



## Cloned human-animal hybrid embryos Scientific and Ethical issues

### Introduction

The Human Fertilisation and Embryology Bill (HFE Bill) allows the creation of four different types of human-animal hybrid embryos. This page deals with the issues raised by cloned human-animal hybrid embryos (also known as cytoplasmic hybrids), which are the main focus of debate about hybrid embryos in the HFE Bill. In our view, although important, **the issues raised by GM embryos, which are one of these four types, are far more important, because it is clear that the Government's aim is eventually to allow the creation of GM children. Please read our web page on GM embryos and support our campaign to reinstate the ban on their creation.**

In 2006, two teams of British scientists applied to the HFEA to create human-animal embryos, by placing human DNA into an animal egg, using the same techniques used to produce cloned human embryos. The rationale for using animal eggs is that because cloning is so inefficient, many eggs are needed, and there are not enough human eggs available, whereas cow or rabbit eggs are plentiful. These scientists were aiming to grow those hybrid embryos in order to extract stem cells from them for research.

Based on the results of public consultation on the review of the Human Fertilisation and Embryology Bill, the Government initially proposed to ban the creation of such embryos. However, following a major campaign by scientists, and a report from the House of Commons Science and Technology Committee, the Government reversed its position, and has subsequently added other types of mixed-species embryo to the list it proposes to legalise.

In the middle of last year, Japanese scientists announced a scientific breakthrough, a method of creating cells which are apparently equivalent in properties to embryonic stem cells directly from adults skin cells. These Induced Pluripotent Stem (IPS) cells would seem to obviate the need for cloning, since they are genetically identical to the patients from which they came. One of the scientific groups which initially proposed to create human-animal hybrid embryos, led by Ian Wilmut, has decided to abandon them, in favour of IPS cells. However the other group, based in Newcastle, is continuing, and has received a license for its research from the HFEA, and is pursuing it.

### What are the issues?

In HGA's view, the concern about these experiments is not that they will lead to the creation of human-animal hybrid monsters. However we have strong objections to the way in which scientists have misled the public over the nature of these embryos and their potential in scientific research. Since they raise significant ethical issues, and because the public is so opposed to them, we are opposed to their legalisation in the HFE Bill.

### 1. Scientific issues

The debate over hybrid embryos has been bedevilled by a number of extremely misleading statements by scientists, concerning the nature of these embryos and their likely usefulness in research.

#### 'These embryos are 99.9% human'

Throughout the hybrid embryos debate, the science lobby has consistently claimed that these embryos are not 'really' hybrids, but are 'basically' human, or 99.9% human. This claim has now acquired the status of fact, and was repeated by the Secretary of State for Health when introducing

the debate on the Bill in the House of Commons. **Yet it is completely scientifically untrue.** The claim is clearly part of a systematic spin strategy to minimise the significance of the interspecies mixing in these embryos, and thereby allay public concerns.

If the egg is the size of a football, the human nucleus that is introduced is roughly the size of the golf ball. The main part of the egg outside of the nucleus is called cytoplasm and its purpose in eggs is to be a large store of protein and other molecules for the earliest stages of development. That is why eggs are the largest cells in the animal kingdom. Until the blastocyst stage, at which the scientists hope to extract stem cells, the vast majority of the material in the embryo will be of animal origin. Gradually, the human genes will be turned on, and some human proteins made, but not until much later than the stage at which the scientists want to extract stem cells will it be possible to say that these embryos are mainly human.

It is not even true that the large majority of the DNA in the embryo will be human. An egg contains upwards of 100,000 mitochondria, subcellular 'organelles' that produce energy for the cell, each of which contains some animal DNA. So actually, even in terms of DNA, it will be approximately 50% human, 50% animal.

It is only possible to describe these embryos as basically human on the basis of a very crude genetic reductionism which assigns excessive importance to the nuclear DNA, and ignores the rest of the cell. This is a fundamental sin of biological thinking which scientists always inveigh against - except when they are doing it themselves. At the early embryo stage, when the human DNA is only beginning to be activated inside an animal egg is the least appropriate moment to claim that the DNA determines the embryo composition and species identity.

#### **'The egg is just a shell to enclose the human DNA'**

Consistent with this genetic reductionism, and minimisation of the animal components is the way that scientists have described the egg cytoplasm as a passive 'shell' or 'container' for the DNA. What is actually happening is a very active process, in which animal proteins in the egg cytoplasm are required to turn off the genes in human DNA that make proteins appropriate to skin cells, and to turn on the genes appropriate to embryos. Without this active intervention from the egg cytoplasm, the human DNA would do nothing, and the success of the reprogramming determines whether the embryos can develop.

