Stem cell research—why is it regarded as a threat?

An investigation of the economic and ethical arguments made against research with human embryonic stem cells • *by Peter Lachmann*

The British House of Lords voted on January 22, 2001 to ease restrictions on the use of human embryonic stem cells. Researchers in the UK are now allowed to use early stage human embryos for therapeutic purposes, mainly to retrieve stem cells. This decision comes amidst a heated debate regarding the medical and economic potential of stem cell research as against its ethical pitfalls. The scientific, legal, ethical and philosophical arguments have been discussed extensively (Mieth, 2000; Colman and Burley, 2001). In this report I therefore propose to take it as established that stem cell technology has great promise for the treatment of a variety of diseases and, indeed, that stem cell therapy may hold exciting prospects for medical advances in the first decades of the 21st century.

What I wish to discuss is why the prospect of stem cell therapy has been greeted, in quite widespread circles, not as an innovation to be welcomed but as a threat to be resisted. In part, this is the characteristic reaction of Luddites, who regard all technological innovation as threatening and look back nostalgically to a fictitious, golden, pre-industrial past. There are, however, also serious arguments that have been made against stem cell research; and it is these that I would like to discuss.

Stem cell technologies would be very expensive and available only to rich countries and to rich people

It is indisputable that most novel medical technologies are expensive. However, they usually get cheaper as the scale on which they are used increases. A good

example is bone marrow transplantation, which initially was extremely expensive. A few decades later, bone marrow trans-

plantation has become a routine procedure that is cheap enough to be used for the treatment of numerous diseases. The same will certainly happen with other therapeutics—be it β -interferon to treat multiple sclerosis, protease inhibitors to block HIV or monoclonal antibodies to target cancer cells. These agents are very expensive now because the cost of their development, testing and production has to be met, but they will rapidly become cheaper as more patients are treated, as the manufacturing process becomes more efficient and as patents expire.

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There is, however, a further argument against this particular threat. One of the major financial problems of health care since World War II has been that major advances in clinical research resulted in ways of controlling diseases rather than curing them. The elderly and many chronically ill people in the First World now live a life of high quality. But this depends on the long-term administration of drugs to treat a number of conditions including high blood pressure, diabetes, rheumatoid arthritis and asthma. Consequently, the cost of health care in these countries has dramatically increased over the last few decades. Even for diseases such as Parkinson's disease that cannot be adequately controlled, continuous ther-

apy is given over many years to relieve symptoms. Stem cell therapy may indeed lead to cures for many ailments. It may become possible to cure Parkinson's disease with grafts of brain cells. It is also likely that diabetes will be curable using stem cell treatment. It may also be possible to achieve at least something approaching a cure for cardiovascular diseases by replacing damaged endothelial cells in the blood vessels or the cardiomyocytes in the heart itself. If these promises hold true, stem cell therapy might result in a reduction in the overall cost of healthcare as a number of currently incurable diseases are cured.

Stem cell research would deviate efforts from other health strategies

It is difficult to tell in advance what type of research will give rise to what type of benefit. The fundamental research from which stem cell technology originated came from studies in developmental biology whose utility could not have been foreseen. Furthermore, current research into the mechanisms of cellular reprogramming and into the growth requirements of different cell lineages will not only advance scientific knowledge, but is also likely to become of widespread value in clinical medicine.

These two preceding arguments are essentially economic. The following are predominantly ethical and should therefore be given greater weight. But before considering them, it is worth remembering Onora O'Neill's eloquent warning against declamatory or polemical ethics at the Millennium Festival of Medicine. Ethics is a subject grounded in philosophy and religion. Ethics cannot be determined by polling people and asking them what they think is right or wrong and simply accepting the view of the majority. It does require support from logically and philosophically coherent arguments.

