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The Unnecessary Evil of 'Therapeutic' Human Cloning

The United Kingdom House of Lords voted last night by an overwhelming majority to allow the creation of human embryos to provide embryonic stem cells that can be used for cell and tissue replacement. Britain stands out as the only country in the European Union to approve of this so-called therapeutic human cloning. **Drs. Mae-Wan Ho** and **Joe Cummins** explain why 'therapeutic' human cloning is both morally unacceptable and scientifically unjustifiable.

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What are stem cells?

Stems cells are cells in mammals including human beings that have the ability to divide and give rise to specialized, differentiated cells. The fertilized egg cell possesses this ability to the highest degree, for it has the potential to divide and develop into the entire organism with the full complement of cell types. The fertilized egg cell is *totipotent*.

Totipotency is retained as the egg divides into two and even four cells, so that each cell, when separated, is capable of developing into a complete foetus. That is how twins, triplets and quadruplets come about; they are natural human clones with identical genetic *and* cytoplasmic makeup.

When the embryo is four days old, and after several rounds of cell division, a hollow sphere is formed, called a *blastocyst*, within which is a cluster of cells called the *inner cell mass*. The outer layer is destined to form the placenta and other supporting tissues needed for the development of the foetus in the womb. The inner cell mass will go on to become all the tissues of the foetus' body. These cells are no longer totipotent, but *pluripotent*, ie, they can give rise to many types of cells, but not all of the ones required for foetal development.

As development proceeds, the inner cell mass divides further and become more restricted in the range of cells they will become. For example, blood stem cells will eventually give rise to red blood cells, white blood cells and platelets, and skin stem cells will give rise to all the various types of skin cells. These more specialized stem cells are said to be *multipotent*.

Pluripotent and multipotent stem cells in the embryo came to be known as *embryonic stem cells* or ES cells.

Stem cells are also found in children and adults, these are known as *adult stem cells*. Blood stem cells, for example, are found in the bone marrow of every child and adult, and in very small numbers, also in the blood stream; they continually replace the supply of blood cells throughout life. Recently, adult stem cells have also been found in brain as well as muscle, liver, skin and other tissues.

One of the main arguments used in favour of 'therapeutic' human embryo cloning is that adult stem cells are much more restricted in their potential to become different cell types than ES cells. However, it is beginning to appear that adult stem cells have the potential to give rise to a far greater range of cell types than previously imagined, and stunning results have been obtained. Furthermore, there are ways to obtain ES cells other than human cloning.

Embryonic stem cells are not all equal

There are three kinds of ES cells. The first is derived from the inner cell mass, a procedure pioneered in Dr. James Thomson's laboratory in the University of Wisconsin using 'excess' embryos from *in vitro* fertilization clinics. The second, embryonic germ cells, is isolated from the regions of the embryo destined to become ovaries or testes. This was first carried out by Dr. John Gearhart's group in John Hopkins' University, using foetuses from terminated pregnancies. The cells resulting from the two laboratories appear to be very similar.

The third kind of ES cells involves somatic cell nuclear transfer, the technique that created Dolly, the lamb cloned from a cell of an adult sheep. Researchers take a normal human (or animal) unfertilised egg and remove the nucleus, replacing it with the nucleus from a somatic cell of a human donor. The perceived advantage of this procedure is that the somatic cell donor could be the patient requiring tissue replacement, thus avoiding problems associated with immune rejection of transplanted cells or tissues that are foreign to the body.

As is clear from the description, the first two categories of ES cells do not involve the creation of human embryos, and research on those ES cells has already been going on for the

past two years. Many people may find research on those stem cells morally acceptable, though it will be difficult to justify research on those cells in view of the latest discoveries on the enormous developmental potentials of adult cells (see below), which make ES cells completely redundant.

It is research on ES cells obtained by nuclear transfer that raises the most serious moral concerns, for it requires the creation of embryos specifically for providing ES cells, the embryos being destroyed in the process.

In December 1998, researchers in the Infertility Clinic at Kyeonghee University in Korea announced that they had successfully cloned a human embryo by transferring the nucleus from the somatic cell of a 30 year old woman into one of her unfertilized eggs. This embryo was reported to have developed to the fourth cell division stage, when it would have been implanted. But it was destroyed on ethical considerations. Meanwhile, researchers in the United States and Australia have created 'human' embryos by transferring the nucleus of human cells into the eggs of the cow and the pig. It is of course questionable whether the embryos created by such procedures are human, and whether they are justifiable on moral grounds. These were destroyed at day 14. It was not clear, however, whether ES cells have been extracted from the embryos before they were destroyed.

Proponents claim that one of the major advantage of ES cells is that established cell lines can be obtained only from ES cells and not adult stem cells; though this may no longer be true (see below).

ES cells carry health risks, and there are major technical difficulties in creating them with nuclear transplant cloning techniques.

- ES cells can give rise to teratomas - malignant tumours (cancers) consisting of a disorganized mass of differentiated cells - on being transplanted.

- Nuclear transplant cloning is a very inefficient process with massive failure rates, requiring a large number of donor eggs.

- Nuclear transplant clones created by transferring human nuclei into cow and pig egg carry even greater risks, as it is well-known that such interspecific nuclear-cytoplasmic hybrids fail to develop normally.

