NEWS

Stem cells derived from 'dead' human embryo

It has no brain, heart or nervous system. So how can researchers tell when an embryo has died? That question is likely to become a focus of debate, as scientists search for ways to create 'ethical' human embryonic stem cells.

Many researchers are investigating methods for deriving such cells without destroying human embryos. Now, one group claims to have developed human embryonic stem cells from a very young embryo that had already died.

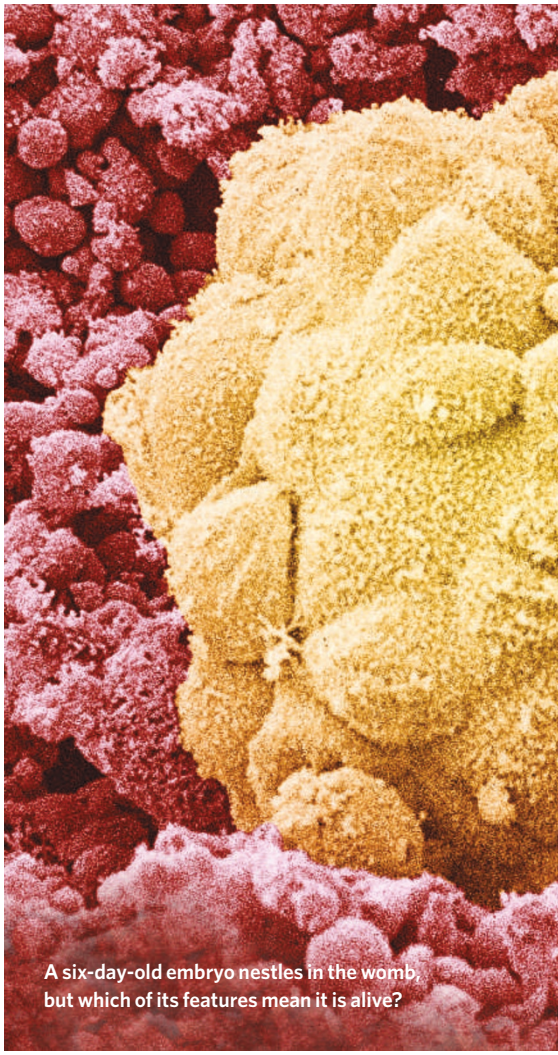
Miodrag Stojković, who led the project at the University of Newcastle upon Tyne, UK, believes his technique may be acceptable to governments in countries such as Germany and the United States. Laws in these countries restrict the use of embryonic stem-cell lines owing to concerns about killing potential humans.

Whether or not the method is judged as harmless will probably depend on whether the lives of such embryos have indisputably ended. "It will intensify the debate over how to define the death of an embryo, because now there is more at stake," says Thomas Murray, president of the Hastings Center, a bioethics research institute in Garrison, New York.

During *in vitro* fertilization (IVF), well over half of human embryos arrest (stop dividing naturally), and are therefore unsuitable for transfer into women. Stojković, now a deputy director of the Prince Felipe Research Centre in Valencia, Spain, used 161 embryos donated by women in two local IVF clinics in his study, published online last week (X. Zhang *et al. Stem Cells* doi:10.1634/stemcells.2006-0377; 2006). Of these embryos, 29 were developing normally until cells were extracted, 119 arrested 3–5 days after fertilization, and 13 arrested 6–7 days after fertilization.

Arrested embryos were monitored for 24 to 48 hours, to check that none of the cells they contained started dividing again. In an IVF clinic, such embryos would meet the standard embryologist's criteria for having terminally arrested, and would typically be thrown away. Even in Italy, which has particularly restrictive laws stating that embryos cannot be destroyed and that all embryos created during IVF must be implanted, embryos which have arrested in this way are discarded.

The team derived healthy human embryonic stem-cell lines from eight of the normally developing embryos, one of the late-arrested embryos and none of the early-arrested embryos. Although many of the cells in the arrested embryos had distorted shapes or damaged chromosomes, a few cells remained healthy. To coax these into growing, the researchers removed the 'zona pellucida' that sheaths the embryo, and



A six-day-old embryo nestles in the womb, but which of its features mean it is alive?

Superconductivity research is down but not out

"Reports of my death have been greatly exaggerated," Mark Twain allegedly said after his obituary was published prematurely. High-temperature superconductivity physicists now know how he felt.

