

# The New York Times

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MONDAY, OCTOBER 17, 2005



Kimimasa Mayama/Reuters

Yesterday north of Muzaffarabad, in the Pakistani-controlled part of the divided region.

## Stem Cell Test Tried on Mice Saves Embryo

### Technique Could Shift Debate on Humans

By NICHOLAS WADE

Scientists have devised two new techniques to derive embryonic stem cells in mice, one of which avoids the destruction of the embryo, a development that could have the potential to shift the grounds of the longstanding political debate about human stem cell research.

The destruction of embryos is a principal objection of anti-abortion advocates who have strenuously opposed federal financing of the research.

The second new technique manipulates embryos so they are inherently incapable of implanting in the uterus, what some see as a possible ethical advantage in the proposed therapy, which converts a patient's skin cell into embryonic cells and then new tissues to repair the body. Both methods are described in today's online edition of *Nature*.

The technique for making embryonic stem cells without compromising the embryo has yet to be adapted to people, but the two species are very similar at this level of embryonic development. "I can't think of a reason why the technique would not theoretically work in humans," said Brigid L. M. Hogan, an embryologist at Duke University.

If it does work in people, which could take many months to find out, the technique might divide the anti-abortion movement into those who accept or reject in vitro fertilization, because the objection to deriving human embryonic stem cells would come to rest on creating the embryos in the first place, not on their destruction.

"This gets around all of the ethical arguments, except for that small minority of the pro-life community that doesn't even support in vitro fertilization," said Representative Roscoe G. Bartlett, Republican of Maryland, whose Web site describes him as "a pro-life legislator."

Until now the only way of deriving human embryonic stem cells has been to break open the embryo before it implants in the uterus, a stage at which it is called a blastocyst, and take out the inner cell mass, whose cells form all the tissues in a human body.

Although the blastocysts used in the procedure are ones that fertility clinics have rejected for implantation, many opponents of abortion say the destruction of any embryo is wrong. Congress has forbidden the use of federal money for any such research, and federally supported scientists can work with only a small number of existing lines of embryonic stem cells that have been exempted by President Bush.

Robert Lanza and colleagues at Advanced Cell Technology, a biotechnology company in Worcester, Mass., have developed an alternative

## Clinic, Hurdles to Clear Before Medicaid Care

RICHARD PÉREZ-PEÑA

Rise on Burnside Avenue in the Morris Heights Health Center, a bustling storefront offering arroz and cheap clothes. The clinical medical safety net for thousands of people, many of whom are struggling.

place of solace and deliverance, just as often, futility and despair, much of it linked to Medicaid government insurance programs for the poor.

Today, the clinic sees patients like T. Shuler, a single mother who has been a Medicaid client for years — and has seen her income cut off just as often, for reasons she does not grasp. She comes to the Heights, pregnant and bare for months, to make her first attempt to enroll. Her application was rejected for mistakes; on her second try, she has all the documents she needs to satisfy New York State.

There are also people like Ronald, an asthmatic and struggling father, who embodies an uncomfortable reality for Morris Heights communities served by the clinic: He can be his own worst enemy, ignoring basic paperwork until the second time, his insurance and his medicine runs out. Thomas Howard's examina-

### PROGRAM DISORDER

On the Front Lines

tion of a fifth-grade girl lays bare another chronic problem. He has to explain to her parents that she has an irregular heartbeat, but cannot see a cardiac specialist for almost half a year. New York pays specialists poorly to participate in Medicaid, and many refuse Medicaid patients.



Andrea Mohin/The New York Times

Angel Pérez of the Bronx, with his mother, Dominga Rosario, faces a five-year wait for ear surgery.

Sixteen months spent inside Morris Heights, listening to patients, clerks, nurses, doctors and administrators, provides a stark education in Medicaid as it is lived at coarse, unpredictable ground level. Those months illuminate Medicaid's sprawling good works, and how they are undermined by inscrutable rules, daunting paperwork, human frailties and, plainly, the puzzling ways New York spends the program's billions of dollars.

