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Newly discovered molecule promises better treatments for heart attacks, heart surgery

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Scientists have discovered a compound that could lead to new treatments for heart attacks as well as methods to protect hearts during open heart surgery and other situations in which blood flow to the heart is interrupted.

In the process, the researchers uncovered cellular mechanisms that help explain how alcohol can protect against heart attack damage. In addition, they have uncovered a possible key to reducing chest pain and the heart attack damage among millions of people of East Asian descent who are genetically unable to respond to nitroglycerin and other cardiovascular treatments.

A research team of scientists at Stanford and Indiana universities schools of medicine reports in the Sept. 12 issue of the journal *Science* that by jump-starting a particular enzyme they were able to significantly reduce the amount of cell death caused by lack of blood flow to the heart.

The group, led by Daria Mochly-Rosen, Ph.D., professor of chemical and systems biology at Stanford, found that administering a compound called Alda-1 activated the enzyme, reducing heart muscle damage in experiments involving rats.

First, however, the researchers studied various mechanisms known to provide cardioprotection to heart muscle cells, including the use of ethanol, to better understand how those mechanisms worked. That work revealed a cellular signaling system that activated a particular enzyme

called ALDH2.

"The idea was to find a small molecule that could bypass the signaling process and activate the enzyme directly," said Thomas D. Hurley, Ph.D., professor of biochemistry and molecular biology and director of the Center for Structural Biology at the IU School of Medicine. Hurley's research has included years of study of the ALDH2 enzyme.

Although the Alda-1 molecule reduced heart tissue damage in laboratory tests, years of work will be necessary to refine the compound into a version that would be potentially effective and safe for human use, Dr. Hurley said.

That benefit could extend to about 40 percent of people of East Asian descent who carry a mutated form of the ALDH2 enzyme, which puts them at increased risk of cardiovascular damage.

Source: Indiana University