A new way to fix a broken heart?

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Researchers seem to have identified a new way to fix a broken heart, a report says.

The scientists have devised a method to coax heart muscle cells into reentering the cell cycle, allowing the mature adult cells to divide and regenerate healthy heart tissue after a heart attack, according to mouse and rat studies described in the July 24 issue of the journal *Cell*.

The key ingredient is a growth factor known as neuregulin 1. The researchers suggest that the factor might one day be used to treat failing human hearts.

"To my knowledge, this is the first regenerative therapy that may be applicable in a systemic way," said Bernhard Kühn of Children's Hospital Boston and Harvard Medical School. For instance, he added, people might one day go to the clinic for daily infusions of the substance over a period of weeks.

"In principle, there is nothing to preclude this going into the clinic. Based on the all the information we have, this is a promising candidate." He emphasized, however, that further studies would be required to demonstrate safety before such treatment could be tested in human patients.

The heart had long been considered an organ largely incapable of repairing itself. Heart muscle cells, also known as cardiomyocytes, do proliferate during prenatal development. Soon after birth, however, the cells become binucleate, meaning that they have two nuclei, and withdraw from the cell cycle, giving rise to the notion that adult cardiomyocytes are incapable of further proliferation.

However, recent evidence has shown that adult heart muscle cells can replace themselves at some low level, with perhaps half of the cells in the heart turning over in the course of a lifetime, Kühn said. The new study offers various lines of evidence for this turnover ability – including video of the cells in action – and indicates neuregulin 1 can ramp up the process.

In the new study, the researchers first tested the ability of various molecules to spur cell division in cultured cardiomyocytes. If cardiomyocytes are to reenter the cell cycle along the border zone of injury, the researchers surmised that there must be an chemical signal that triggers the response, Kühn explained.

They looked to several factors known to drive cardiomyocyte proliferation during prenatal development. Of those, neuregulin 1 had the most significant effect, inducing the division of those cardiomyocytes with one nucleus instead of two.

By manipulating neuregulin 1 levels, the scientists said they showed they could increase or decrease cardiomyocyte proliferation in living animals. Moreover, injecting neuregulin 1 in adult mice sparked cardiomyocyte cell-cycle activity and promoted the regeneration of heart muscle, leading to improved function after the animals suffered a heart attack. The regeneration could not be traced to progenitor cells, the researchers said.

The scientists added that they aren't sure whether neuregulin 1 is responsible for the natural repair process, but their findings show that it clearly can enhance it. They also note

that neuregulin 1 and its receptor, or molecular “gateway” facilitating its transmission and use, are always present in the adult heart, though it is not clear if they are in the right place or in sufficient quantities.

Before making the leap to the clinic, Kühn’s group plans to further explore how the treatment works at the fundamental level. They will also examine the response in pigs, which have more in common with humans than rodents do. Ultimately, such a treatment might serve as a useful alternative or complement to treatments designed to seed damaged hearts with regenerative stem cells, Kühn said.