For the people who turn to Morris Heights and Medicaid for care, and for those at the clinic who labor to help them, Medicaid's faults and handicaps boil down to three fundamental, dispiriting truths that strike at the heart of its lofty ambitions:

¶ People like Ms. Shuler have trouble getting health care through Medicaid because they do not understand the system, especially the enrollment process. That is one reason about one million eligible New Yorkers are not in the program, according to researchers. New York has recently made enrollment easier, yet it still demands more extensive documentation from applicants than any other state, requirements that can thwart qualified people and, according to experts across the political spectrum, do little to prevent fraud.

¶ Patients like Mr. Shinnery often

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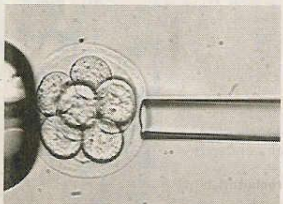
# Stem Cell Technique Tried on Mice Saves Embryo

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vide three times until it contained eight cells, a stage just before the embryo becomes a blastocyst. Removing one of these cells, they then coaxed it into growing in glassware and forming cells that have all the same essential properties as embryonic stem cells derived from the inner cell mass, Dr. Lanza's team reports.

The seven-cell embryo was implanted in the mouse uterus and grew successfully to term. This part of the procedure is known to work with humans too, because it is the basis of a well-established test known as preimplantation genetic diagnosis. In the test, one cell is removed from each of a set of embryos and tested for any of 150 genetic defects, giving the parents the choice of implanting an embryo that is disease free.

Dr. Lanza's technique is likely to be welcomed by many in the middle of the debate, although it has not won over the United States Conference of Catholic Bishops. Richard M. Doerflinger, its deputy director for pro-life activities, dismissed the tech-



Advanced Cell Technology

A mouse embryo at the eight-cell stage, shown just before a blastomere is to be extracted.

nique, saying that preimplantation genetic diagnosis itself is unethical.

The technique "is done chiefly to select out genetically imperfect embryos for discarding, and poses unknown risks of future harm even to the child allowed to be born," Mr. Doerflinger said in an e-mail message.

Only a procedure that generated embryonic stem cells without creating or destroying embryos "would address the Catholic Church's most fundamental moral objection to embryonic stem cell research as now pursued," Mr. Doerflinger said in testimony last December to the President's Council on Bioethics.

Senator Sam Brownback, a Kansas Republican and a leading pro-life advocate did not return a call to his office. Edmund D. Pellegrino, the new chairman of the President's Council on Bioethics, said through a spokeswoman that he had no comment.

But Markus Grompe, a leading stem cell scientist and a Roman Catholic who supports the church's teaching on the unacceptability of destroying embryos, praised the Lanza approach, provided that the extracted cell could not develop into an embryo by itself. "I find it clearly less objectionable than the outright destruction of the embryo," said Dr. Grompe, who studies liver stem cells at the Oregon Health and Science University.

In response to Dr. Grompe's reservation, Dr. Lanza said individual human blastomeres, as the cells are known at this stage, had never been shown to create viable embryos.

growing a culture of perfectly matching embryonic stem cells.

The cells would be available throughout the child's life for the kind of tissue and organ repair that it is hoped stem cells will one day provide. In many of the degenerative diseases of old age, from heart attacks to Parkinson's, the body loses vital cells and fails to replace them, an omission that could perhaps be overcome if embryonic cells like those present at the beginning of life were available to generate replacement cells artificially.

With the parents' consent these cells could also be used for research, providing many new embryonic stem cell lines for laboratories. The procedure might be even be offered for all embryos generated in fertility clinics when its theoretical risk has been better assessed.

"I can see a day when every fertility clinic embryo has a cell removed and banked for future tissue use or organ replacement," said Ronald M. Green, an ethicist at Dartmouth.

Children born after the preimplantation diagnosis procedure have the same incidence of birth defects as those who did not undergo the procedure. So far, after some 10 years of experience, there is no indication that it causes health problems in humans, said Andrew R. La Barbera, scientific director of the American Society for Reproductive Medicine.

