

Human Fertilisation and Embryology Bill

A briefing for MPs on the need for research involving human and human admixed embryos. Prepared by the Academy of Medical Sciences, the Medical Research Council, the Royal Society and the Wellcome Trust. The Association of Medical Research Charities supports the content of this briefing.

We welcome the provisions in the Human Fertilisation and Embryology Bill that relate to research. We particularly support provisions regulating the creation and use of human admixed embryos, which will open new avenues for understanding and treating disease. The Bill will help to maintain the tightly regulated environment that has enabled embryo research to progress in the UK with the confidence of patients, scientists and the wider public.

Summary

- The UK is currently a world leader in stem cell and embryo research and has a deserved reputation for its robust and responsive regulatory framework which allows such research to flourish while maintaining public confidence.
- We welcome the introduction of the Human Fertilisation and Embryology Bill, and specifically the provisions to modernise and update the regulation of research using embryos.
- Stem cell research offers a valuable opportunity to understand and develop new treatments for debilitating diseases such as Alzheimer's disease, Parkinson's disease, motor neurone disease, multiple sclerosis, cancer, HIV and AIDS, as well as treating infertility.
- Stem cells from three different sources are currently used in research: adult (including reprogrammed cells), fetal and embryonic stem cells. Research on stem cells from these different sources is complementary – at present, it is not known which route will ultimately be most effective, and closing off any one avenue of research could be detrimental to the potential development of therapies.
- The creation of human admixed embryos (HAEs) is one important option to overcome the limited availability of donated human eggs – one of the major barriers to embryonic stem cell research. HAEs will reduce the number of human eggs and embryos used to produce stem cells for research.
- The Bill allows research, under license, on four types of HAEs, which contain both human and animal material. This briefing provides further information about these different types and their importance for research.
- The Bill includes robust safeguards to ensure research is regulated in a responsible and appropriate way, including clear prohibition both on implantation of human admixed embryos in a woman or animal and on research on all embryos beyond 14 days of development.
- The Human Fertilisation and Embryology Authority (HFEA), an independent regulator, will continue to regulate all embryo research, and will only grant a licence for research using human or HAEs if it is satisfied that the research is necessary and desirable.

- Consultation has shown that the majority of the public support research using human embryos and HAEs to find treatments for diseases. Surveys by MORI in 2003 and for the HFEA in 2007 showed that the vast majority of the British public – 70% and 79% respectively - support the use of human embryos for medical research to find treatments for serious diseases and for fertility research.
- Through the Association of Medical Research Charities and the Genetic Interest Group, over 200 charities and patient organisations have also recently written to MPs in support of the research provisions in the Bill.
- If research involving HAEs is prohibited, UK scientists will no longer be able to work at the cutting edge of stem cell research. This will be to the detriment of patients. The UK will also lose its competitive advantage in the field.
- The scientific, ethical, and safety issues around HAE research have been rigorously reviewed by scientists, the HFEA, research funders, patient groups and others; the current Bill has been exposed to many levels of parliamentary scrutiny.
- We will continue to provide further briefings as the Bill progresses through the House of Commons. We are happy to provide more detailed information, including 1-1 meetings with scientists involved in stem cell research. Contact details are provided below.

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A meeting of the All Party Parliamentary Group on Medical Research will take place in the House of Commons at 12pm on Tuesday 6 May. Scientists, doctors and other researchers will be available to talk about stem cell research and the HFE Bill. For further information on the APPG meeting please contact Nancy Lee, 020 7611 8751

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Human Fertilisation and Embryology Bill – further information

1. Stem cell research in the UK

The UK is currently a world leader in human reproductive technologies and stem cell research. This was demonstrated by the award of the 2007 Nobel Prize for Physiology or Medicine to Sir Martin Evans FRS FMedSci from Cardiff University, in recognition of his work in stem cell research. The UK also has world-class researchers in developmental and reproductive biology and the UK Stem Cell Bank – a national repository of human stem cell lines used in research and therapy. These strengths present valuable opportunities for the UK to influence the international agenda, to drive the translation of research in the laboratory into benefits for patients, and to attract skilled scientists and international investment in stem cell research.

The Wellcome Trust and the Medical Research Council have made considerable funding commitments to the area of stem cell research, including individual projects, the UK Stem Cell Bank and specialist centres. For example in 2005/2006 the MRC spent over £14 million on stem cell research, split roughly 60:40 between embryonic and adult stem cell research (see section 4 for definitions).

Stem cell research offers an unprecedented opportunity to understand and develop new treatments for debilitating diseases such as Alzheimer's disease, Parkinson's disease, motor neurone disease, multiple sclerosis, cancer, HIV and AIDS, as well as treating infertility.

