

Briefing on the second reading of the Human Fertilisation and Embryology Bill, Monday 19 November 2007.

Prepared by the Medical Research Council, Royal Society and Wellcome Trust

The Medical Research Council, Royal Society and Wellcome Trust welcome the sections of the Bill that have been laid before Parliament relating to the regulation of research using embryos. We fully support the aims of the Bill to modernise and update the regulatory framework for these activities. This will ensure that UK scientists working at the cutting edge of stem cell and embryo research will be able to continue to carry out their work under the tightly-regulated environment that has enabled this type of research to flourish in the UK to date.

We will carefully follow the progress of the Bill through Parliament to **ensure clarity around drafting of various provisions**, for example:

- around the definition of 'gametes' and 'germ cells';
- access to HFEA data for research; and
- consent provisions so far as they relate to creation of inter-species embryos.

We welcome the following aims addressed in provisions included in the Bill as follows:

- clarification of definitions
- inclusion of inter-species embryos (ISEs) within licensable research and the regulatory power to extend this definition for research purposes
- extension of HFEA powers and clarification of the licensing and appeal process
- removal of the prohibition on altering the genetic structure of embryos for research
- extension of storage limits
- the extension of research purposes
- facilitation of the use of data on treatment held by the HFEA for medical research

Background

The aims of the Human Fertilisation and Embryology Bill are to modernise and update the Human Fertilisation and Embryology Act (the Act) to ensure it keeps pace with the scientific and medical developments in the field whilst maintaining public confidence in the regulatory framework within which such research is approved. **We are pleased that the Government has taken into account the recommendations from the scientific community** when preparing the Bill.

The development of this Bill has involved extensive consultation with a broad spectrum of the scientific and wider community, including professional bodies and scientific experts, since the Government first published draft legislation in May 2007. A Joint Parliamentary Committee has undertaken pre-legislative scrutiny of the draft Bill and sought a wide range of evidence before publishing their recommendations on 1 August 2007. The Human Fertilisation and Embryology Authority (HFEA) carried out a comprehensive public consultation on hybrids and chimeras which was published in October 2007. The Academy of Medical Sciences created a working group of experts to examine the issue of interspecies embryos which reported in June 2007.

Reasons to support research provisions of the Bill

The **United Kingdom is currently a world leader** in human reproductive technologies and stem cell research. One recognition of this was the award of the 2007 Nobel Prize for Medicine to Sir Martin Evans FRS, from Cardiff University, in recognition of his work in stem cell research.

Research covered by the Bill spans a broad range of basic and applied science including reproductive technologies and stem cell research. **Stem cell research offers a potentially revolutionary way to repair diseased and damaged body tissues**, replacing them with healthy new cells.

The Bill will **allow the creation** and use of interspecies embryos, for research purposes, **within a tightly regulated framework**, overseen by the HFEA. The ability to undertake such work will allow the development of techniques to overcome the shortage of human eggs available for use in medical research and the production of stem cells, eg for research into the genetic basis of disease.

The Bill **clearly prohibits** the implantation of interspecies embryos in a woman. Furthermore, interspecies embryos cannot be kept after the earliest of the following: the appearance of the primitive streak, or the end of a period of 14 days beginning with the day on which the process of creating the interspecies embryo began.

Any amendments to the Bill which prohibit research on ISEs under these strict conditions would deny researchers the opportunity to fully pursue embryonic stem cell research and could significantly undermine the UK's position as a world leader in stem cell research, a position that the Government, scientists, regulators, ethicists and funders have worked hard to achieve. This work not only has eventual therapeutic potential, but significantly contributes to the countries scientific and economic competitiveness.

The UK is well positioned, because of its flexible and facilitative regulatory regime and its commitment to stem cell research, to identify and realise the therapeutic potential of stem cells. It also has world-class researchers in developmental and reproductive biology and the UK Stem Cell Bank. These strengths present valuable opportunities to influence the international agenda, drive the translation of basic research to clinical benefits and attract skilled scientists and international investment in stem cell research.

Further details regarding current research using stem cells, including work funded by the MRC and the Wellcome Trust is attached.

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The potential of stem cells and current research:

It is hoped that stem cells could ultimately replace any damaged or degenerate tissue, for example, **cardiac muscle after a heart attack, brain tissue in Parkinson's or Alzheimer's disease or pancreatic islet cells in type 1 diabetes**. Stem cells given to the patient would differentiate into the tissue which requires replacement or repair.