#### **These embryos are very unlikely to develop or produce stem cells**

The process of reprogramming the human DNA that has just been described is extremely difficult, which is why cloning is so inefficient, and why many of the animals that are born have deformities, and die. The root of the problem is that it is completely unnatural to try to force the reprogramming of the skin cell in this way - animals have evolved to reproduce sexually, and there are several inbuilt biological barriers in the way of cloning.

Because cloning is so difficult, despite nearly 10 years of effort there has been no progress with human 'therapeutic cloning' and no stem cells derived from cloned human embryos. It is certain that it will be even more difficult when there is a species mismatch between the cytoplasm and the nucleus. Firstly, the subtle differences between animal and human proteins mean the animal proteins will not be properly able to recognise the right place to bind to on the human DNA. Secondly, rabbits have a different developmental programme to humans, so the rabbit proteins will tend to impose a rabbit model of embryo development upon the human DNA.

The following table lists the biological problems with mixed species cloned embryos. It is hard to think of a way of creating an embryo that would produce more problems for it, or a type of embryo that would have less developmental potential.

Source of problem	Problem	Consequences for embryo
Cloning procedure	Eggs not properly matured through post-mortem hormonal treatment of ovaries	Poor developmental potential
Cloning procedure	Physical damage to embryo	Fragility, poor developmental potential
Cloning	Skin cell DNA does not go through gamete development, DNA methylation (imprinting) errors	Incorrect gene expression
Cloning	Incomplete reprogramming of nuclear gene expression by cytoplasmic factors	Incorrect gene expression
Species mismatch	Cytoplasmic factors will mis-recognise nuclear correlates, leading to incorrect reprogramming	Incorrect gene expression
Species mismatch	Cytoplasmic animal factors will tend to impose animal developmental programme on human DNA	Incorrect gene expression
Species mismatch	Mitochondria with proteins from different species will not function properly	Impaired energy metabolism

The hope that this work will succeed is based on one scientific paper, published in 2001, whose results have never been repeated even by the original laboratory. It is argued that animal eggs are needed because human eggs are in short supply. **But the strategy of using cow or rabbit eggs simply because there are more of them available is a strategy of simply applying brute force of numbers to the problem of cloning's inefficiency. The chosen solution will make the efficiency even lower, thereby cancelling out any gains.** In our view the biological problems outlined above in interspecies hybrids are likely to mean that that the scientists will waste a huge amount of time and taxpayer money, creating thousands of embryos with very little positive result. If they must insist on using nuclear transfer, their time would be better employed in studies of the mechanism of reprogramming, in order to improve its efficiency.

### **Embryonic stem cell lines from cloned interspecies hybrid embryos will be abnormal**

Even if ES cell lines can be obtained from cytoplasmic hybrid embryos it is almost certain that they will contain subtle abnormalities which will invalidate any experimental results obtained with them. It is now well established that cloned animals are abnormal due to failures in reprogramming. These abnormalities resulting from nuclear transfer will undoubtedly be compounded by further errors and abnormalities resulting from the interspecies mismatch, and from the presence of animal mitochondria. Overall, these experiments are likely to be a study primarily of experimental artefacts.

**It is extremely unfortunate that there has been such an extraordinary degree of hype about these experiments and that hopes of cures have been raised that are extremely unlikely to be fulfilled.**

## Induced Pluripotent Stem Cells

Finally, given that induced pluripotency is now being widely used and that Ian Wilmut has abandoned his plans to create intracellular hybrids, in favour of IPS cells, it is extremely hard to see why the Newcastle/King's teams are persisting with such an extreme long shot. **A number of disease specific IPS cells already exist and although IPS cells are not perfect models, they are clearly scientifically and ethically far superior to cloned human-animal hybrids.**

### Scientific conclusion

The arguments made above are quite obvious, and basic. Human Genetics Alert has repeatedly put them forward, and but has found it impossible to find scientists willing to debate them publicly, or in detail. This vindicates our conclusion that they are correct. We have recently been in correspondence with three British Nobel Prize winners, who although they have not agreed with our conclusions about whether the research should be permitted, have not found fault with these scientific arguments. It is not enough for politicians to claim that all the major medical and scientific institutions supports this research, unless they can demonstrate that these arguments are wrong. If science has any claim whatever to be a methodology with superior access to truth than others, then it must engage with critical arguments. Scientific correctness does not rest upon the authority of senior scientists, but upon evidence and arguments.