The UK is well positioned to identify and realise the therapeutic potential of stem cells because of its robust and responsive regulatory regime and its commitment to stem cell research. In a report for the Government on stem cell research in the UK and its future potential, Sir John Pattison FMedSci identified the UK as a 'world leader in stem cell research.' and recommended that funding should be available to ensure the UK maintained its position. The Government accepted the recommendations of Pattison's review in December 2005.

2. The HFE Bill and research

The aim of the Bill is to modernise and update the 1990 Human Fertilisation and Embryology Act to ensure it keeps pace with scientific and medical developments, whilst maintaining public confidence in the regulatory framework within which research using embryos is approved.

The Bill allows scientists working at the cutting edge of disease and fertility research to pursue a range of complementary and important avenues of research within tightly specified legislative guidelines. The Bill has been the subject of extensive consultation with a broad spectrum of society, including the scientific community, with input from many professional bodies:

- Publication of a Government White Paper and public consultation in December 2006.
- In January 2007, the House of Commons Science and Technology Committee conducted an inquiry into 'Government proposals for the regulation of hybrid and chimera embryos'. The Committee concluded that the creation of human-animal chimeras and specifically cytoplasmic hybrid embryos is necessary for research, and that the Government should provide a robust framework for regulation of such research.
- Following publication of the draft HFE Bill in May 2007, a Joint Parliamentary Committee undertook pre-legislative scrutiny of the draft Bill and sought a wide range of evidence from scientific, regulatory and ethical experts, before publishing recommendations in August 2007.
- The Academy of Medical Sciences established a working group of experts to examine the issue of inter-species embryos which reported in June 2007. The working group concluded that human admixed embryos research is vital for understanding and treating human disease.¹

¹ www.acmedsci.ac.uk/p99puid105.html

- The HFEA carried out a comprehensive consultation in late 2007, including a study of public attitudes, which demonstrated that the majority of the public support medical and scientific research on hybrids and chimeras (human-animal embryos).
- The Bill was introduced into the House of Lords in December 2007. In January 2008, the House of Lords voted against a proposed ban on the creation of HAEs for research by 268 votes to 96.

3. Human Admixed Embryos

A key goal of stem cell research is to be able to produce cells and tissues, and ultimately organs such as the liver or bladder, which are genetically matched to the patient. The techniques needed to do this are complex, and a shortage of human eggs on which to carry out this research is impeding scientists' progress.

The term Human Admixed Embryo (HAE) refers to an artificially created entity which behaves like an embryo and which contains both human and animal material. The creation of HAEs is an important potential route in enabling researchers to overcome the shortage of human eggs. Human admixed embryos will help to advance knowledge of a range of diseases, from developmental abnormalities in children to cases of stroke, spinal cord injury and cancer. Learning how to control stem cell development could allow the production of cells to treat conditions such as childhood diabetes and Parkinson's disease, and could eventually allow transplantation of cells containing a patient's own DNA, thus avoiding problems of tissue rejection. The Bill defines four types of HAEs which may be created under licence:

Cytoplasmic hybrid embryos are created by inserting the nucleus of an adult human cell such as a skin cell into an animal egg which has had essentially all of its genetic material removed. This would be grown for approximately five days until human stem cells can be extracted. The animal egg simply acts as an 'incubator', allowing the human stem cells to develop. The only residual animal DNA is in the mitochondria - the 'batteries' of the cell - equating to only less than 1% of the total DNA. Using animal eggs to create cytoplasmic hybrid embryos will allow more rapid progress of stem cell science and spare the use of valuable human eggs [referred to in Clause 4(5)(a) of the Bill].

Transgenic human embryos are human embryos into which sections of animal DNA has been inserted. There are already good scientific reasons to conduct these kinds of experiments. For example, they could be used to better understand how genes function in very early life (up to the 14 day limit), thus aiding research into re-programming, stem cell derivation, early cell commitment, differentiation and early embryo development. Such work has already commenced in mouse models. The use of transgenic human embryos would allow scientists to investigate further how stem cells become selected and differentiated into specific cell types. In addition to increasing understanding of stem cell potential, such work could be used to improve assessments of embryo quality prior to assisted reproduction, and so potentially increase the success rate of IVF treatment [referred to in Clause 4(5)(c) of the bill].

Chimeric human embryos are human embryos into which one or more animal cells have been integrated. Such research could help to determine the relationship between embryonic stem cells and normal embryo cells and to investigate how stem cells differentiate into specialised cell types [referred to in Clause 4(5)(d) of the Bill].

