phrase 'necessary or desirable' is not defined and may be subject to legal challenge in the case of cell nuclear replacement research. The definition of 'serious disease' is also unclear.

No international consensus has been reached regarding embryo research or 'therapeutic cloning'.

2.3 Ethical sourcing of embryos and oocytes

In the UK, most embryos used for research are surplus embryos from *in vitro* fertilisation (IVF) treatments. Embryo donors are protected by requirements in the HFE Act for informed consent. Detailed consent and information forms prepared by the UK Stem Cell Bank for couples asked to donate embryos for ES cell research are currently being trialled at IVF clinics.

There are also more subtle social and psychological issues to be considered, including the extra burden placed on couples at a highly stressful time and the difficulties for them of evaluating the psychological risks and benefits of donation.

Questions also surround the 'value' placed on embryos by different groups in society. For donor couples, the transformation of embryos from intended babies, to 'waste' or 'left over' material and then finally to a source of precious stem cells is a complex and value-laden process.

Couples who consent to donation must do so without financial reward, but the embryos they donate may lead to the development of materials or treatments that have considerable commercial value. Although most commentators support a ban on the 'sale' of embryos, the issues are not clear-cut.

The donation of oocytes for embryos created for research purposes raises ethical questions, as oocyte donation carries significant medical risk for the donor. Cell nuclear replacement research exacerbates the problem of oocyte sourcing because of the extremely low efficiency of the process.

3. Other issues raised by stem cell research

There are other issues that are not unique to stem cell research, but must be taken into account.

3.1 Sourcing of other tissues for stem cell research and transplant: legal issues

Donations of tissue other than gametes and embryos, such as stem cells from adults, must be made in accordance with prevailing laws including laws on consent. The Human Tissue Act 2004 requires a researcher to obtain 'appropriate consent' before using or storing a tissue sample for the purposes of



research or transplant. The precise steps involved in securing 'appropriate consent' may eventually be stipulated by the courts or, more likely, in codes prepared by the Human Tissue Authority.

Once a cell line is created, it falls outside the Human Tissue Act; thus the penalties for failing to obtain or act in accordance with appropriate consent cannot then be enforced.

3.2 Embryo and stem cell research in an age of global science

Biomedical research, including stem cell research, is a global enterprise. Differences in moral and cultural values may raise a dilemma when scientists wish to import material for stem cell research. The consent process may meet the rules of the country of collection but not the standards of ethical sourcing that apply in the country of destination.

Legal standards in the UK (under the HFE Act and the Human Tissue Act) try to avoid the worst risks of exploitation whilst recognising that valuable imports will be stopped if European standards are strictly insisted upon.

3.3 Clinical studies

When stem cell research moves into clinical experimentation, media attention and 'hype' may lead patient-subjects to have unrealistic expectations, despite explanations that they are unlikely to benefit personally from experimental treatments. The design of clinical studies should be such that patients are not subjected to unjustifiable risks. Those conducting early-stage clinical studies should consider a flexible, patient-oriented study design.

Choosing which diseases should be a priority for stem cell therapy may be difficult. Where no other treatment is available, high-risk experimental treatments can be justified but if relatively effective therapies are available (for example for type 1 diabetes), the decision to enrol children or young adults in clinical trials of stem cell therapies is a serious one.

4. Issues raised by stem cell therapy

4.1 Regulation of product development

The safety of human tissue products for clinical application is currently regulated by a variety of laws and codes under administration in the UK by the Medicines and Healthcare products Regulatory Agency (MHRA). Codes published in 2000 and 2002 will need to be brought up to date for the purposes of stem cell therapy.

4.2 The EU Tissue Directive

The regulatory framework applicable to stem cell therapy is required by 2006 to incorporate the provisions of the EU Tissue Directive (2004), which sets standards for 'donation, procurement, testing, processing, preservation, storage and distribution' of human tissues and cells intended for human application.

4.3 Obtaining market approval

The general regulatory regime for market approval will be relevant to stem cell therapies. A key question is whether transplantable material derived from stem cells is appropriately dealt with according to the Medicinal Products Directive or the Medical Devices Directive. This and other uncertainties and inconsistencies have led the European Commission to propose a special system of market approval for tissue-engineered products; new draft legislation is expected during 2005. In the meantime, UK regulatory authorities have recommended that 'regulatory guidance should be obtained from the medicinal authorities on cell lines/tissues arising from stem cell technologies'.

4.4 Securing the trust of donors

The EU Tissue Directive specifies that all cells and tissues for clinical use must be traceable from donor to recipient and vice versa. Although there are sound public health reasons for this policy, it has implications for donor privacy. Information arising from medical testing of donors and donated





tissue must be kept confidential. There is also the question of whether donors wish to be informed about anything of medical importance that is discovered through use of their donated material.

Traceability requirements may have implications for the supply of donated material. Couples may be unwilling to donate embryos if their connection to them as 'parents' cannot be severed.

4.5 Securing the trust of patients offered stem cell therapies

Steps have been taken to secure the safety and quality of stem cell therapy but some other factors relevant to end-users have been neglected in comparison. For example, the regulatory system does not adequately address compliance, or do enough to ensure that manufacturers are sufficiently accountable to patients, rather than official regulators. It may be difficult for a patient harmed by a tissue therapy to seek compensation.

Governance documents fail to address the right or wish of recipients to know that their treatment results from destructive research on embryos, or contains material originally derived from embryos.

4.6 Intellectual property rights

The granting of patents on ES cell lines is contentious at present. Such lines are patentable in the UK (though not the *processes* used for deriving them, which are excluded because they involve 'uses of human embryos'). The European Patent Office, however, currently views such lines as not patentable. As a consequence, applicants seeking a patent over an ES cell line will not be able to apply to the European Patent Office for a patent valid in countries that are signatories to the European Patent Convention, but will have to apply to the national patent offices in each separate country.

4.7 Gaps and problems in the regulatory framework

Uncertainties surrounding the regulatory framework for stem cell therapy raise the question of whether a special regulatory regime is necessary to maintain public confidence. A better approach, however, may be to encourage greater coordination of both regulations and regulators, and more accessible descriptions of current ethical and legal standards.

4.8 Opportunity costs and equity

Stem cell based therapies are likely to be expensive and technologically demanding, with substantial opportunity costs for cash-limited healthcare systems. If, on the other hand, taxation-funded health services decide not to fund stem cell therapies, they may be available only to the wealthy few.

Other questions of social justice may arise. For example, cell lines in stem cell banks may fail to include less-common tissue types, thus disadvantaging minority racial and ethnic groups.

4.9 Longevity, 'immortality' and individual identity

Replacement of degenerating tissue by stem cell therapy might make a more significant difference to lifespan than other types of treatment. The social consequences of a significant increase in longevity are unknown. It has also been suggested that transplants of stem cells into the brain could result in the recipient losing his individual identity and essentially becoming another person. However, such scenarios seem, at present, too remote to prompt serious policy consideration.

5. Concluding remarks

Many issues in stem cell research and therapy would benefit from further legal and social science research. It is to be hoped, however, that the approach to policy development in the UK – broadly permissive but with provision for rigorous ethical and legal oversight – will enable policy to evolve in a way that is rational and commands broad public support.

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