

UW-Madison: Metabolic switch may regenerate heart muscle following heart attack

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MADISON – Research from the University of Wisconsin-Madison finds that a new therapeutic approach for heart failure could help restore cardiac function by regenerating heart muscle.

In a study recently published in the journal *Circulation*, the UW team describes its success in improving, in a mouse model, the function of heart muscle by temporarily blocking a key metabolic enzyme after a heart attack. This simple intervention, the researchers say, could ultimately help people regain cardiac function.

“Our goal was to gain new understanding of how the heart can heal itself following injury at the molecular and cellular level and see if there was a way to restore cardiac function to an earlier state,” says UW-Madison’s Ahmed Mahmoud, professor of cell and regenerative biology in the School of Medicine and Public Health. “We know that a metabolic switch occurs in the heart following birth, which contributes to the loss of capacity for cardiac regeneration. But we didn’t know which mechanisms regulate that metabolic switch. So that’s where we started our research.”

That metabolic switch involves a change to the way in which cells produce energy, transitioning from a process called glycolysis to one called oxidative phosphorylation.

Earlier studies showed that a metabolic compound called succinate, produced by cells, can accumulate in the heart when it’s deprived of oxygen, such as during a

heart attack. This can trigger a cascade of events that leads to the production of harmful molecules, called reactive oxygen species, that can damage heart cells.

Previous studies also showed that blocking another cellular compound, succinate dehydrogenase, could prevent the accumulation of succinate and subsequent damage. Inhibiting the compound can also prompt a metabolic shift in cells to glycolysis, which promotes heart regeneration.

Mahmoud's team investigated whether they could alter this metabolic switch and preserve the ability of the heart to regenerate following damage. First, they focused on succinate, which in newborn mice reduced the regeneration of new heart cells and caused DNA damage following myocardial infarction.

Then, in young mice, the research team used a metabolite called malonate, which blocks succinate dehydrogenase, to see if it would preserve the capacity of heart cells to regenerate following a heart attack. The treatment not only resulted in complete heart regeneration, it also restored heart function.

STORY CONTINUES AT <https://news.wisc.edu/metabolic-switch-may-regenerate-heart-muscle-following-heart-attack/>