Reprogramming heart muscle cells to repair damage from heart attacks

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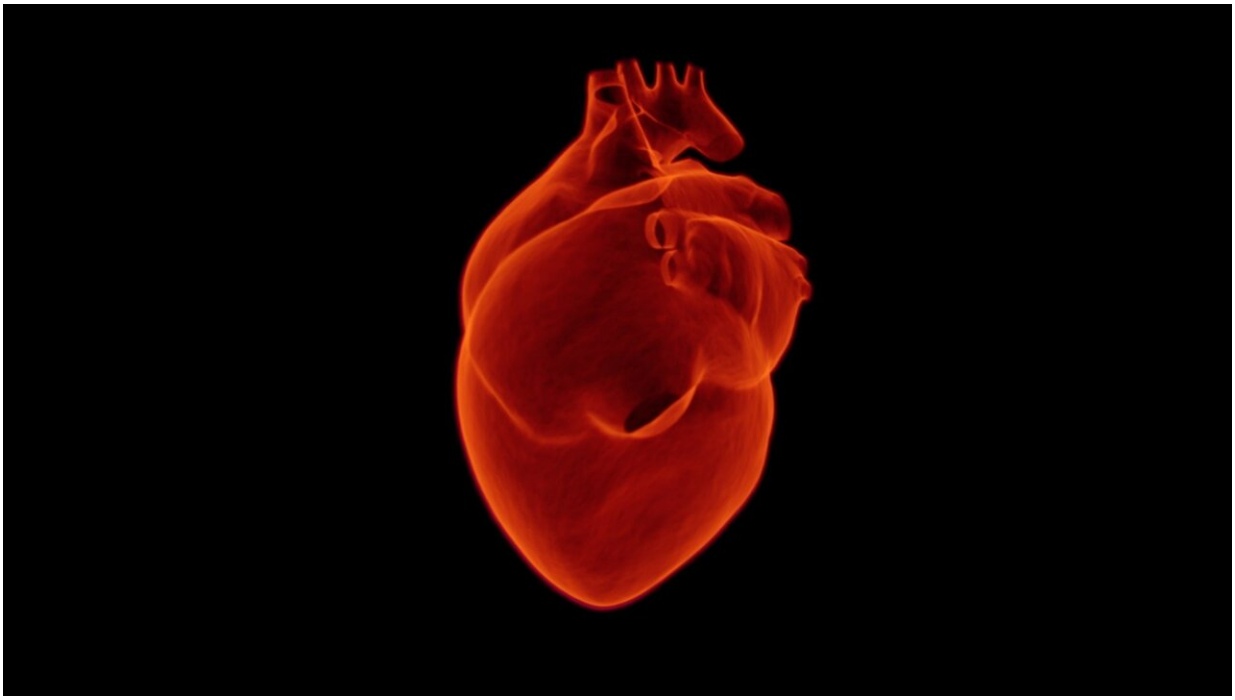

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A team of researchers affiliated with several institutions in Germany and one in Canada has found that it is possible to reprogram heart muscle to repair damaged tissue. In their paper published in the journal *Science*, the group describes their approach to repairing damaged hearts in mice and how well it worked when tested.

There are two main kinds of heart attack. The first occurs when something prevents the heart from beating. The second occurs when blood flow is restricted to parts of the heart, preventing the muscle in that area from beating. The first kind is generally fatal unless the heart can be restarted very quickly. The second is generally less serious, but can leave permanent, debilitating scarring. In this new effort, the researchers have found a way to prevent such scarring—at least in mice.

The work built on prior research that showed that in the case of a baby experiencing heart damage in utero, the heart can repair itself because the cardiomyocyte cells are in a state that allows rejuvenation. This is not the case after birth or later in life, as the cardiomyocytes have no ability to regenerate. After several years of effort, the researchers discovered a way to get adult cardiomyocytes to revert back to fetal-like cardiomyocytes by reprogramming them using the Yamanaka factors c-Myc, Klf4, Sox2 and Oct4. Their research showed that such factors express for cell renewal. The reprogramming also featured an on/off switch using the antibiotic doxycycline.

The researchers then tested their approach by giving mice with reprogrammed cells doxycycline just prior to and after inducing heart damage. They found that under both scenarios, heart regeneration occurred along with heart function improvement. The researchers also tried giving similar test mice doxycycline six days after experiencing heart damage and found it had no impact. Thus, the window of repair is short. Further testing also showed that if doxycycline was administered for too long a period, cancerous tumors developed. Much more work is required to determine if a similar approach might work for humans, and if it can be done without increasing the risk of cancer.

More information: Yanpu Chen et al, Reversible reprogramming of cardiomyocytes to a fetal state drives heart regeneration in mice, *Science* (2021). DOI: 10.1126/science.abg5159