If current trends continue, research into high-temperature superconductivity (high T_c) will come to a standstill some time between 2010 and 2015, according to a report by Andreas Barth and Werner Marx, respectively at FIZ Karlsruhe and the Max Planck Institute for Solid State Research in Stuttgart, Germany. That news hasn't gone down well.

Barth and Marx scoured databases owned by the Chemical Abstracts Services (CAS) and the physics and engineering abstracts service Inspec to find how interest in the field was holding up. They searched for all papers published and patents granted until the end of 2005 that involve alkaline earth cuprates containing rare earth elements. These materials show extremely low resistance to electricity at temperatures up to around −200 °C. This is much warmer than temperatures normally associated with superconductors. But nobody has been able to work out how such high-temperature superconductors work.

Barth and Marx plotted the falling number of publications over time, then extrapolated the results to predict that the number of publications on these compounds will drop to zero between 2010 and 2015 "if no ground-breaking discoveries happen to occur".

Superconductivity scientists admit the field has slowed since the flurry of research that followed Georg Bednorz and Alex Müller's 1987 Nobel prize for their discovery of ceramic high-temperature superconductors. "There was a gold rush," says Jan Zaanen of Leiden University, the Netherlands. "It's a very deep problem — all the easy things have been done."

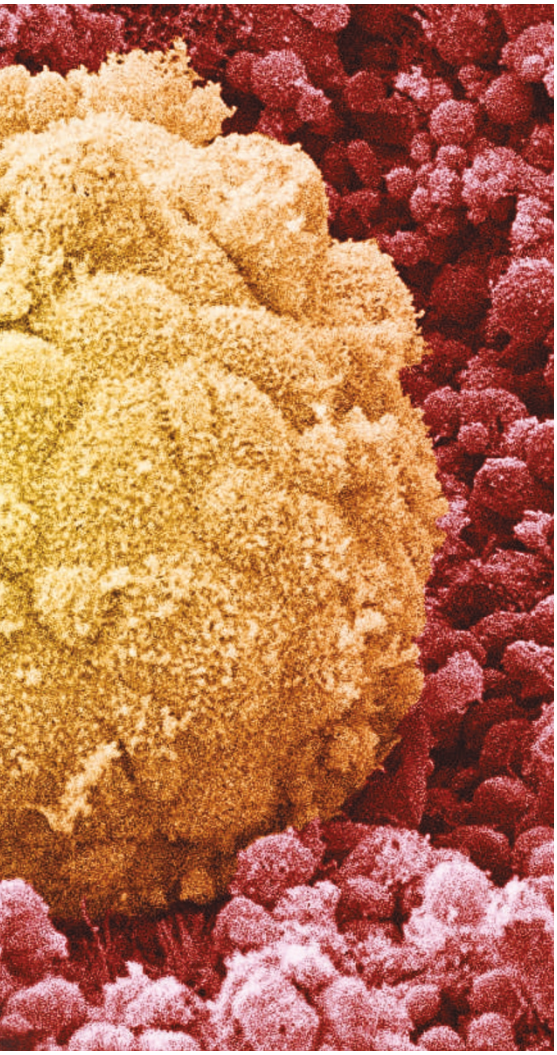
"All fields of condensed-matter physics undergo periods of ebb and flow," says Paul Grant, who has worked at IBM on high-temperature superconductors. "The general field of superconductivity is wide open."

After high-temperature superconductivity was discovered there was a huge spike in publications. Dreams of creating levitating trains, making a fortune and getting a Nobel prize for finding out how these systems work kept the field alive for a while. But as problems remained unsolved, people started to leave. "High T_c made me

©2006 Nature Publishing Group

F. ABRAHAMS/HRW

BLOGGERS RALLY OVER 'TRIPOLI SIX'
Follow the story of the medics in Libya accused of infecting children with HIV.
www.nature.com/news



Y. NIKAS/WELLCOME PHOTO LIBRARY

used different culture conditions.

The cell line from the arrested embryo seems to behave normally and can generate other tissue types, although "scientists will have lingering doubts about the 'health' of the cell line, if it's derived from a poor-quality embryo," cautions stem-cell researcher George Daley of the Children's Hospital Boston in Massachusetts.

Some stem-cell scientists are excited by Stojković's achievement. "There is no destruction of an embryo involved," says Hans Schöler, a director at the Max Planck Institute for Molecular Biomedicine in Münster, Germany. "If everything is confirmed, I don't see how anyone could attack such cell lines as unethical."

