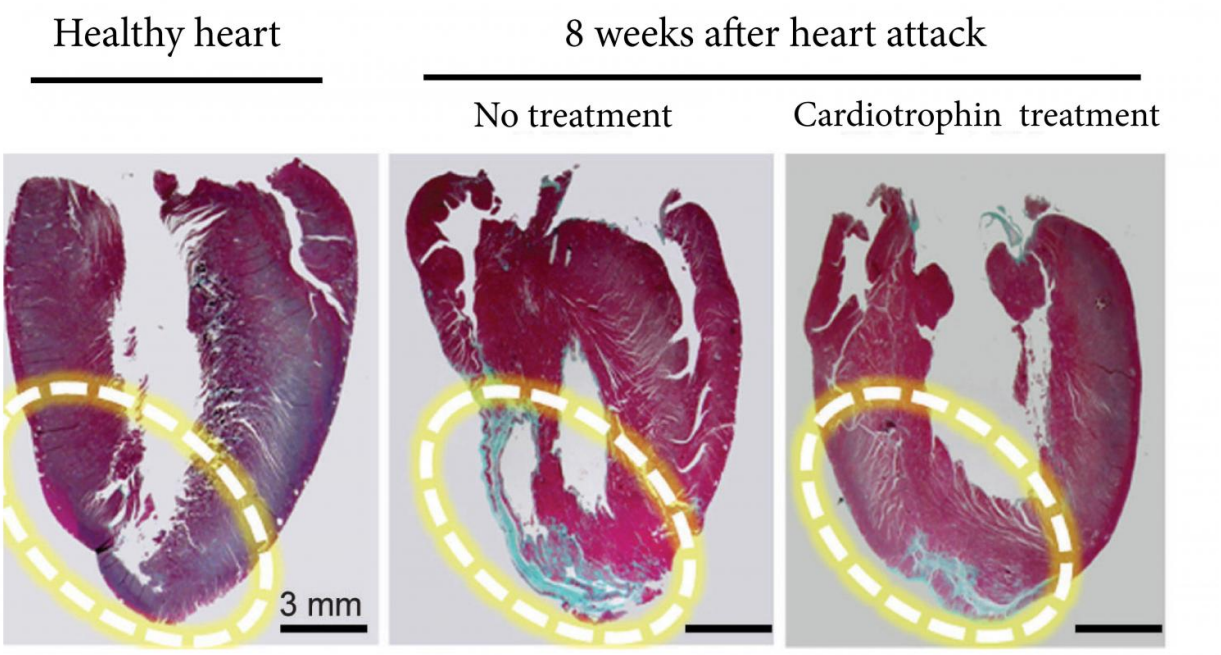
How to trick your heart into thinking you exercise

August 8 2017



The far right image shows how a cardiotrophin treatment repaired heart muscle after a heart attack in a rat model. The blue areas are scar tissue and the red sections are healthy heart muscle. Credit: *Cell Research*

Researchers have discovered that a protein called cardiotrophin 1 (CT1) can trick the heart into growing in a healthy way and pumping more blood, just as it does in response to exercise and pregnancy. They show that this good kind of heart growth is very different from the harmful

enlargement of the heart that occurs during heart failure. They also show that CT1 can repair heart damage and improve blood flow in animal models of heart failure. The results are published in *Cell Research*. The research team is from The Ottawa Hospital, the University of Ottawa, the University of Ottawa Heart Institute and Carleton University.

Heart failure is a leading cause of death and disability in high-income countries and a growing problem around the world. It occurs when the heart can't pump enough blood through the body, often because a heart attack has damaged the heart muscle tissue.