True hybrid embryos are created by the fusion of human and animal gametes. Although we are not aware of any current need to generate true hybrid embryos, given the speed of this field of research, the emergence of scientifically valid reasons in future cannot be ruled out. In light of the difficulties of defining all future applications, we believe it is sensible to future-proof the legislation, but it is important to note that such work would still require researchers to obtain a licence from the HFEA by demonstrating the importance and relevance of this research to human health. The legislation currently allows the creation of hamster egg-human sperm

hybrids to test sperm quality and we do not believe true hybrid embryos should be treated any differently [referred to in Clause 4(5)(b) of the Bill].

The Bill will allow the creation and use of any one of the four types of HAEs for research purposes only, within a tightly regulated framework, overseen by the Human Fertilisation and Embryology Authority (HFEA). The HFEA will only license research that is judged to be necessary and desirable.

The Bill clearly prohibits the implantation of HAEs in a woman or animal. Furthermore, it will continue to be the case that no embryo can be used for research beyond 14 days of development.

Any amendments to the Bill which prohibit research on HAEs under the strict conditions imposed will deny researchers the opportunity to pursue fully stem cell research which could shed light on devastating illnesses and diseases.

4. Stem Cell Research: A brief guide

Stem cell research offers a potentially revolutionary way to repair diseased and damaged body tissues, replacing them with healthy new cells.

Stem cells are immature cells that have not yet developed into the specialised cells that make up our organs and tissues. They are found in many parts of the body and are present from just after fertilisation of an egg right through adulthood. Unlike specialised cells, stem cells are able to generate many different types of cells, such as the beating cells of the heart or the insulin producing cells of the pancreas. And they have the ability to renew (make identical copies of) themselves almost indefinitely. There are three main sources of stem cells:

Embryonic stem cells come from embryos that are about five days old – a ball of about 50-100 cells. This type of cell can give rise to all cell types in the body – they are 'pluripotent'. The most common source is from couples who donate embryos left over from IVF treatments.

Adult stem cells are less ethically controversial than embryonic stem cells, but at the moment they can be induced to develop into only a limited number of cell types. Adult stem cells are already widely used in bone marrow transplantation where bone marrow cells are reimplanted following chemotherapy to replace bone marrow cells destroyed during therapy.

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. Fetal tissue has also been studied to provide multipotent cells for clinical trials to repair injured tissues such as neuronal cells in Parkinson's disease or spinal cord injury.

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 may reject cells that do not exactly match those of the recipient. This is why recipients of organ transplants such as a kidney must take long-term medication to suppress their own immune system to avoid 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 that genetically match the patient.

Stem cells may also be used in the lab 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 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.

Somatic cell nuclear transfer (SCNT) to produce HAEs.

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 a human admixed embryo (sometimes termed a 'cytoplasmic hybrid embryo.') of the type described in Clause 4(5)a of the Bill.

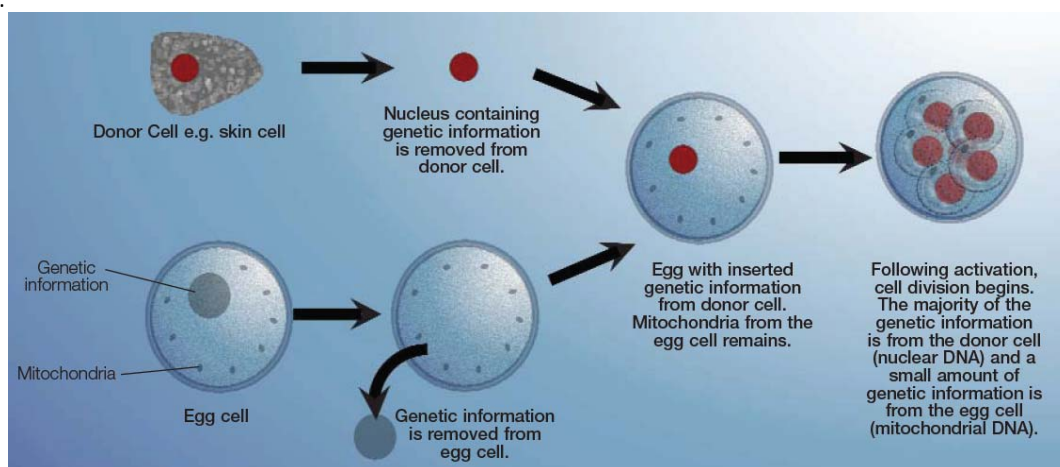


Fig: Somatic cell nuclear transfer (SCNT)

There are three main avenues of research attempting to derive autologous (matched) pluripotent stem cell lines: SCNT using human eggs, SCNT using animal eggs, and reprogramming of adult somatic cells to create Induced Pluripotential stem 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 licensed by the HFEA would 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, building on the Induced Pluripotential stem cell work announced in November 2007. 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.