SCIENCE NEWS
This Week

Stem Cell Success

Mice fuel debate on embryo cloning

A handful of mutant mice have fired up the debate over the cloning of human embryos to produce cells for medical use. After genetically engineering cells that had been generated by cloning mouse embryos, investigators have partially repaired the defective immune system of these animals.

The two new studies, which will appear in an upcoming *Cell*, represent the first evidence that the strategy dubbed therapeutic cloning could someday provide sick people with genetically matched cells, tissues, or organs, say the researchers. "We felt we needed to put some evidence on the table that this could indeed work," says William M. Rideout III of the Whitehead Institute of Biomedical Research in Cambridge, Mass., a coauthor of one study.

Yet a rival researcher openly challenges the significance of the experiments. "This does not address the issue of whether therapeutic cloning will work or not," argues Robert Lanza of Advanced Cell Technologies in Worcester, Mass. His company recently claimed to have cloned human embryos as a first step toward therapeutic cloning (*SN: 12/1/01, p. 341*).

A more favorable assessment of the mouse work comes from Irving Weissman of Stanford University, who recently chaired a national advisory panel that called for continued work on therapeutic cloning but a ban on cloning intended to create babies (*SN: 1/26/02, p. 52*). Noting that the mouse experiments offer the first evidence in a scientific journal that cloned stem cells can be therapeutic, he says the reports "should completely change the tenor of the debate."

The debate to which Weissman refers concerns the bill introduced by Sen. Sam Brownback (R-Kan.) and Sen. Mary Landrieu (D-La.) that would ban the cloning of human embryos to produce either a baby or tissues for transplantation. Since the House of Representatives has passed a similar bill, and President Bush supports the legislation, approval of the Brownback-Landrieu bill would effectively outlaw human therapeutic cloning.

Some scientists argue that such research will simply continue in countries with less restrictive policies. In fact, the Wall Street Journal recently reported that investigators in China have cloned human embryos to derive stem cells.

Therapeutic cloning, in theory, offers patients lab-grown replacement cells that won't be rejected by their immune system. For example, a woman with diabetes might receive insulin-secreting islet cells cloned from her own body and therefore genetically identical to the rest of her cells. Such transplants could preclude the need for immune-suppressing drugs.

The Whitehead Institute researchers tested therapeutic cloning on mice that have a gene mutation leaving them unable to make immune cells known as T and B cells. A small number of people have similar conditions, which leave them vulnerable to infections. In the cloning step of the experiment, the scientists clipped cells from the tail of one mouse and implanted its DNA into another mouse's eggs, which they had stripped of DNA. They then stimulated the eggs into dividing to the embryonic stage from which they could extract so-called stem cells, which can develop into any tissue.

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The scientists then repaired the original mouse's genetic defect in the stem cells and allowed the cells to mature until the team could isolate ones with blood-forming properties similar to bone marrow of adults. "What we were looking to achieve [in the mice] was the equivalent of a bone marrow transplant without any of the rejection problems," says Rideout.

Next, the researchers added to the stem cells a gene called *HoxB4*. Experiments conducted by a Whitehead Institute team led by George Daley had shown that the activity of this gene helps such cells survive after being transplanted.

Finally, the investigators transferred the cells into mice with the same immune defect that the original mice had. The animals are all from the same inbred line, so their genes are virtually identical. The expectation was that the transplanted cells would produce normal blood cells, including the missing T and B cells. The plan did not work at first. "Even though the cells were genetically identical [to the recipients'], they were being rejected," says Daley.

He, Rideout, and their colleagues ultimately concluded that the cells before transplantation hadn't matured enough to sport the proper identifying proteins, so some immune cells of the host mice attacked the transplanted cells as foreign. By performing the same experiments in mice in which those patrolling immune cells were absent or suppressed, the investigators finally were able to get the transplanted cells to take hold and produce new T and B cells.

The researchers estimate that they restored only about 5 percent of a mouse's normal T and B cell function. "It does not rise to the level of a cure," says Daley. "That's for the future."

"As in most areas of biology, the first results, although definitive, are not as robust as one would take to the clinic," agrees Weissman.

Lanza takes a harsher view. Since the mice used are inbred, and, in his opinion, don't have a particularly sophisticated immune system to begin with, he argues that the experiments didn't actually test whether therapeutic cloning creates tissue that avoids rejection. "The real challenge is to get things to work in large animals with sophisticated immune systems similar to a human's," he says.

Several newspapers have reported that Advanced Cell Technologies has used therapeutic cloning to derive bovine stem cells and create kidneys that it has transplanted into adult cows. Lanza confirmed those reports but declined to offer any further details, noting that the company planned to publish its results soon.
—J. TRAVIS

Telescope Tuned Up

Back to work for orbiting observatory

A rejuvenated Hubble Space Telescope floated away from the space shuttle Columbia on Saturday, March 9, after astronauts spent a week renovating the observatory.

Columbia's crew began the mission March 1. Despite a problem with the shuttle's cooling system early on, the trip progressed as planned, and Columbia's robotic arm clamped onto Hubble last Sunday.

Over the next 5 days, four astronauts performed 36 grueling hours of space walks to replace worn components and add new devices (*SN: 3/2/02, p. 132*).

The most crucial task was to replace Hubble's power-control unit, which had lost some of its capacity. The unit hadn't been designed to be removable, says Holland Ford of the John Hopkins University in Baltimore. The procedure required shutting Hubble's power off for the first time in its 12-year history.