Recent work with adult stem cells, however, has made some researchers question whether a tight focus on ES cells is necessary. Small numbers of stem cells exist in adult tissues, where they help to repair our bodies. Compared with ES cells, these adult versions are thought to have a more restricted capacity for development into different tissue types. But if they could be used as a source of replacement tissue, adult stem cells would avoid the destruction of a human embryo — a fundamental moral objection to approaches based on ES cells.

Adult stem cells could be harvested from healthy donors and used to grow replacement tissues for patients needing grafts. Once again immunosuppression or tolerance would probably be needed, but a novel way of using adult stem cells might provide a suitable tolerance strategy. Bone marrow contains haematopoietic stem cells (HSCs), which give rise to all of our blood cells, including those of the immune system. When HSCs are transplanted into the bone marrow of the recipient, the immune system can enter a 'chimaeric' state in which some of its cells are derived from the transplanted HSCs. These would, in theory, prevent the immune system from reacting against other cells transplanted from the same donor[9]. Last year, for instance, Judith Shizuru, Irving Weissman and their colleagues at Stanford University in California showed that mice given transplants of highly purified HSCs subsequently accepted heart grafts from mice genetically identical to those from which the HSCs came[10].

But if a patient's own stem cells could be used to grow replacement tissues, there would be no need to worry about rejection. With this aim in mind, researchers are again looking to bone marrow to provide a solution. Bone marrow contains stem cells that can give rise to a range of tissues including bone, cartilage and muscle. In April 1999, researchers with the company Osiris Therapeutics in Baltimore showed that cultures of these cells retain this potential[11]. And in this issue of *Nature*[12], Piero Anversa of the New York Medical College in Valhalla and his colleagues describe experiments in which they injected stem cells from mouse bone marrow directly into the cardiac muscles of mice with damaged hearts. They found that the stem cells developed into muscle cells and blood vessels, helping to repair areas of dead tissue. These experiments raise the possibility of repairing a patient's failing heart with cardiac muscle grown from his or her own bone marrow stem cells[13].

Career change

Recent experiments in mice have also revealed that adult stem cells can develop in entirely unexpected ways. Neural stem cells from the brain, for example, have been transplanted into bone marrow, where they developed into blood cells[14]. Bone marrow stem cells have also been shown to migrate to the brain after being injected into the bloodstream, where they develop into cells that appear to be neurons[15,16]. These experiments have fuelled hopes of treating patients with their own adult stem cells.

But even the enthusiasts accept that there is a long haul ahead before therapies based on these discoveries are ready for the clinic. "We need to make this more robust," says Helen Blau, who works on adult stem cells at Stanford. Showing that small numbers of stem cells can migrate to another site in the body and develop into a cell type appropriate for that tissue is one thing; using them to repair damaged or diseased tissues is another.

Improving the situation will entail a search for cell-surface markers to identify the stem cells that can transform into a wide range of tissue types, and the development of methods to purify and selectively culture them. It may also require the discovery of the biochemical signals that attract stem cells to sites of tissue damage and direct their development to effect a repair.

Given these obstacles, some researchers believe it is also worth taking on the field's toughest challenge — finding a way to reprogramme any of the body's cells to create ES-like cells matched to the intended recipient without cloning an embryo. Interest stems in part from experiments reported in 1997, in which researchers led by Azim Surani of the Wellcome/CRC Institute of Cancer and Developmental Biology in Cambridge fused mouse white blood cells with embryonic germ cells[17] — cells from the developing reproductive system that share many characteristics of ES cells. The white blood cell nuclei appeared to return to an embryonic state.

Researchers at several of the leading com-

A tortured tale of supply and demand

Given the breadth of their potential, one might expect that human embryonic stem (ES) cells would be the focus of attention for hundreds of research groups. But so far, only a dozen or so teams have entered the field. The issue was initially one of a shortage of cells. But now the main problems are political — with fears that the new US administration will ban federal funding for ES-cell research looming large.

So far, the main distributor of human ES cells has been the WiCell Research Institute, a non-profit spin-off from the University of Wisconsin in Madison, where in 1998 the cells were first cultured in James Thomson's lab[2]. His work was funded by the company Geron of Menlo Park, California, which has certain exclusive commercial rights to develop the ES cells for therapeutic applications.

In February last year, the University of Wisconsin announced that WiCell would soon start making Thomson's ES cell lines available to other research groups. Some researchers were initially concerned that WiCell wanted wide-ranging rights to rescind permission to work on the cells and to demand that they be destroyed. Those rights have since been restricted, and will only be enforced under specific circumstances — for instance if researchers use the cells for additional projects without written permission.

Given the time that has elapsed between the cells' creation and WiCell's formation, say stem-cell researchers, Geron got an important head start. Although researchers who use WiCell's ES cell lines can patent discoveries made using the cells, they may find that much of this territory has already been staked out. "We have submitted 36 patent filings on these cells," says David Greenwood, Geron's senior vice-president for corporate development.

Other supplies are now available. A group headed by Alan Trounson at Monash University, near Melbourne in Australia, is responding to requests to obtain cells from its human ES cell lines[6] — although high demand is putting the lab under pressure. "We are short on staff," says Trounson. Other ES cell lines are soon expected to become available from the Rambam Medical Center in Haifa, Israel.

But increased availability does not mean open access. Current legislation in France and Germany, for instance, prohibits embryo research, including work on ES cells — although the French government is proposing to lift its ban. In the United States, meanwhile, uncertainty as to whether federal funds will be freed to support ES-cell research is hampering progress.

Last summer, the previous US administration concocted a compromise that would allow researchers to use federal funds to work on ES cells, provided the ethically contentious step of isolating the cells from a human embryo had been achieved using other funding sources. But President George W. Bush's administration may now block the use of federal funds for ES cell research. And in the current state of limbo, few scientists have responded to a call from the National Institutes of Health (NIH) for ES-cell research proposals. By the 15 March deadline for documents to show that proposed research will comply with NIH guidelines, just three submissions had been received.

Even if federal funding is released, there may still be problems. The NIH has published criteria — including standards for informed consent from 'parents' of the embryos from which the cells were harvested — with which suppliers of ES cells to federally funded researchers must comply. WiCell's current cell lines do not meet these standards, and the NIH is still reviewing compliance documents submitted from Monash.

Joanna Downer