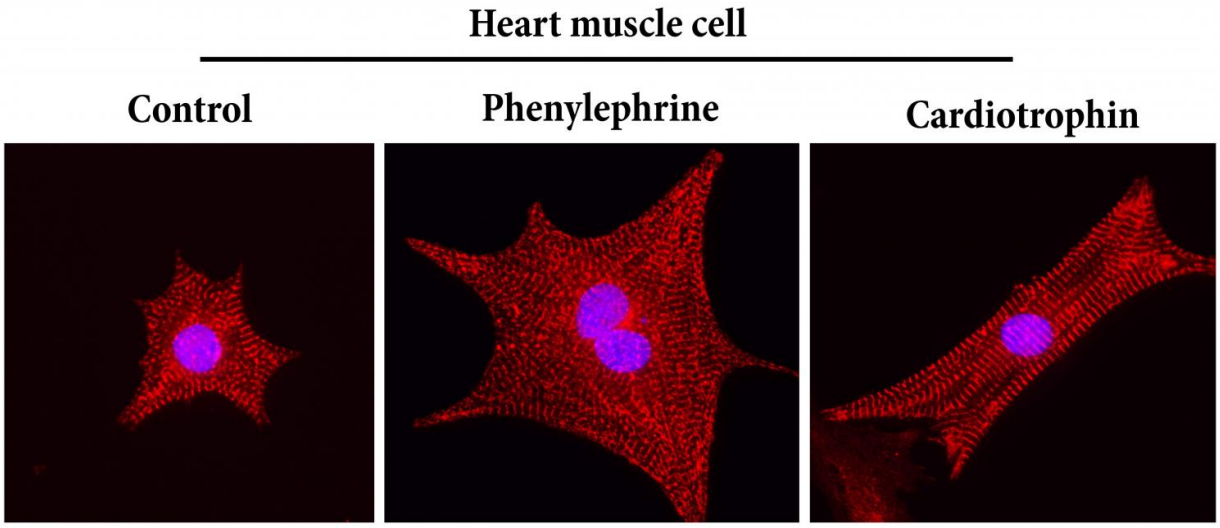
"When part of the heart dies, the remaining muscles try to adapt by getting bigger, but this happens in a dysfunctional way and it doesn't actually help the heart pump more blood," said Dr. Lynn Megeney, senior author of the study and a senior scientist at The Ottawa Hospital and professor at the University of Ottawa. "We found that CT1 causes heart muscles to grow in a more healthy way and it also stimulates blood vessel growth in the heart. This actually increases the heart's ability to pump blood, just like what you would see with exercise and pregnancy."

Dr. Megeney and his colleagues conducted a variety of studies in mice, rats and cells growing in the lab. In addition to CT-1, some of the studies involved a drug called phenylephrine (PE), which is known to cause the bad kind of heart growth. They found:

- Heart muscle cells treated with CT-1 become longer, healthier fibres, while those treated with PE just grow wider.
- CT-1 causes blood vessels to grow alongside the new heart muscle tissue and increases the heart's ability to pump blood, while PE does neither.
- When CT-1 treatment stops, the heart goes back to its original condition, just like it does when exercise or pregnancy end. However, the dysfunctional heart growth caused by PE is

irreversible.

- CT-1 dramatically improves heart function in two animal models of heart failure - one caused by a heart attack (affecting the left side of the heart) and one caused by high blood pressure in the lungs (pulmonary hypertension, affecting the right side of the heart).
- Both CT-1 and PE stimulate heart muscle growth through a molecular pathway that has traditionally been associated with promoting cell suicide (apoptosis), but CT-1 has a better ability to control this pathway.



Cardiotrophin 1 stimulates a good kind of heart muscle growth, generating long healthy fibres (right panel). Heart disease causes an unhealthy kind of heart muscle growth, similar to what is seen with phenylephrine treatment (middle panel). Credit: *Cell Research*

"This experimental therapy is very exciting, particularly because it shows

promise in treating both left and right heart failure," said Dr. Duncan Stewart, a cardiologist, senior scientist and co-senior author on the paper who is also Executive Vice-President of Research at The Ottawa Hospital and a professor at the University of Ottawa. "Currently, the only treatment for right heart failure is a transplant. And although we have drugs that can reduce the symptoms of left heart failure, we can't fix the problem, and left heart failure often leads to right heart failure over time."

"An intriguing aspect of this research was how human CT1 was able to promote a healthy growth response in multiple animal models," said co-author Dr. Patrick Burgon, scientist at the University of Ottawa Heart Institute and assistant professor at the University of Ottawa. "This suggests the action of CT1 is universally conserved and puts us much closer to therapy."

The researchers also note that while exercise could theoretically have the same benefits as CT-1, people with heart failure are usually limited in their ability to exercise.

Dr. Megeney and Dr. Stewart have patents pending for the use of CT-1 to treat heart conditions and they hope to develop partnerships to test this protein in patients. If this testing is successful it will take a number of years for the treatment to become widely available.

More information: Mohammad Abdul-Ghani et al. Cardiotrophin 1 stimulates beneficial myogenic and vascular remodeling of the heart, *Cell Research* (2017). DOI: 10.1038/cr.2017.87

Provided by Ottawa Hospital Research Institute