House of Commons Science and Technology Committee

Government proposals for the regulation of hybrid and chimera embryos

Evidence from the Medical Research Council and the Wellcome Trust

Introduction

1 The Medical Research Council (MRC) and the Wellcome Trust welcome the opportunity to provide input to the Science & Technology Committee. It is our view that research involving embryos, particularly the generation of embryonic stem cells, holds great promise and has enormous potential to alleviate human disease.

2 In 2004/5 the MRC was funding 140 projects of direct relevance to stem cells, equating to an annual spend of £14.2million. The MRC, with the Biotechnology and Biological Sciences Research Council (BBSRC), also funds the UK Stem Cell Bank[1]. The research that MRC funds ranges from basic research into stem cell growth and development, to studies that may be suitable for clinical trials and ultimately, therapeutic use. We also have an active programme of engagement with the general public on stem cell research, including a touring exhibition[2] and discussion documents.

3 Between 2002 and 2006 the Wellcome Trust has awarded over £40 million for stem cell research, including core funding for the newly created Wellcome Trust Centre for Stem Cell Research at the University of Cambridge (also part funded by the MRC). The Wellcome Trust also provides core support to the Wellcome Trust/Cancer Research UK Gurdon Institute at Cambridge and the Wellcome Trust Centre for Cell Matrix Research at Manchester, both of which carry out significant stem cell research. The Trust has also been involved in a multi-million pound joint funding initiative with the Juvenile Diabetes Research Foundation in an effort to promote the UK's contribution to stem cell research. The Trust supports ethical and accountable research involving embryonic and adult stem cells from humans and animals. The Trust also funds research into the use of embryonic stem cells in research through our Biomedical Ethics Funding Programme.

4 We have consulted the BBSRC and the Economic and Social Research Council (ESRC), who have informed us that they do not expect to fund the generation of animal/human chimeras as the research is unlikely to fall within their remit. They will therefore not be responding separately to this inquiry. However, the BBSRC and ESRC recognise the importance of human stem cell research for understanding the basic biology of human stem cell development and differentiation, and support the view that research on hybrid and chimera embryos is important, and should be permitted within the current statutory requirements concerning human embryos.

5 There are obvious difficulties associated with obtaining human eggs for use in the creation of embryos for research purposes. Most donated human eggs are currently used for infertility treatment. The availability of human eggs for research is currently

[1] UK Stem Cell Bank website: www.ukstemcellbank.org.uk
[2] Stem Cell Science: Hope not Hype? information at www.mrc.ac.uk/NewsViewsAndEvents/Events/Reports/StemCellScience-HopenotHype/

severely limited.[3] This is the main reason at the moment that there is a need to create human-animal embryos for research, but other reasons may arise in the future. Moreover, the generation of human embryos from which stem cells can be harvested using somatic cell nuclear transfer is extremely inefficient, with a success rate currently less than 0.1%. Using animal eggs to uncover the reasons why this process is so inefficient with human eggs should enable scientists to make better use of human eggs in the future, and would accelerate the progress of this work toward clinical applications.

6 The MRC and the Wellcome Trust recognise that there are strongly held views both for and against the creation and use of hybrid and chimera embryos for research. It seems that most opposition to this research arises from those who are opposed to any form of embryo research, on absolute moral grounds. Whilst respecting this position, it is clear that the Government and a substantial majority of the public accept stem cell research aimed at producing new treatments and we strongly believe it is in the interests of patients and the public for research involving hybrid and chimera embryos to be permitted, under strict limits and subject to regulatory control, including ethical and scientific review by bodies with a mix of relevant scientific expertise and lay involvement.

The scientific background

7 Fusing human and animal cells is not a new research procedure. Previous research has created hybrid cells, grown exclusively in tissue culture, between human cells and other species, such as mice, which have been used for many years as powerful tools in genetic research.

8 There is a vast array of scientific evidence providing examples of the potential health benefits of carrying out research using cells containing hybrid human and animal DNA. For example, the mouse has long been used to model human genetic diseases and much of this research has employed methods to modify the genetic makeup of mice so as to provide more authentic and relevant mouse models of human disease. Although most such models involve simple 'knock-out' of a single gene, others are more complex and include the insertion of human genetic material into the mouse genome – essentially the creation of genetic hybrids. Two examples, both developed in this country, illustrate the importance of such techniques to medical research. The first is the creation, by Gillian Bates and colleagues of King's College London, of two mouse strains whose genome includes the aberrant human DNA sequence that underlies the neurodegenerative disorder Huntington's Disease. These Huntington's mice have enormously accelerated the progress of research on this devastating neurological disorder[4]. A more recent example is the MRC- and Wellcome Trust-supported research, published in the journal *Science* in 2006, and widely reported in the media at the time, in which a mouse line was created that carries an almost complete extra copy of human chromosome 21. This development by researchers at the MRC National Institute for Medical Research and at University College London[5] is expected to have a huge impact on Down's Syndrome research; researchers are able to study these mice to shed light on the key gene (or genes) responsible for the many different symptoms seen in Down's Syndrome.