ES stem cell research serves commercial interests, not public good

There are powerful commercial interests in ES stem cells. Geron Corporation of Menlo Park California gained first rights to exploit cells commercially, and also funded the isolation of embryonic germ cells. A total of ten companies were involved in exploiting stem cell technology and stem cells in 2000. Geron already owns dozens of patents on ES cells.

Companies investing in adult stem cell technology include Nexell Therapeutics of Irvine California and Anastrom Biosciences of Ann Arbor. Osiris Therapeutics of Baltimore identified mesenchyme stem in the supportive tissue that surrounds the bone marrow, and

has patented systems for isolating and producing those cells, and launched two clinical trials. Mesenchyme cells can differentiate into cartilage, muscle and even neurons. Neural stem cells came on the scene later, but already clinical trials have begun.

It is clear that the major impetus for both ES and adult stem cell research is coming from the biotech companies and scientists working with them. Therapy is likely to be very costly on account of the multiple license fees that have to be paid, not only on cells and cell lines but on isolation procedures.

Public opposition to ‘therapeutic’ human embryo cloning has been fierce. Apart from the moral objection to the creation of human embryos that are destined to be destroyed, many groups feel that ‘therapeutic’ human cloning is a slippery slope to reproductive cloning and the re-emergence of eugenics. The Clinton administration had forbidden such research in federally funded projects; and no European Government, with the exception of the United Kingdom, is in favour of such research.

The British government first announced plans to relax the law on human embryo cloning to allow the creation of human embryos up to 14 days to provide ES cells. Parliament voted in favour of the new law in December, against the advice of the European Group of Ethics in Science and New Technologies (EGE). The House of Lords endorsed Parliament’s decision with an overwhelming majority last night.

The EGE had warned that the creation of embryos by somatic cell nuclear transfer (‘therapeutic cloning’) for research on stem cell therapy would be premature", drawing attention to the rapidly developing research in adult stem cells. The EGE recommended that the EU should set up a budget to explore non-cloning sources of stem cells, especially adult tissue, and to enable the results of such research to be "widely disseminated."

Promises of adult stem cells

Mammals appear to contain some 20 major types of somatic stem cells. Stem cells have been described that can generate all the cells in the brain, the liver, pancreas, bone and cartilage. These adult stem cells are increasingly found to have the potential to become practically as many different cell types as ES cells. Furthermore, it appears that differentiated adult cells can be made to revert to cells remarkably similar to stem cells, and to have the ability to multiply for long periods in cell culture. Some of the findings are highlighted below.

- Mouse bone marrow stem cells can give rise to skeletal muscle and brain cells. Liver /pancreas stem cells can give rise to blood cells and brain cells. Brain cells can give rise to all previous cells types including the peripheral nervous system and smooth muscle. Brain cells have been found to differentiate to muscle, blood, instestine, liver and heart.

- Catherine Verfaillie of the University of Minnesota in Minneapolis is reported to have isolated bone marrow cells from children and adults that can become brain, liver, and muscle cells as well. These were found in adults between 45 and 50 years old. This research has not yet appeared in print.

- Scientists from the National Neurological Institute and Stem Cell Research Institute in Milan, Italy, succeeded in growing skeletal muscle from stem cells originating from an adult brain, both in culture and in animals receiving the transplanted stem cells (Galli, R. et al (2000) *Nature Neuroscience* 3, 986-991).

- A researcher in Britain, Dr. Ilham Abuljadaye, has just announced an efficient method for creating large quantities of adult stem cells from white blood cells, and her findings have been independently replicated, though not yet published. The method involves inducing the white blood cells to de-differentiate in the test-tube into stem cells (" Stem cell discovery reverses time" *The Times*, 15 Jan 2001, http://www.thetimes.co.uk/article/0,,2-68170,00.html). That means it will be feasible to prepare stem cells from the patient who is in need of cell or tissue transplant, greatly simplifying the procedure, avoiding immune reactions and reducing cost.

- Two research teams at University College London found that adult rat cells can be made to divide hundreds of times when provided with the right mixture of nutrients, and without taking on the undesirable characteristics of cancer cells, such as uncontrollable growth (Cohen, P. (2001). *New Scientist* 18 Jan. latestnews@newscientist.com). Adult human cells may have the same capacity.

- Another possibility is that the patient's own stem cells could be stimulated to multiply and replace cells and tissues within the body itself (McKay, R. (2000). *Nature* 406,361-364.)

Conclusion

We reject research on ES cells created by human 'therapeutic' cloning on the following grounds.

- It is totally unnecessary, given the promise of adult stem cells and adult cells from the patients themselves, which can be most effectively used for cell and tissue replacement.

- It is morally unacceptable to create human embryos for providing ES cells.

- It is a slippery slope to human reproductive cloning.

- Nuclear transplant cloning has very low success rates and generates many abnormalities.

- Cloning procedures involving transplanting human nuclei into animal eggs carry even greater risks.

- ES cells are already available using 'excess' embryos from *in vitro* fertilization clinics and aborted fetuses.

- ES cells carry cancer risks on being transplanted.

- ES cells are subject to multiple patents, on cloning and isolation procedures as well as on the cells themselves; this will make their use in cell or tissue replacement therapy very costly.

- Adult stem cells are already showing great promise in cell and tissue replacement; and are likely to be much less costly.

'Therapeutic' human cloning is an unnecessary evil. We call on the UK Government to reject it in line with the other EU countries, and to support research into non-cloning sources of stem cells, especially adult cells, with special emphasis on methods that do not involve patented procedures and cell lines.

General References

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