Can Scientists Bypass Stem Cells' Moral Minefield?

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Having already stirred bioethical controversy by fusing a human cell and a cow cell to create something resembling a hybrid embryo, scientists at a small biotechnology company in Massachusetts are again fomenting debate by proposing to create purposefully disabled embryo-like entities.

The goal is to create a developing mass of mostly human cells that's crippled enough to prevent its development into a person, yet healthy enough during the first week of existence to produce the crucial "stem cells" that scientists want to collect.

Company officials and other experts said they believe the approach may allow researchers to get around the emotional debate over the ethics of conducting research on human embryos, since the fatally flawed creations might be seen as standard laboratory-grown cells rather than as potential people.

But others are concerned that the strategy raises a serious ethical problem by making defective, mostly human embryos that are doomed to die soon after their creation.

"On the one hand you could say these types of cells are okay because they could never grow into a person, but others could say you're generating lethal mutations," said an official at the White House Office of Science and Technology Policy, speaking on the condition of anonymity. The science office will advise President Clinton on the issue.

The dilemma is part of an expanding controversy over the definition of "human," and in particular the definition of "human embryo," in an era when it has become easy to combine genes from different species and when embryos and embryo-like entities can be made in novel ways.

Michael West, president of Worcester-based Advanced Cell Technology (ACT), said he believed his approach would allow embryonic stem cell research to go forward not only at his privately financed company but also at federally funded laboratories, which are precluded by Congress from conducting human embryo research.

To ensure that the entities he's creating cannot be considered embryos, West envisions mutating the cells in advance. The trick, he said, will be to do just enough damage to preclude the cells from developing into a viable being, but not so much as to interfere with the growth of stem cells, which he hopes to harvest.

Stem cells are primitive, embryonic cells that have not yet become specialized into heart cells, brain cells or other kinds of cells. Scientists see them as a raw material from which they may grow replacement tissues in laboratory dishes, for transplantation into patients with diseases such as Parkinson's and Alzheimer's.

"We believe there are ways that technology could be engineered so as to eliminate the possibility of these [embryo-like entities] becoming a human being," West said. "There would be a lot less concern if we could assure people that these cannot grow into a person or an animal."

West's approach to getting stem cells is to combine a human skin cell and a cow's egg from which most DNA has been removed. The result is an expanding mass of cells that resembles an embryo and seems to contain the stem cells he wants. But no one knows whether that mass meets the technical definition of an embryo, since no one has transferred one to a womb to see whether it can develop into a fetus. That means one knows what the mass's moral status is.

Many cross-species hybrids made in this fashion are inherently nonviable—and so probably would not qualify as embryos—because of incompatibilities between the so-called nuclear DNA of one cell (in ACT's case, human) and remaining bits of so-called mitochondrial DNA in the other cell (in ACT's case, a cow's egg).

In experiments by Carlos Moraes at the University of Miami, for example, cells that contained a mixture of human nuclear genes and chimpanzee or gorilla mitochondria generally survived. But combinations of human DNA with mitochondria from more distant relatives such as orangutans, baboons and lemurs were not viable.

"The conclusion is, if the two species diverged more than 10 million years ago they are not going to be able to work together," Moraes said. And since humans and cows diverged an estimated 110 million years ago, he said, "it seems obvious" that ACT's combination is nonviable.

But other experiments leave open the question of a cow-human hybrid's viability.

Neal First and colleagues at the University of Wisconsin in Madison fused cow egg cells (whose nuclear DNA had been removed, but whose mitochondrial DNA remained) with cells from sheep, pigs, monkeys and rats, which contained all their nuclear DNA. In several instances the team got viable embryos, and there was no correlation with how closely related the species were. Several even grew into fetuses after being transferred to the wombs of cows, although none survived to term.

Even if further tests suggest that cow-human hybrid cells cannot grow into viable embryos—a conclusion that would allow ACT and others to grow such creations for their valuable stem cells—other problems may arise. Some scientists suspect, for example, that cow-human hybrid stem cells may not be as medically useful as completely human ones.

Indeed, West is already looking into the possibility of removing the bovine mitochondria from his cow eggs. That might make better stem cells but also would make his creations more fully human and definitively viable, with all the ethical problems that come with that.

