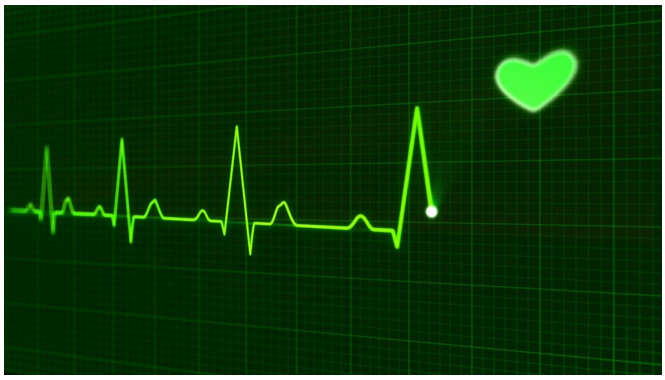
Compound identified that improves heart function in rats

28 January 2019, by Mandy Erickson



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Heart attack survivors may think the worst is behind them. But many later develop heart failure, a progressive disease marked by shortness of breath and swelling in the legs. Symptoms can prevent patients from working, exercising—even picking up grandchildren.

Heart failure occurs after a heart attack when enough of the heart muscle dies, causing the rest of the heart to overwork, which leads to more damage. To protect an overworked, failure-prone heart, cardiologists typically prescribe medications that encourage the heart to take it easy, said Daria Mochly-Rosen, Ph.D., professor of chemical and systems biology and the George D. Smith Professor in Translational Medicine.

Mochly-Rosen is hoping to tackle heart failure at the molecular level. She and her colleagues developed a compound that in preliminary tests appeared to improve heart function in rats with heart failure caused by a heart attack.

The study was published Jan. 18 in *Nature Communications*. Julio Ferreira, Ph.D., a professor at the University of Sao Paulo, is the lead author.

One contributor to heart failure following a heart attack is the accumulation of broken or dysfunctional mitochondria, the small organelles in cells that produce energy. The researchers identified a pair of proteins that, when bonded, gum up the normal activity of mitochondria and contribute to heart failure. One of those proteins, protein kinase C beta 2, is found in higher levels in failing human and rodent hearts.

The researchers tapped their chemistry know-how to develop a compound called SAM?A (pronounced "samba"), which can prevent these proteins from bonding, thereby improving mitochondrial function and providing more energy for the heart.

In tests, post-heart-attack rats that developed heart failure and were treated with SAM?A had better cardiac function—measured by how well their left heart ventricles pumped blood with each heart beat—than rats that weren't treated with SAM?A.

"We greatly improved their hearts," Mochly-Rosen said. "If humans are going to be like rats, perhaps we can treat them with a drug that prevents this deterioration."

She added that they also gave healthy rats doses of SAM?A "and it had absolutely no effect," an indication that the compound is nontoxic.

Mochly-Rosen and Ferreira suspect that SAM?A will also be effective in humans. If so, it has the potential to be developed into a drug for human heart attack patients, they believe.

"I'm hopeful SAM?A will be accepted by the industry for drug development because it appears very promising," Mochly-Rosen said.

More information: Julio C. B. Ferreira et al. A selective inhibitor of mitofusin 1-?IIPKC association improves heart failure outcome in rats, *Nature Communications* (2019). DOI:

10.1038/s41467-018-08276-6