"I don't see how anyone could attack such cell lines as unethical."

But others say the technique will be dogged by ambiguity over what constitutes a dead embryo. In theory, the approach is similar to harvesting organs from dead people — but in the latter case there are clearly defined criteria for proclaiming someone irreversibly brain dead. There are no such rules for an embryo. And even the remote possibility that an embryo could revive would make this procedure unacceptable to some.

Donald Landry at Columbia University Medical Center, New York, is working to establish "ironclad" criteria to define embryo death. He and co-workers have observed 444 arrested human embryos; of these, 142 had fewer cells at the five-day mark and never developed into a normal blastocyst (D. W. Landry *et al. Regen. Med.* **1,** 367–371; 2006). "They were truly dead," he says. Landry is now planning to study embryo death at other stages of development and to find molecules that are only produced by terminally arrested embryos.

Stojković's technique is just the latest proposal for creating 'ethical' human embryonic stem cells. A recent *Nature* paper by Robert Lanza and colleagues from Advanced Cell Technology in Worcester, Massachusetts, sparked criticism after claiming to have made two such lines by taking single cells from embryos; they proved the principle, but did in fact destroy the embryos they used. Earlier this month, the body that operates the US National Stem Cell Bank agreed to distribute Lanza-style cell lines — if the federal government will fund research on them.

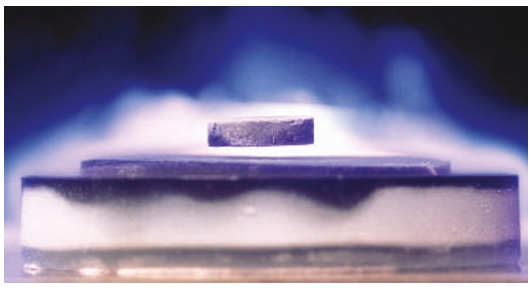
But without a change in current restrictions, most US scientists are unlikely to get their hands on 'ethical' lines. Legislation known as the Dickey Amendment prevents federal money from being spent on research that harms human embryos. Even if new techniques are deemed to leap this hurdle, President George W. Bush has banned federally funded studies on any human embryonic stem-cell lines derived after 9 August 2001.

James Battey, who heads the National Institutes of Health (NIH) Stem Cells Task Force, says the institutes won't seek legal advice on whether new lines could be funded until they receive a grant application for such work. But Landry hopes that embryonic stem cells derived from dead embryos might finally persuade the Bush administration to change its mind. "I think it would pass muster," he says. ■

Helen Pearson and Alison Abbott

feel old," says Zaanen. Only the diehards remained, he says, some of whom acquired reputations for having large egos and even making superconductivity something of a religion. Zaanen claims those egos have been toned down but says the field is still too intimidating to attract young blood.

Barth and Marx did not include such influences as these in their study. Marx says his aim was to "demonstrate the potential of databases and search systems for generating meta-information that could be interesting in a specific field". As a piece of scientometrics the work is robust, according to Paul Peters, who works at the CAS: "Given the fact that multiple sources and different approaches all indicate the same demise, I would think this is quite accurate."



D. PARKER/IMI/UNIV. BIRMINGHAM HIGH TC CONSORTIUM/SPL

A magnet levitates above a ceramic superconductor cooled by liquid nitrogen.

But he warns: "Science may prove them wrong." There are signs that high-temperature superconductivity could be having a resurgence. The US Department of Energy's basic energy sciences office recently ran a workshop on superconductivity. Pat Dehmer, the office's associate director, says: "Funding will be very seriously considered for this field," although she remains coy about revealing details before the federal budget announcement in February. A demonstration project using high-temperature superconductor wires in the US national energy grid is also starting this year.

Marx agrees that the field could revive given a breakthrough such as the discovery of superconductors that work at even higher temperatures or are in a new class of materials, or the development of a theoretical explanation of the phenomenon. He also admits that his study has limitations. "Extrapolations are always problematic," he says. "The word 'zero' is perhaps not an optimal expression here. It may be taken seriously but certainly not literally."

That doesn't stop some from taking the conclusion personally. The extrapolation is "utter nonsense" according to Zaanen. "It's a vivid illustration of the blindness of bean counting." ■

Katharine Sanderson

©2006 Nature Publishing Group