Scientists isolate elusive embryonic stem cells

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Imagine being able to grow in a laboratory unlimited quantities of human tissues for transplantation--anything from heart muscle to bone marrow and brain tissue. While the idea seems like the theme of a science fiction novel, scientists in the United States have brought it one major step closer to reality.

In what marks a major advance in biological medicine, two scientific teams--one at John Hopkins Medical Center in Baltimore and another at the University of Wisconsin, Madison--have successfully isolated and cultivated embryonic stem cells, which are the progenitors of all tissues in the body.

The importance of embryonic stem cells rests in their lack of specialisation. These basic cells are present in the earliest stages of developing embryos and are able to develop into virtually any type of cell and tissue in the body. Being self-renewing, they offer a potentially limitless source of cells and tissue.

Capturing and cultivating embryonic stem cells has profound implications for transplant medicine, for the testing and development of new drugs and for the scientific understanding of basic developmental biology.

James Thomson, a developmental biologist who heads the Madison research team, wrote in the journal *Science:* 'You can derive and culture these cells, and it opens the possibility for some dramatic new transplantation therapies. Although a great deal of basic research needs to be done before these cells can lead to human therapies, I believe that in the long run they will revolutionise many aspects of transplantation medicine.'

Scientists have been investigating stem cells for over a decade but their capture has proven elusive as they only exist for a short time. In the Madison research, stem cells were obtained from in-vitro fertilised embryos less than a week old--known as blastocysts. A blastocyst is a hollow ball of about 140 cells that develops several days after fertilisation. Embryonic stem cells are derived from the inner cell mass of the blastocyst at an early period of embryogenesis.

The embryos used by the Madison research team were clinically produced in a laboratory dish for couples having difficulty achieving pregnancy. The remaining blastocysts were donated specifically for the project by the couples involved who were informed and gave written consent.

The researchers were able to establish five independent cell lines from 14 blastocysts and were able to grow them indefinitely in culture. They observed the stem cells differentiate into the three primary cell types that make up the body-- endoderm, ectoderm and mesoderm--and subsequently into an array of neural, gut, muscle, bone and cartilage cells.

At the John Hopkins Medical Centre in Baltimore, scientists adopted a different strategy. By searching small samples of aborted non-living human fetal tissue, they were able to isolate what they call primordial germ cells (PGC) that would have become eggs and sperms. The PGCs were cultured on mouse connective tissue cells in a broth of nutrients and specialised growth factors. Under the right conditions, the PGCs developed into a tightly knit cluster of stem cells and then into the three basic layers of cells found in all mammalian embryos.

Professor John Gearhart, who led the Baltimore team, explained: 'The potential of these unique, versatile cells for human biologic studies and medicine is enormous. These cells will rapidly let us study human processes in a way we could not have done before. Instead of having to rely on mice or other substitutes for human tissues, we will have a unique resource that we can start applying to medicine.'

The next and crucial stage of research is in understanding how to direct the transformation of the stem cells into different types of cells such as muscle, tissue and blood. While scientists have been able to observe embryonic stem cells differentiate, it has been to a random, mixed population of cells.

The ability to grow particular tissue types would allow the treatment of a range of ailments that at present require waiting time for donors. Thomson's team is now working with clinical scientists and transplant surgeons to carry out the basic research needed to develop human

embryonic cell-based therapies to repair or replace damaged or diseased tissues and even organs.

The new techniques have the potential to resolve one of the central difficulties involved in transplants--tissue and organ rejection. Gearhart explained: 'Not only should scientists be able to generate specific nerve, muscle, skin or other cells for transplantation, but we should also be able to alter these cells, as has been done in mouse studies, to reduce the likelihood of rejection. We could make universal donors. More specific cells could become transplant therapies for diabetes, spinal cord injury, neurodegenerative disorders like Parkinson's disease, muscular dystrophies, atherosclerosis and wound healing.'

The first application of embryonic stem cell technology may be in the area of drug discovery. Treating specific cell types with chemicals and measuring their response offers a short cut to isolating and testing medicines that can be used to treat diseases specific to those tissues.

Stems cells will also provide a window into the earliest stages of human development which have been difficult if not impossible, to study in the past and may allow, through a greater knowledge of the events that occur in the first stages of life, the treatment and even prevention of abnormalities in human beings.

Theological opposition

There is no question as to the significance of the initial breakthroughs and the importance of further research into embryonic stem cells. Yet the research is facing considerable opposition. In fact, in the United States there is a legal prohibition on the provision of federal funds for research on embryonic cells.

Dr Lori Andrews of the Chicago-Kent College of Law, a legal expert on reproductive technology, commented: 'Any time you take a cell off a blastocyst, that cell could be used itself to create a human being, so some groups in our society believe that in making it transplantable you have derailed it into becoming a kidney or some other tissue'.

The groups to which she refers are mainly churches and religious groups. For instance, Dr Kevin Fitzgerald, a Jesuit priest at Loyola University Medical School, raised objections to research on embryonic stem cells because he regards it as 'disputing the viability of life, and we are back to the question of how to justify destroying life for the purposes of scientific advancement'.

To equate the use of a tiny group of cells or a blastocyst with the taking of a human life is not based on science but on the religious superstition that this primitive biological structure is invested with a human soul. On the same basis the Roman Catholic Church and other religious groups oppose the right of women to abortion and virtually all forms of contraception. Not only do these groups set the rules for their own members but seek to impose their views on others via their considerable political clout within the US Congress.

The blastocysts used in the Madison research were clinically produced and would otherwise have been discarded. These primitive embryos only have the potential to become human life, firstly, because of the astonishing advances in medical science and, secondly, if they are subsequently implanted in a willing female recipient. Yet despite having the written consent of the donor couples, scientists are ineligible for US federal funding--for research that has enormous potential to save lives.

The development of any medical procedure undoubtedly requires careful testing, monitoring and supervision. But the primary concern of medical researchers should be for the potential benefits, and any associated dangers, of a particular therapy for the present and future generations as judged on the basis of science, not theology.

Opposition to research on embryonic stem cells is not confined to the United States. A proposal has been put forward by the European Parliament to deny EU research money to projects that result in destroying human embryos. This could have far-reaching implications as scientists perform research on embryos to learn more about the causes of infertility, to find safer forms of contraception, to detect genetic disorders or sex-linked hereditary disorders and to develop procedures to benefit embryos.

While governments place bans on embryonic stem cell investigations, industry can do as it pleases. The over-riding drive for the research as it exists presently, is to find what is most profitable for the companies concerned. One of the most significant discoveries of modern medicine is in the hands of the Geron corporation, which funded the research teams at Madison and Baltimore and, as a result, holds the licence to develop the technology.