That's why West would like to go one step further and induce specific mutations in his starter cells, so that the resulting hybrid entity has no chance of actually growing into a viable embryo but still would make healthy and medically useful stem cells.

John Fletcher, an emeritus professor of bioethics at the University of Virginia in Charlottesville, said he was optimistic about the approach, even though it could raise the issue of "wrongful life"—the controversial legal and ethical doctrine that says it is immoral to bring a fatally defective life into existence. On balance, he said, "I think it's an avenue worth pursuing."

Others, however, said they were not sure the approach would solve the problem. "Anytime you remove something from a viable cell to make it nonviable is problematic," said R. Alta Charo, a professor of law at the University of Wisconsin in Madison and a member of the National Bioethics Advisory Commission, which is preparing a report on stem cell research for Clinton. "It can be seen as killing, albeit over a long period of time."

Ultimately, Charo said, the ethics of the approach may depend on whether the mutation takes its toll before or after the earliest stages of embryo development—that is, whether there was ever a moment of potential life.

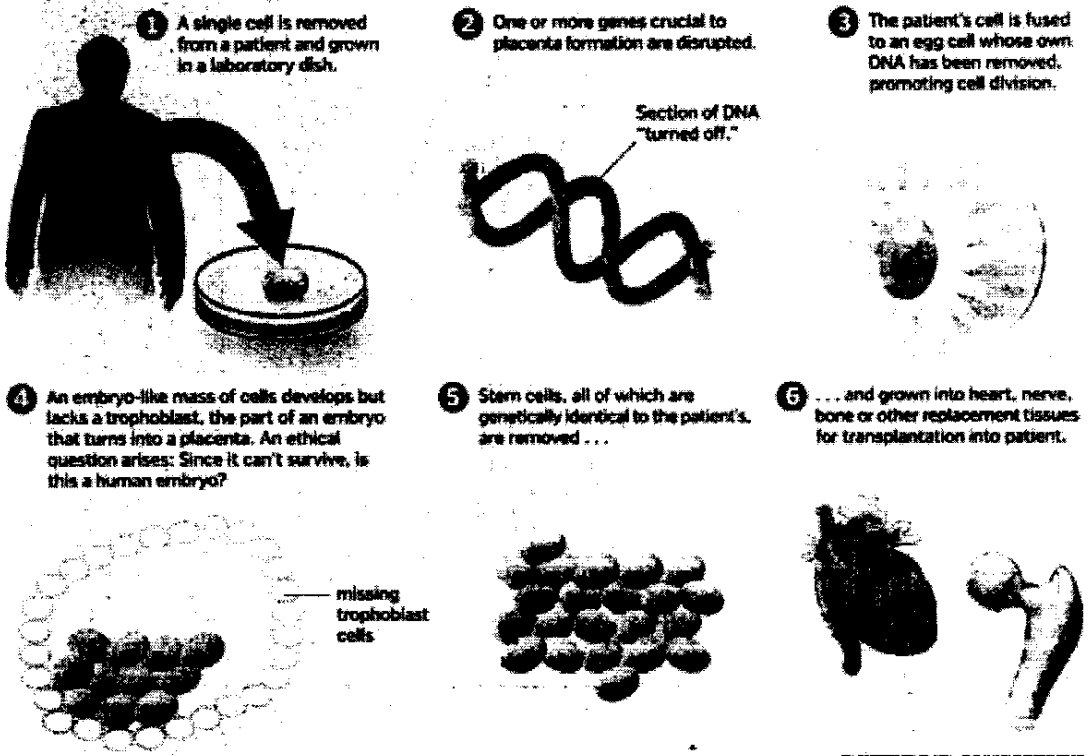
"If you engineered the cells so that they never have a chance to develop into an entity that can become a baby, but only an entity that can be useful for medical purposes, you might have avoided the problem," she said.

The bioethics commission will start its analysis of human stem cell research at its next meeting in January. It hopes to produce a final report on the topic within about six months.

Looking for an Ethical Path to Growing Human Spare Parts

Scientists are considering various ways of engineering human "pre-embryos" that have no potential to develop fully into a baby but would still produce a supply of stem cells, which could be harvested and used in new medical treatments.

One possible scenario:



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