Researchers Create New Rat Heart in Lab

By LAWRENCE K. ALTMAN
Published: January 13, 2008

Medicine's dream of growing new human hearts and other organs to repair or replace damaged ones received a significant boost on Sunday when University of Minnesota researchers reported success in creating a beating rat heart in a laboratory.

Experts not involved in the Minnesota work called it "a landmark achievement" and "a stunning" advance. But they and the Minnesota researchers cautioned that the dream, if it is ever realized, is still at least 10 years away.

Dr. Doris A. Taylor, the head of the team that created the rat heart, said that she followed a guiding principle of her laboratory — "give nature the tools and get out of the way."

"We just took nature's own building blocks to build a new organ," Dr. Taylor said of her team's report in the journal, Nature Medicine.

The researchers removed all the cells from a dead rat heart, leaving the valves and outer structure as scaffolding for new heart cells injected from newborn rats. Within two weeks, the new cells formed a new beating heart that conducted electrical impulses and pumped a small amount of blood.

With modifications, scientists should be able to grow a new human heart by taking stem cells from a patient's bone marrow and placing them in a cadaver heart that's been prepared as a scaffold, Dr. Taylor said in a telephone interview from her laboratory in Minneapolis. The early success "opens the door to this notion that you can make any organ: kidney, liver, lung, pancreas — you name it and we hope we can make it," she said.

"Doris Taylor's work is one of those maddeningly simple ideas that you knock yourself on the head, saying why didn't I think of that," said Todd N. McAllister, of Cytograft Tissue Engineering of Novato, Calif. His team has used a snippet of a patient's skin to grow blood vessels in a laboratory and then implanted them to restore blood flow around a patient's damaged arteries and veins.

The field of tissue engineering has been growing rapidly. For many years, doctors have used engineered skin for burn patients. Engineered cartilage is used for joint repairs. Researchers are investigating use of stem cells to repair cardiac muscle damaged by heart attacks. Also, new bladders grown from a patient's own cells are being tested in the same patients.

Dr. Taylor is a newcomer to tissue regeneration. She began her professional career at the Albert Einstein Medical School in the Bronx investigating gene therapy and then cell therapy. She said she switched to tissue regeneration when she realized the limiting step in trying to generate an organ was not the number of cells needed, but the complexity of creating a three-dimensional structure.

“The heart is a beautiful organ, and it’s not one that I thought I’d ever be able to build in a dish,” Dr. Taylor said.

Her view changed about three years ago when she recalled that cells are removed from human and pig heart valves before they are used to replace damaged human ones. As she contemplated replacing the old rat cells with new ones, Dr. Taylor followed another of her mantras: “trust your crazy ideas.”

Progress came in fits and starts. “We made every mistake known, did every experiment wrong and had to go back and do them right,” Dr. Taylor said.

She poured detergents like those in shampoos in the rat’s arteries to wash out the heart cells and then injected neonatal cardiac cells. The first two detergents she tested failed. But a third concoction led to a clear, translucent scaffold that retained the heart’s architecture.

After injecting the young rat heart cells into a scaffold, she stimulated them electrically and created an artificial circulation as the equivalent of blood pressure to make the heart pump and produce a pulse. The steps also helped the cells mature. Tests like examining slices of the heart under a microscope showed they were living cells.

To test the biological compatibility of the new hearts, the team transplanted them into the abdomen of unrelated live rats. The hearts were not immediately rejected. A blood supply developed. The hearts beat regularly. And cells from the host rats moved in and began to re-line the blood vessels, even growing in the wall of the hearts.

Dr. Taylor is now conducting similar experiments on pigs as a step toward human work. “Working out the details in a pig heart made a lot more sense” because the anatomy of the porcine heart is the closest to humans and pigs are plentiful, she said.

“The next goal will be to see if we can get the heart to pump strongly enough and become mature enough that we can use it to keep an animal alive” in a replacement transplant, Dr. Taylor said.

As for human hearts, the best-case scenario would be to obtain them from cadavers, remove their cells to make a scaffold and then inject bone marrow, muscle or young cardiac cells from a patient. The process of repopulating the scaffold with new cells would take a few months, she said.

The body continually replaces its proteins every few months, so the hope is that the body will create a matrix that it recognizes as its own.

One potential problem is that anti-rejection drugs might be required to prevent adverse immune reactions from the scaffold. In that case, Dr. Taylor hopes such therapy would be needed only temporarily.

Many things that work in experiments on animals fail in humans because of the species barrier. Dr. McAllister said that in Dr. Taylor’s case “the principal problem in escalating it to humans is one of scale, not of cell biology, and that is an easier problem to solve potentially.”

“If it works, it means that there’ll be many more organs available for transplants,” Dr. Taylor said.

Because the components of the biologic matrix differ for every organ, Dr. Taylor expects that scientists will be able to do tests to answer two fundamental questions: Can a stem cell be placed anywhere in the body and still produce a heart, kidney or other organ? Or must a stem cell be placed in its anatomic position to do so?

Such tests might include taking stem cells from one organ, say a kidney, and putting them in a kidney, liver or heart to begin to understand if the stem cells are innately committed to produce kidneys or whether they will convert to produce livers or hearts.

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