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## **Stem cell transplant advance 'thrilling'**

*U.S. scientists use embryonic tissue from humans to repair hearts in rats*

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In a major scientific advance, U.S. researchers have used human embryonic stem cells to repair damaged heart tissue in rats that had suffered cardiac arrests.

The "thrilling" accomplishment, released in a study yesterday, seems to overcome two of the most persistent and perplexing hurdles that have thwarted use of the promising embryonic cells for organ repair.

"One was how to coax the human embryonic stem cell to turn into (heart) cells," says Dr. Charles Murry, director of cardiovascular biology at the University of Washington's Institute for Stem Cell and Regenerative Medicine. The other was to keep them alive after transplantation.

"Embryonic stem cells can turn into hundreds of different cell types and the trick was to turn them into the cell type of interest, to the exclusion of all this other stuff. It's like getting the roulette ball to go into the right slot in the wheel."

The study was published yesterday in the journal *Nature Biotechnology*.

Janet Rossant, deputy scientific director of the non-profit Canadian Stem Cell Network, says the ability to make large numbers of heart cells and to have them live after transplant "are big steps forward."

But Rossant, a scientist with the federal funding agency Canadian Institutes of Health Research, says the paper has not shown that the implanted heart tissue is functioning as existing tissue would, or that the new cells will survive in the long term.

"There's still a lot of questions remaining before taking that forward to therapy," she says. "But it's certainly an interesting step forward."

Embryonic stem cells appear soon after conception and can transform themselves into any tissue in the body.

The study authors also created a concoction of compounds that helped the newly created heart cells survive once they'd been transplanted into the damaged rat organs.

Typically, new cardiac cells died after past implantations, due to inflammation, the lack of a vascular network to feed them and their inability to integrate with existing organ tissues.

"We used to just squirt them (the cells) in a saline solution and say, 'See you boys,' and hope for the best," Murry says. "That was pretty dismal."

After 18 months of work, Murry's team came up with a cocktail of six ingredients that would allow the new cells to take root and thrive once they'd been injected into the damaged hearts.

The concoction included a cellular glue-like substance – known as Matrigel – that allowed the new cells to attach themselves to the existing heart tissue.

In the past, failure to properly attach meant transplanted cells did not receive the "survival signals" that are passed via different messenger enzymes between their connected counterparts.

The "pro-survival cocktail," which was injected into the heart along with the cells, also included compounds that shovelled energy to the implanted cells and protected them against the harsh, inflammatory environment that exists after a heart attack.

But coaxing the embryonic stem cells to become heart cells in the first place involved an entirely different bag of tricks.

Sifting through a slew of biochemical factors that were known to be involved in heart formation, researchers came up with a formula that greatly increased the yield of heart tissue from the stem cells.

"Typically one tenth of 1 per cent of the (stem) cells would make heart muscle, maybe 1 per cent on a really good day," Murry says. "Now we're getting 38 to 50 per cent of the cells turning into heart muscle."

In total, the combined procedures increased the proportion of successful cell grafts from 15 per cent to 100 per cent in the rodents, who went through lab-induced heart attacks.

The size of those grafts went from "tiny clusters of cells" under the old methods to upwards of 10 per cent of the damaged heart region under the new.

Murry hopes to bring the research into clinical human trials within three years, but will test it on pigs or other large mammals first.

He says it may have applications for stem cell therapies on other organs that have similar production and transplantation hurdles.

"The problem with cell death in cell transplantation (for example) is something that has plagued repair of all solid tissues so far," Murry says. "It's our hope that this will be useful outside of the heart as well."