Interference with the genome involves 'playing God'

This argument reflects the view that divine creation is perfect and that it is inappropriate to alter it in any way. Such a point of view is particularly difficult to sustain in Western Europe where every acre of land bears the marks of more than 2000 years of human activity, and where no primordial wilderness remains. Ever since *Homo sapiens* gave up being a hunter and gatherer and took to herding animals and agriculture, he has modified the environment. All major food plants and domestic animals have been extensively modified over millennia. It is therefore impossible to sustain the idea that genetic interventions for food plants, animals and the therapy of human diseases are a categorical break from what has gone on throughout evolution.

The proposition that any attempt to interfere with the 'perfect divine creation' is morally wrong is also not widely held by theologians. The following quotation is from Professor Iain Torrance, Professor of Divinity in Aberdeen (personal communication), on the subject of co-creation:

'Creation, understood in the light of the trajectory of the incarnation, is not a simple act. It is an enabling: a process in which a created realm is brought to its own reality and enabled to be itself. I suggest that this may give us a charter for some acts in which we do co-operate with God, though it would be rash ever to claim confidently that any specific act were such. I believe we are invited to share in this activity of enabling, which brings the created world closer to perfection. We never know what perfection is or when we have arrived there. Art is a kind

of creation of beauty and may in some sense act as an analogy.

I believe we have an authority to intervene, so as to heal and restore, but not to manipulate and destroy.'

Unfortunately, the idea of a perfect creation was adopted by the early evolutionary biologists who, understandably, were greatly impressed by the elegance of evolutionary adaptation. They therefore

fittest to survive under those selective pressures that exist at any one time.

The idea of 'playing God' also carries with it the proposition that there is knowledge that may be too dangerous for mankind to know. This is an entirely pernicious proposition, which finds few defenders in modern democratic societies. On the other hand, there is a general agreement that there are things which

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tended to replace a perfect divine creation with a perfect evolutionary adaptation. But when scientists began to study the molecular mechanisms of evolution, it turned out that there are only a limited number of strategies available to achieve adaptation. The evolution of many molecular systems demonstrates that adaptation is by no means a perfect process but very much a matter of 'muddling through'. It is perfectly clear, for example, that no competent engineer would design a creature walking on two legs as badly adapted to the upright posture as is Man. If Man were really made physically in the image of God, it would be bad news for an immortal God.

There has been a desire among political figures as widely separated as Karl Marx and Adolf Hitler to incorporate 'scientific Darwinism' into their particular political theories. They have generally failed to understand the nature of the evolutionary process, particularly in believing that natural selection produces an overall, optimal phenotype. To give a current example, if the HIV pandemic continues unabated it will provide a very strong selective pressure in favour of those few people who lack the receptors—CD4 and CCR5—to which the virus attaches. One can imagine that, in due course, their progeny could become dominant in large parts of the world. However, there is no reason whatsoever to believe that these survivors would necessarily be particularly intelligent, beautiful, moral or have other survival characteristics. Furthermore, mutation of the receptor genes may impair their immune system's ability to deal with other diseases. Survival of the fittest—an unfortunate phrase in any case—simply describes those who are

should not be done—in science as in other areas of life. In the context of stem cell research, this may be summed up by Kant's injunction that 'humanity is to be treated as an end in itself'. The intention of stem cell research is to produce treatments for human diseases. It is difficult not to regard this as a worthy end, and more difficult to see that there could be any moral objection to curing the sick, as demanded by the Hippocratic oath.

Somatic cell nuclear transfer is immoral as it involves creating embryos only to destroy them

The essential problem here is to decide at what stage of development a human embryo acquires the interests—and the rights to protect these interests—that characterize a human being, i.e. when does an embryo become part of humanity? This is a problem that has occupied a great deal of theological and philosophical attention and the arguments have been extensively discussed (Dunstan, 1990; Dunstan and Sellar, 1988).