If Dr. Lanza's technique succeeds in generating human embryonic stem cell lines, Dr. La Barbera said, "I suspect that indeed it will become routine to generate stem cells for everyone who undergoes preimplantation genetic diagnosis."

But Kathy Hudson, director of the Genetics and Public Policy Center at Johns Hopkins University, said there was "little data that documents the safety and efficacy" of the preimplantation diagnosis procedure, even after 2,000 births. She urged the American Society for Reproductive Medicine to create a national database to address the safety issue.

The other alternative method reported in Nature today addresses an ethical objection to therapeutic cloning, the idea of treating patients with new tissues generated from their own cells.

The cells would be obtained by taking the nucleus from a patient's skin cell and injecting it into a human egg whose nucleus had been removed. The egg develops into a blastocyst from which embryonic stem cells can be derived in the usual way. Critics say this nuclear transfer technique creates embryos only to destroy them.

To counter this objection, Alexander Meissner and Rudolf Jaenisch of the Whitehead Institute in Cambridge, Mass., have created mouse nuclear transfer embryos that are inherently incapable of implanting in the uterus. They did so by switching off a gene in the donor nucleus that is needed for the implantation process. The gene was switched back on later

**Two techniques, one that leaves an embryo viable, address ethical concerns.**

because it is needed to form the intestinal tissue



Rick Friedman for The New York Times

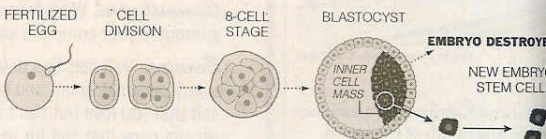
Robert Lanza and colleagues have experimented with mice to develop a technique to generate stem cells but leave the embryo viable.

## A New Way to Create Embryonic Stem Cells

In an effort to satisfy those who have moral objections, scientists have developed a new method to generate embryonic stem cells that does not destroy the embryo. One of the new methods is shown below.

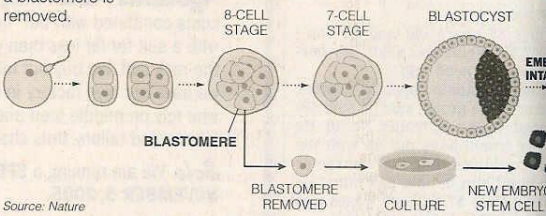
### CURRENT METHOD

1. A fertilized egg undergoes cell division, becoming a mass of cells called a blastocyst after 5 days.
2. Stem cells are taken from the inner cell mass of the blastocyst, destroying the developing embryo.



### A NEW METHOD

1. After the third division, at the 8-cell stage, a single cell called a blastomere is removed.
2. The blastomere is cultured with an established embryonic stem cell line and then separated to form new lines.
3. Because the blastocyst is left intact, the developing embryo can still be implanted in the uterus.



Source: Nature

The New York Times

be created. This is still his position, he says.

Scientists hope that alternative approaches to embryonic stem cell research may ease the political obstacles in their path, but they also wish to avoid being compelled to abandon existing approaches before new ones have been shown to work.

Irving Weissman, a stem cell biologist at Stanford, notes in a commentary in Nature that there have been calls in Congress for a moratorium on generating new stem cell lines until the two new techniques have been adapted to people, a prospect which he describes as "highly speculative."

Representative Bartlett said the Lanza method "has come at a very propitious time" because the Senate is considering various stem cell bills, including a counterpart to legislation he proposed in the House advocating

Dr. Lanza's company, Advanced Cell Technology, is well known in the cloning field, having accomplished solid achievements as well as some that veered toward the merely attention getting, like letting a human nucleus develop to very early stage in a cow's egg. The company is headed by Michael West, who as founder of Geron initiated support for the research that led to the first derivation of human embryonic cells.

It will take a lot more research and maybe several years before advanced Cell Technology and others can tell if the new method works in humans and how applicable it might be.

In preimplantation genetic diagnosis, there is very little time before the disease-free embryo must be planted in the uterus, perhaps too little to allow an embryonic stem line to be generated, as Dr. La