### 2. Weighing scientific benefit and ethics

We would note that the scientific debate about the usefulness of the proposed research on cytoplasmic hybrids has followed a familiar pattern. At the early stages we have seen a large number of very strong positive statements claiming that these experiments are 'vital medical research'. However, as might have been expected from the history of the debates on gene therapy and stem cells, scientific bodies are now making much more cautious statements about the value of the research. The Academy of Medical Sciences (AMS) report retreats to the highly defensive position that 'Although it is not yet clear how useful approaches involving cytoplasmic hybrid embryos will be, there is widespread agreement within the scientific community that uncertainties will only be resolved by actually carrying out the necessary experiments.'

**This may seem like a reasonable argument, but it is a far cry from the bullish statements that were initially made about this research. The point is that the public and the Government have been persuaded to overcome ethical concerns and their resistance to human-animal hybrids on the basis that this is vital and promising medical research, not on the basis that, 'Well it might work, so lets have a try'.**

**The likely value and success of research is a crucial factor in deciding whether we are prepared to cross established ethical lines for the sake of the knowledge that it may bring. In our view, since these experiments are so unlikely to succeed, and they raise severe ethical problems, it is wrong to let them proceed.**

The debate on the Bill in the House of Commons resounded with the argument that all research possibilities must be kept open. But this does not reflect the real world. Science-funding bodies rightly close off certain avenues of research every day by refusing to fund research proposals of poor quality, or those that do not fit with current scientific thinking. The call to keep all research avenues open has much more to do with an ideological fixation of the scientific community, which rejects any notions of that non-scientists might place limits on research for ethical reasons, except in the most extreme cases. In HGA's view, this is undemocratic and irresponsible, especially considering that it is taxpayers money that funds much scientific research.

### **3. Ethical issues**

#### **Creation of embryos purely for research is unethical**

Human Genetics Alert is not a pro-life organisation. We are not opposed to research on surplus embryos. However, creation of embryos purely for the purposes of research is unethical, because the embryo is then created not for the purposes of human procreation, but merely as a tool for scientific research. It turns the embryo into nothing more than a source of biological raw material for the experiments. This is not consistent with the concept of the embryo as a morally significant entity, deserving of respect, which underlies the law. This is why, although many countries allow embryo research, only a handful allow the creation of embryos purely for research. The EU has banned the creation of embryos purely for the purposes of research in its research funding programmes.

#### **The opposition to mixing species is rational**

For most people the very idea of human-animal hybrid embryos makes them very uneasy, if not positively disgusted. Many people find it hard to put into words their reasons for these feelings. However, in fact they are based on perfectly rational arguments.

If we look at nature, we see its working depends on species being distinct and different. If everything could breed with everything else, we wouldn't have oak trees and roses, pigs and birds, it would all be one grey mush. Species are the result of long slow process of design through natural selection. When natural selection designs a bird, it creates an integrated system in which all the parts work well together. When we look at nature, and find it beautiful the beauty comes from the internal harmony and the way the design perfectly suits the lifestyle of that species. And then, along comes a scientist who takes two entirely different systems, and in an instant of time shoves them together, violently disrupting that close internal harmony. If we could appreciate beauty at the molecular level, and we looked at these hybrid embryos they would look very ugly, a complete mess, precisely because they are so unnatural.

The creation of such mixtures epitomises humanity's lack of wisdom and respect for nature. The reason that biologists find no problem in doing this is because nowadays they focus entirely on molecules and cells and have lost their grasp of the larger whole. From this viewpoint, species barriers appear arbitrary and unreal, since all organisms are composed of very similar molecules. Scientists tend to dismiss opposition to species mixing as irrational, and they deride it as 'the yuk reaction'. In our view, revulsion at the violence they do to the integrated systems of nature is completely rational. We should not simply trust scientists, because, like everyone else, they have their own very particular way of seeing the world, which is far from objective.

#### **Conclusion**

The science lobby has severely misled the Government, MPs and the public about the nature of human-animal hybrid embryos, and their usefulness in medical research. In reality, they are very unlikely to be useful and there scientifically and ethically superior alternatives. Certainly, no convincing case has been made about the value of these hybrids that should lead us to override the public's resistance to them, and the ethical problems that arise from creating embryos purely for the purposes of research.

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