One difficulty with any transplantation procedure is that the human body can reject cells that do not exactly match those of the recipient. This is why recipients of organ transplants such as liver, kidney or heart/lung must take long-term medication to suppress their own immune system to reduce the risk of rejection. Using transplanted tissue originally from the recipient (*autologous*), would remove this problem and could also improve the availability of therapy. **Thus the aim of much stem cell research is to create stem cells containing nuclear DNA from cells derived from the recipient.**

Stem cells may also be used *in vitro* as models for cells and tissues with specific diseases enabling drug therapies to be tested or disease progression to be studied in detail. Many cancerous cells behave like stem cells and greater understanding of the mechanisms by which stem cells develop and function will have some application in oncology research.

Current stem cell research is directed towards:

- exploring the use of adult stem cells, such as the use of bone marrow stem cells in **heart repair**.
- exploiting embryonic stem cells for the treatment of **paediatric, heart, pancreatic, liver and brain conditions**
- using fetal stem cells as **treatments** for **neurodegenerative conditions** and eye conditions
- exploring the use of endogenous stem cells, naturally resident in tissues of the human body, to **direct the repair of damaged or diseased cells and tissues**
- increasing our **understanding and treatment of cancer** through studies of endogenous adult stem cells
- generating embryonic stem cells with the same nuclear genetic material to that of the patient using therapeutic cloning techniques, to avoid the potential rejection of cell therapies.
- using stem cell lines as **tools in drug discovery and development**

Sources of stem cells.

There are three sources of stem cells:

1. Embryonic:

these are pluripotent cells (they can turn into any cell type). They could be used either

- a. To create autologous matched cell lines using SCNT (see below). These would initially be used to provide models of disease and test therapies but eventually might be the source of stem cell therapies
- b. To create cell lines that could be used by a large number of recipients. These lines can also be used to study the processes involved in cellular development and differentiation.

2. Fetal:

- a. Fetal cord blood contains adult type stem cells. Some organisations offer banking of this blood in the hope that in the future it may provide stem cells for the donor. At present the techniques do not exist to make this a reality.
- b. Fetal tissue has also been studied to provide multipotent cells to repair injured tissues such as neuronal cells in Parkinsons disease or spinal cord injury. After the

embryonic stage most fetal tissue will be, at most, multipotent, unless it can be modified to regain pluripotency.

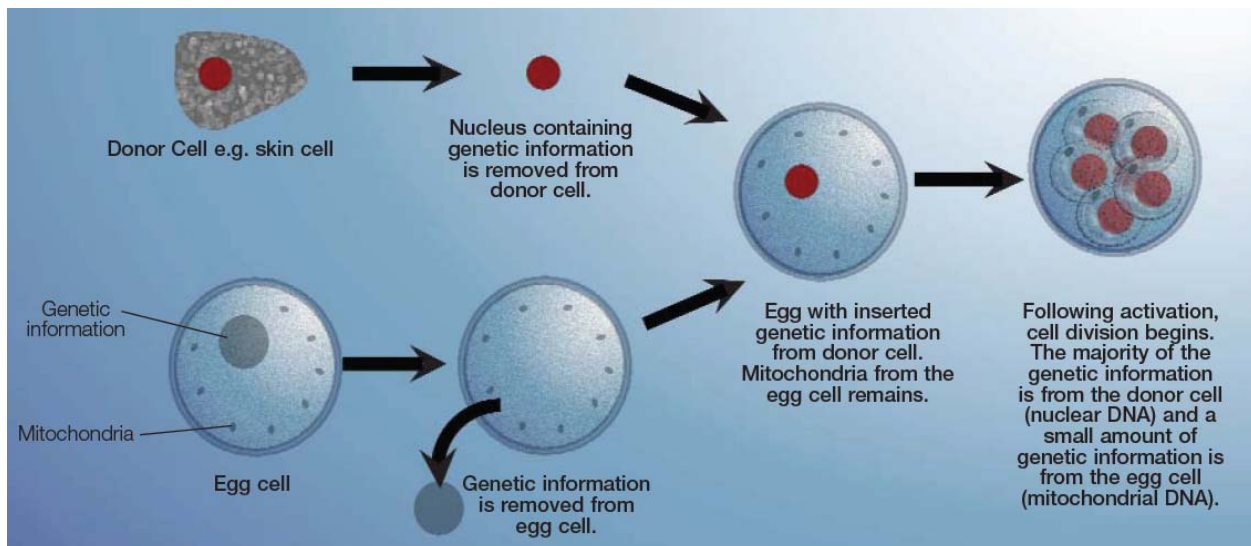
3. Adult:

This is the most attractive route to remove many of the ethical arguments that arise over the use of gametes, embryos or fetuses.