One principal condition is regarded as sufficient to confer interests and the right to defend them—sentience. In this context, sentience is neither the ability to think—which is in any case very difficult to define—nor is it the ability to feel pain. Sentience is defined as the ability to form any links with the outside world. Until an organism has a rudimentary central nervous system and some sense receptors—be it for pain, touch, smell, taste, sight or sound—it cannot form any contact with the outside world and therefore is not sentient. It therefore does not seem possible

to attribute sentience to a pre-implantation embryo, or indeed even to an implanted embryo until it has developed some form of nervous system and sense organs. Along the same line, we now universally accept that a human being is dead when no contact with the outside world can be demonstrated by central nervous function. Certainly, death is regarded as having occurred well before every individual cell of the body has died.

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The medieval church took the view that an embryo acquired a soul, or it became *animatus*, at the same time that it became *formatus*, i.e. when it acquired recognisable human form. This doctrine was derived from Aristotle who curiously believed males to become *formatus* at 40 days, whereas females were not so until 80 days of gestation. The medieval church held that the abortion of an embryo that was neither *formatus* nor *animatus* was only a fineable offence; and it was only after an embryo had become *animatus* that abortion became a mortal sin. At the core of the refusal of the Roman Catholic Church to countenance embryo research is a doctrine by Pope Pius IX, who declared in 1869 that an embryo acquires full human status at fertilization. This may have been partly in response to an increased frequency of abortion but it is likely also to have been influenced by a desire to bring Christian doctrine into line with 19th century embryology.

But women lose large numbers of pre-implantation embryos throughout their reproductive life. These embryos are not mourned, they are not given burial and no one says prayers for them. The intra-uterine coil, widely used as a method of contraception—though not permitted by the Roman Catholic church—is designed to prevent implantation of embryos and, again, is not regarded as being morally reprehensible.

Further difficulties for the view that full human status is acquired at fertilization arise from advances in reproductive biology. Somatic cell nuclear transfer does not involve fertilization and thus turns the Pius IX doctrine *ad absurdum*, since it makes it possible to see in any somatic cell whose nucleus can be introduced into an oocyte, the potential for giving rise

to a complete human being. When reprogramming of cells becomes better understood, it may be possible to convert somatic cells into embryos without the need for an oocyte. If, ultimately, any somatic cell has the potential of being grown into a complete embryo and, subsequently, into a human being, it would logically mean that we should ascribe a moral status to every cell in the body—a concept that is clearly ridiculous.

The view that an embryo does not acquire the status of a human being until it is obviously of human form with a central nervous system and organs (as is the view of the Protestant church), or even until it is delivered (which is the view of the Jewish religion), is more defensible on philosophical grounds than is stating that human status is acquired at fertilization. Of course, any decision relating to the particular point in development at which an embryo acquires full human status must be partially arbitrary. There are other cases where there is blurring at the interface of two categories or where distinctions are made slightly arbitrarily. This is the case in distinguishing between plants and animals; in distinguishing between male and female; and in distinguishing between the living and dead at the end of

ple of the Wedge is that you should not act justly now for fear of raising expectations that you may act still more justly in the future—expectations which you are afraid you will not have the courage to satisfy. A little reflection will make it evident that the Wedge argument implies the admission that the persons who use it cannot prove that the action is not just. If they could, that would be the sole and sufficient reason for not doing it, and this argument would be superfluous.’ (Cornford, 1908). It is inherent in what Cornford writes that the fear that one may not behave justly on a future occasion is hardly a reason for not behaving justly on the present occasion.

In addition to this philosophical argument, one should consider that there are also cogent biological reasons for opposing reproductive cloning using cell nuclear transfer. This is a form of vegetative reproduction, a technique used only by plants and a few lower animals. The late William Hamilton pointed out (Hamilton *et al.*, 1990) that primitive animals which have the opportunity of adopting vegetative reproduction have uniformly failed to do so. He argues that it is the challenge of parasitism that makes the use of sexual reproduction, with its re-assortment of genes at each generation, advantageous in evolutionary terms.

In fact, the use of reproductive cloning can be defended only for farm animals, where this technique may be the best for producing, for example, cows that are

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life. But the fact that making distinctions can sometimes be difficult is not an argument for making fundamentalist distinctions or making no distinction at all.

