Scientists reverse advanced heart failure in an animal model

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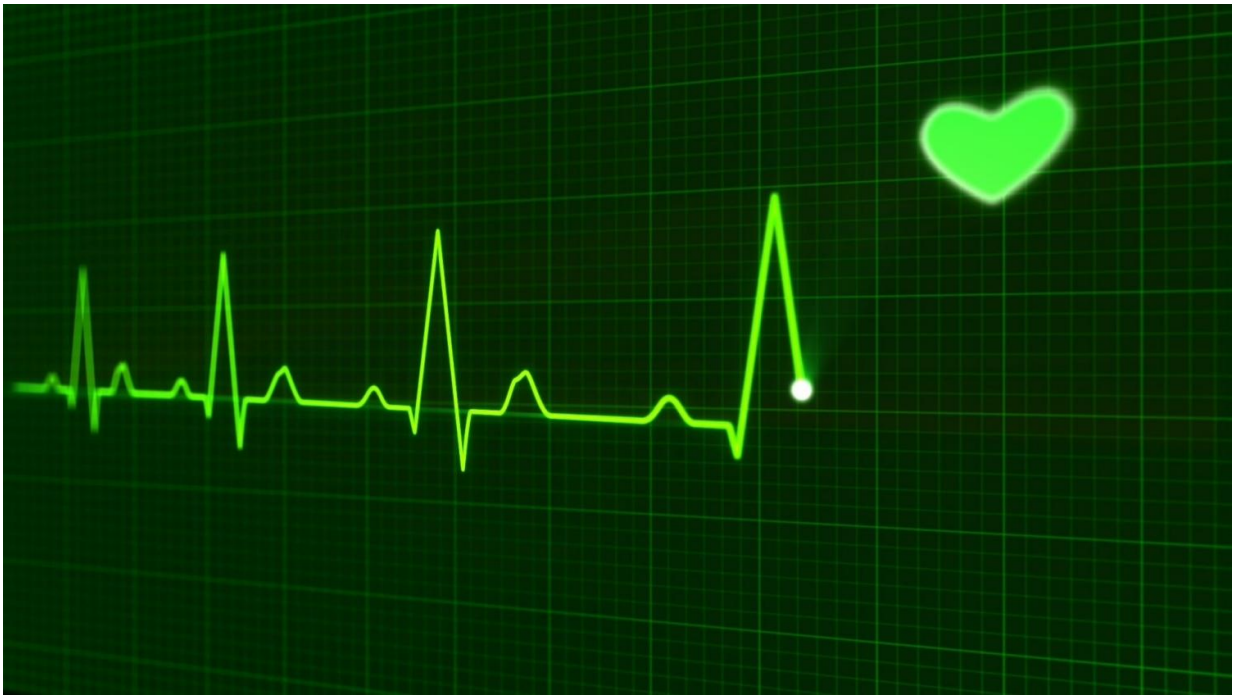

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Researchers have discovered a previously unrecognized healing capacity of the heart. In a mouse model, they were able to reverse severe heart failure by silencing the activity of Hippo, a signaling pathway that can prevent the regeneration of heart muscle. The study appears in the journal *Nature*.

"Heart failure remains the leading cause of mortality from heart disease. The best current treatment for this condition is implantation of a ventricular assist device or a heart transplant, but the number of hearts available for transplant is limited," said corresponding author Dr. James Martin, professor and Vivian L. Smith Chair in Regenerative Medicine at Baylor College of Medicine and director of the Cardiomyocyte Renewal Lab at the Texas Heart Institute.

During a heart attack, blood stops flowing into the heart; starved for oxygen, part of the heart muscle dies. The heart muscle does not regenerate; instead it replaces dead tissue with scars made of cells called fibroblasts that do not help the heart pump. The heart progressively weakens; most people who had a severe heart attack will develop heat failure.

"One of the interests of my lab is to develop ways to heal heart muscle by studying pathways involved in heart development and regeneration," Martin said. "In this study, we investigated the Hippo pathway, which is known from my lab's previous studies to prevent adult heart muscle cell proliferation and regeneration."

"When patients are in heart failure there is an increase in the activity of the Hippo pathway," said first author John Leach, a graduate student of molecular physiology and biophysics in the Martin lab. "This led us to think that if we could turn Hippo off, then we might be able to induce improvement in heart function."

Encouraging results

"We designed a mouse model to mimic the human condition of advanced heart failure," Leach said. "Once we reproduced a severe stage of injury in the mouse heart, we inhibited the Hippo pathway. After six weeks we observed that the injured hearts had recovered their pumping

function to the level of the control, healthy hearts."

The researchers think the effect of turning Hippo off is two-fold. On one side, it induces heart muscle cells to proliferate and survive in the injured heart, and on the other side, it induces an alteration of the fibrosis. Further studies are going to be needed to elucidate the changes observed in fibrosis.

More information: Hippo pathway deficiency reverses systolic heart failure after infarction, *Nature* (2017). DOI: 10.1038/nature24045

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