9 Two key points should be borne in mind when considering the issue of the creation of hybrid and chimera embryos for research, in the manner proposed in, for example, the two research projects recently submitted to the HFEA for consideration:

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[3] The HFEA has recently consulted on egg sharing for research. The MRC's response to the HFEA consultation is at: www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC003455. The Wellcome Trust's response is at www.wellcome.ac.uk/assets/WTX035514.pdf

[4] See www.sciencedaily.com/releases/1997/04/970402124046.htm

[5] MRC press release: www.mrc.ac.uk/NewsViewsAndEvents/News/MRC001790

a. The ultimate goal of the research is not to create hybrid or chimera embryos that might be implanted and develop further, but to create blastocysts containing only human nuclear DNA, from which stem cell lines can then be derived. The use of animal egg cells (oocytes) has been proposed as a readily available alternative to using human eggs, which are scarce. The animal oocyte has its nucleus removed and the nucleus from a human *somatic* cell (i.e. not a germ cell) is inserted. The animal oocyte cytoplasm then acts as an 'incubator' for the human cell, allowing it to develop as a stem cell. The only residual animal DNA is in the mitochondria, the 'batteries' of the cell. This equates to only a tiny proportion of the total DNA in the cell (less than 1%); and has minimal impact upon the cell's developmental programme, which is directed by the human nuclear DNA. Indeed, there is the possibility that even the cytoplasm of the animal egg, which contains the mitochondria, might be replaced with that of the human somatic cell.

b. Although the human cells would grow initially in the form of an *in vitro* blastocyst, the intention is to remove cells from the blastocyst and use these to develop disease-specific embryonic stem cell lines. We are not aware of any intention, reason or ability to develop such embryos beyond the blastocyst stage, and certainly not beyond the 14-day limit currently imposed. [We do not suggest that this requirement should be changed]. One research proposal involves developing neuronal stem cells in order to study brain cell function in relation to neurodegenerative diseases. In these diseases, for obvious reasons, it is virtually impossible to obtain samples of living brain cells from patients.

10 The MRC and the Wellcome Trust are continuing to monitor the views of the academic and clinical community regarding the scientific possibilities and challenges emanating from this research. The Academy of Medical Sciences is convening a working group, chaired by Professor Martin Bobrow FRS FMedSci, to discuss issues surrounding embryos containing human and non-human material. In addition to examining definitions of hybrid and chimera embryos, this group will identify key research opportunities in the field, together with an assessment of how these opportunities are balanced by both safety and ethical concerns. Following an initial meeting in March, the working group will publish its output later in the Spring, to feed into the HFEA consultation and Parliamentary process around the forthcoming Bill. It is likely that the MRC and the Wellcome Trust will be observers on this working group.

Public Attitudes

11 While we have no evidence of general public attitudes on the creation of hybrid embryos, in 2003 the MRC, the Wellcome Trust and a coalition of organisations with a common interest in stem cell research commissioned MORI Social Research Institute to carry out a national survey of the public's views about the use of human embryos in medical research. As far as we are aware, this is the most recent representative public opinion survey on this subject. The survey indicated that around 70 per cent of the British public support the use of human embryos for medical research to find treatments for serious diseases and for fertility research[6].

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12 We believe the creation of hybrid embryos by combining human and animal embryos and/or stem cells is likely to prove helpful in understanding the growth and development of human embryonic stem cells and the treatment of serious diseases and conditions.

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[6] More at www.mrc.ac.uk/NewsViewsAndEvents/InvolvingThePublic/Consultations/Useofhumanembryosinmedicalresearch2003/index.htm

13 Given this potential, we agree with the view of the House of Commons Science and Technology Committee,[7] that it should be lawful to create hybrids or chimeras for research purposes if they are destroyed in line with the current 14-day rule for human embryo cultures subject to suitable legal and regulatory controls, including the requirement that the embryos must not be permitted to develop beyond 14 days.

14 If it is the Government's intention to prohibit the creation of human-animal hybrid and chimera embryos for research in all circumstances, we would not support this. It would deny researchers the opportunity fully to pursue embryonic stem cell research, and would also stifle research on transgenic disease models that involve the transfer of human DNA to animal lines. Such a prohibition would have a significant impact on the progress of medical research. We also fear it would undermine the UK's position as a world leader in stem cell research, a situation that the Government, scientists, regulators, ethicists and funders have worked hard to achieve. Much current stem cell research is in relatively early development, but it is our view that we are now at the stage where this research needs to be done – both in terms of therapeutic potential, and scientific and economic competitiveness.

15 If, on the other hand, it is the Government's intention to introduce draft legislation prohibiting the creation of human-animal hybrid and chimera embryos other than under licence for the purposes of research, the MRC and the Wellcome Trust would support that approach, in principle. In particular, we would support a proposal to regulate and license the activity in the same way that the use of human embryos is currently regulated and licensed, and to modify or clarify the current law as necessary to achieve this.

16 However, we are concerned that it might prove impossible to create hybrid or chimera embryos, or use stem cells derived from them, for research purposes, until new primary and secondary legislation is put into place, and that the delay this will cause to the progression of the research in this country will be damaging for the reasons detailed above. We would therefore wish to see urgent action to clarify or address the position, so that the activity can continue to proceed.

17 In summary, the MRC and the Wellcome Trust believe that, subject to appropriate controls, the creation of human-animal embryos and cells for research purposes should be permitted, and that if it were to be prohibited, temporarily or permanently, this would significantly impede research involving embryonic stem cells and the potential health benefits that could flow from that.

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[7] Human Reproductive Technologies and the Law: Fifth report of the Science and Technology Committee, 2005; HC 7-I