- a. Adult stem cells are already widely used in bone marrow transplantation where the multipotent bone marrow cells are reimplanted following chemotherapy to replace the bone marrow cells destroyed during therapy. Some success has been reported using similar cells to repair heart damage after infarction. There is however, dispute as to whether these cells actually differentiate into cardiac tissue or have other effects (for example, on the immune system) that improve outcomes in this situation.
- b. Work has also focused on processes that could allow adult somatic (not gametes – eggs or spermatozoa) cells to be 'reprogrammed' to regain the properties of multipotency or, ideally, pluripotency. There have been some reports of success in this research but, as yet, none have been sufficient to be certain that this technique will be an effective source of stem cell lines.

Somatic cell nuclear transfer (SCNT)

To produce stem cells **exactly** matched to the recipient, researchers remove the genetic material (the nucleus) from a normal (somatic) cell in the patient's body and place it into an unfertilised egg. The nucleus then behaves as it would in an embryo, and stem cells exactly matched to the donor of the nucleus can be cultured, and encouraged to grow into the specific cell type(s) needed to repair damage. The generation of embryos from which stem cells can be harvested using somatic cell nuclear transfer is extremely inefficient, with a success rate in animals currently less than 0.1%. Promising research in non-human primates has recently been reported, but the technique has not yet been achieved in humans. The egg used may either be human or animal. The latter creates an interspecies embryo of the type described in section 4A (5)b of the Bill. This is sometimes termed a 'cytoplasmic hybrid'.



There are three main avenues of research attempting to derive autologous pluripotent stem cell lines.

1. SCNT using human eggs
2. SCNT using animal eggs
3. Reprogramming of adult somatic cells

It is our view that, at present, there is no conclusive evidence as to which of these three routes will ultimately prove most effective. Techniques developed in pursuing one avenue will be applicable to the others. For example, creation of cytoplasmic hybrids would allow researchers to work on much more easily available eggs from animals. Current proposals to be submitted to the HFEA for licensing use cow eggs obtained from an abattoir. Techniques developed could then be applied to human eggs, donation of which is limited and subject to other considerations. In a similar way knowledge relating to the development of cells following SCNT may aid progress in reprogramming adult cells to 'regress' to become pluripotent. We believe that it would be detrimental to close off any of these avenues of research and that all should proceed in a carefully regulated environment.

Examples of current Stem Cell Research funded by the MRC and the Wellcome Trust

Disease Modelling

Work undertaken by Wellcome Trust funded scientists at the Wellcome Trust Centre for Stem Cell Research based at the University of Cambridge aim to focus on the genetic and biochemical mechanisms that control how stem cells develop into particular types of cells. This work will help provide the techniques and knowledge for the engineering of stem cells to model particular diseases, drug discoveries and regenerative medicine.

Blindness

MRC-funded scientists at the University College London Institute of Ophthalmology are researching stem cell transplants to treat people with hereditary retinal disease and age-related macular degeneration – two major causes of vision problems and blindness in the UK which have a lack of effective treatments. The investigators hope to use stem cells to generate replacement retinal cells that could be used to restore vision.

Diabetes

Dr Neil Hanley and his team at the University of Southampton are attempting to generate human embryonic stem cells that can be used to replace the insulin producing beta cells in patients suffering from type 1 diabetes.

Osteoporosis

Stem cell technology holds promise for many people with bone problems, such as arthritis and osteoporosis patients, people with bone injuries and those who need joint replacement operations. MRC-funded scientists at Imperial College London have successfully grown cartilage cells from human embryonic stem cells. Their achievement may mean that one day replacement cartilage could be grown for transplantation into patients.

Biology of embryonic stem cells

Researchers at the Wellcome Trust Institute for Stem Cell Research, at the University of Edinburgh are investigating the development of applications to understand how embryonic stem cells maintain their potential during self-renewal and how they then switch to the production of particular, specialised cells. Work in this field has the potential to lead to the ability to develop replacement cells and tissues for treatment of degenerative diseases including juvenile diabetes. This work could also lead to improved cell based assays as an alternative to animal tissue for screening new pharmaceuticals.

Stem cell bank

Based at the National Institute for Biological Standards and Control at South Mimms, Hertfordshire, the UK Stem Cell Bank was established in 2002 as the world's first stem cell bank. It is funded jointly by the BBSRC and the MRC. The Bank recently made its first four research-grade stem cell lines available, with the release of further research-grade lines imminent. It is also embarking upon the construction of its Good Manufacturing Practice (GMP) facilities for the deposition and ultimate distribution of clinical-grade stem cell lines for transplantation. Confidence in the UK oversight arrangements has persuaded a number of overseas labs to deposit lines – of the 40 registered some 20 are non-UK derived.