

# Human Embryonic Stem Cells Found?

Biologists who ponder the remarkable process by which an embryo develops into an adult will long remember 1997. First came the cloning of Dolly the sheep. Now, investigators report they may have isolated for the first time human embryonic cells that have the potential to develop into muscle, blood, nerves, or any other tissue in the body.

"I feel fairly confident that they will be demonstrated to be totipotent," says John D. Gearhart of Johns Hopkins Medical Institutions in Baltimore, who described the cells at last week's International Congress of Developmental Biology in Snowbird, Utah.

With these mother cells, scientists may someday create many sorts of tissues to treat conditions such as spinal cord injuries, diabetes, leukemia, and even neurodegenerative disorders like Parkinson's disease.

In the long run, the use of the stem cells may make moot the furor over transplanting cells from aborted fetuses to relieve some of these conditions. In the short run, however, the cells may reignite the controversy, since Gearhart's group derived them from terminated pregnancies.

Like Dolly, the stem cells are also apt to trigger concern about how this scientific advance might be misused. In theory, for example, the cells could generate a human baby if properly implanted into a woman's womb.

Gearhart and other researchers stress that such a scenario is not currently achievable or even under consideration.

"To concentrate on the risks [of human embryonic stem cells] is to deny potential health benefits to a lot of people," asserts Brigid L.M. Hogan of Vanderbilt University in Nashville, who has worked with mouse embryonic stem cells.

Scientists have used such mouse stem cells for nearly a decade to create genetically altered mice. By deleting a specific gene in embryonic stem cells and injecting the altered cells into a developing embryo, scientists can create a chimera—a creature whose cells are of two distinct genetic types. With chimeras, scientists can breed progeny that lack the chosen gene. Mice made this way can mimic human diseases or reveal what proteins guide embryogenesis.

To understand the development of human embryos and to generate tissue for transplantation, several research teams had searched for human embryonic stem cells, with no success. Gearhart's group and others, following the path blazed by mouse scientists, initially tried to tease apart human blastocysts, clusters of 100 or so cells that constitute a

stage of embryonic development.

Gearhart then decided to adopt the strategy of two other research groups, one led by Hogan, that in 1992 had collected primordial germ cells, the cells that give rise to sperm or eggs. Grown under certain conditions, these mouse cells come to resemble stem cells derived from blastocysts.

Working with aborted fetuses 5 to 9 weeks old, Gearhart and his colleagues gathered primordial human germ cells and have kept some of them alive in the laboratory for more than 7 months.

The cells are shaped like mouse embryonic stem cells, carry several of the same surface proteins, and make telomerase, an enzyme thought to keep stem cells virtually immortal (SN: 11/25/95, p. 362). They can spontaneously form embryoid bodies, clusters of differentiated cells also formed by embryonic stem cells. Gearhart has found that these clusters contain various tissues, including blood cells, although he hasn't yet found every cell type.

Debate continues over whether primordial germ cells are the equivalent of blastocyst-derived stem cells. As germ cells develop into sperm or eggs, some genes receive a sex-specific chemical imprint that governs their activity during development. This imprinting may compromise the use of such germ cells as stem cells, says Hogan.

Stem cell investigators caution that Gearhart has not yet published his work. "They're obviously very interesting cell lines . . . but we don't really know their properties," says Anne L. McLaren of the University of Cambridge in England.

Before publishing their findings, Gearhart and his colleagues plan to implant the putative stem cells into mice that have no effective immune system and therefore will not reject them. At the implant sites, the cells should multiply and differentiate into a variety of cell types.

Investigators expect they will one day be able to control this differentiation.

"If these are totipotent cells, they should have the ability to form anything in the body. Basic developmental biology isn't at the point where you can direct [stem cells] into any cell type you want, but there've been tremendous strides recently," says James A. Thomson of the University of Wisconsin-Madison Regional Primate Center, who in 1995 reported isolating embryonic stem cells of monkeys (SN: 8/26/95, p. 139).

In fact, a description of progress toward generating blood stem cells from mouse embryonic stem cells followed Gearhart's talk in Utah. If similar efforts prove suc-

cessful with human embryonic stem cells, they could eliminate the use of bone marrow tissue or umbilical cord blood to treat blood disorders such as leukemia. While such tissues contain blood stem cells, the cells are rare and may not proliferate as well as those derived from embryonic cells.

Gearhart envisions altering genes of embryonic stem cells to ensure that they will not be rejected by the immune system. "We may end up with universal donor tissue," he says.

Irrespective of their medical uses, human embryonic stem cells could shine a light on such mysteries as how developing cells commit to becoming neurons or other types of cells. "There's a lot of interesting, straightforward biology that could come from them," says Hogan, noting that little is known, for example, about what genes human fetal cells use or what growth factors they secrete.

To study conditions such as Down's syndrome, Gearhart plans to use the cells as a source of chromosomes unaltered by the changes that normally occur as an organism develops.

The availability of totipotent human stem cells may offer difficult ethical issues. Instead of generating a baby via the union of sperm and egg, fertility specialists might be able to implant stem cells to create offspring.

Such a feat seemed impossible, even in mice, until 1993, when researchers combined mouse embryonic stem cells with a chromosomally abnormal mouse embryo. Before the defective embryo degenerated, it helped the stem cells implant and ultimately give rise to a new mouse by themselves, says Janet Rossant of Mount Sinai Hospital in Toronto and a member of the research team that conducted the 1993 experiment.

Bioethicist Ronald M. Green of Dartmouth College in Hanover, N.H., suggests that this year's frenzy over Dolly (SN: 4/5/97, p. 214) may temper people's reaction to news of human embryonic stem cells. While the cells could, in theory, spawn many clones, the procedure does not raise as many questions of personal identity as would the Dollylike cloning of an adult, he contends.

Gearhart himself wonders who, if anyone, will regulate the use of embryonic stem cells. Johns Hopkins University officials have already filed for patents on the cells and the procedures used to create them. One or more companies may soon buy the rights to their research, adds Gearhart, noting that the stem cell research has been conducted without any federal funding. —J. Travis