Allowing stem cell research is the thin end of a wedge leading to neo-eugenics, ‘designer’ children, and discrimination against the less-than-perfect

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ple of the Wedge is that you should not act justly now for fear of raising expectations that you may act still more justly in the future—expectations which you are afraid you will not have the courage to satisfy. A little reflection will make it evident that the Wedge argument implies the admission that the persons who use it cannot prove that the action is not just. If they could, that would be the sole and sufficient reason for not doing it, and this argument would be superfluous.’ (Cornford, 1908). It is inherent in what Cornford writes that the fear that one may not behave justly on a future occasion is hardly a reason for not behaving justly on the present occasion.

The Universal Declaration on the Human Genome (<http://www.unesco.org/ibc/uk/genome/projet/>), which UNESCO hopes will be incorporated into national laws, specifically prohibits the use of genetic manipulation to ‘improve’ humans. Vigilance will certainly always

be needed to prevent the misuse of this technology, but it is unlikely that the use of stem cells carries any particularly devastating dangers.

Eventually, an 'immortal' population could evolve and that would create its own moral problems

This proposal derives from John Harris who is sufficiently impressed by the promises of stem cell therapy to believe that we may have to face a population that can live two or even more centuries (Harris, 2000). Success on that sort of scale seems a long way off—but it would be an accolade to medicine to have that set of problems to face!

I wish to close with another quotation from the *Microcosmographica Academica*: 'There is only one reason for doing something; the rest are arguments for

doing nothing.' The Luddites can always produce a variety of more or less plausible arguments for resisting technological innovation. But without innovation we would not have moved on from the Stone Age to the Computer Age in only ~100 generations. The present arguments for doing nothing are no more potent than all preceding ones.

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Myth, menace or medical blessing?

The clinical potential and the problems of genetic vaccines • by Wolfgang W. Leitner

Some day in the near future, when children have to see a paediatrician to get their immunizations they may encounter a much less painful procedure than today's children do. Instead of the dreaded needle and syringe, the doctor will hold a gene gun to the child's arm and, with a blast of helium, painlessly shoot tiny gold particles into the skin. These particles are coated with plasmid DNA containing the nucleotide sequences for viral or bacterial surface proteins. Upon their introduction into host cells, the protein is produced which triggers an immune response as it would normally in the case of an infection. As a result, the child will be protected from further attacks by the respective virus or bacterium, as in the case of any vaccination.

This procedure is painless, bloodless, clean and—as far as we know today—completely safe. However, such a scenario is likely to send cold chills down

the backs of most European parents who, in general, tend to be more reluctant in their acceptance of DNA-based technologies than North Americans, who seem to be less concerned about the idea of 'genetic immunization' or 'gene vaccines'. Oddly, the idea of a 'gene transfer' raises irrational fear in many people who do not realize that we are under constant attack by viruses, bacteria and parasites, which—as part of the infectious process—force their genes into our cells and use them as factories to produce their progeny. In the face of all the criticism and opposition that other 'gene-based' products and therapies have spawned in Europe, it may appear premature to believe that genetic vaccines will soon become acceptable to the public.

Indeed, there are some risks involved with genetic vaccines, comparable to those that an infection might have. Some researchers are concerned that vaccine sequences might be integrated into the

genome of the patient's cells. Inserted in the wrong location, these genes could theoretically have oncogenic potential, for instance by disrupting cancer-suppressor genes. It will require extensive clinical trials to test this approach and to convince the public of its safety.

DNA vaccines represent a good example of a successful collaboration between immunology and molecular biology. Since their discovery, plasmid DNA constructs have been extremely useful tools for molecular biologists, but their more recent application as vaccines has dragged them out of the laboratory and into the public spotlight. Plasmids are circular, extrachromosomal pieces of DNA that can be modified to carry genes of interest. When introduced into mammalian cells *in vitro*, they cause these cells to produce the respective protein of interest. For this reason, it was not very surprising to find that injection of plasmid DNA into the leg muscles of mice resulted