Protein helps protect tissues from damage after a heart attack

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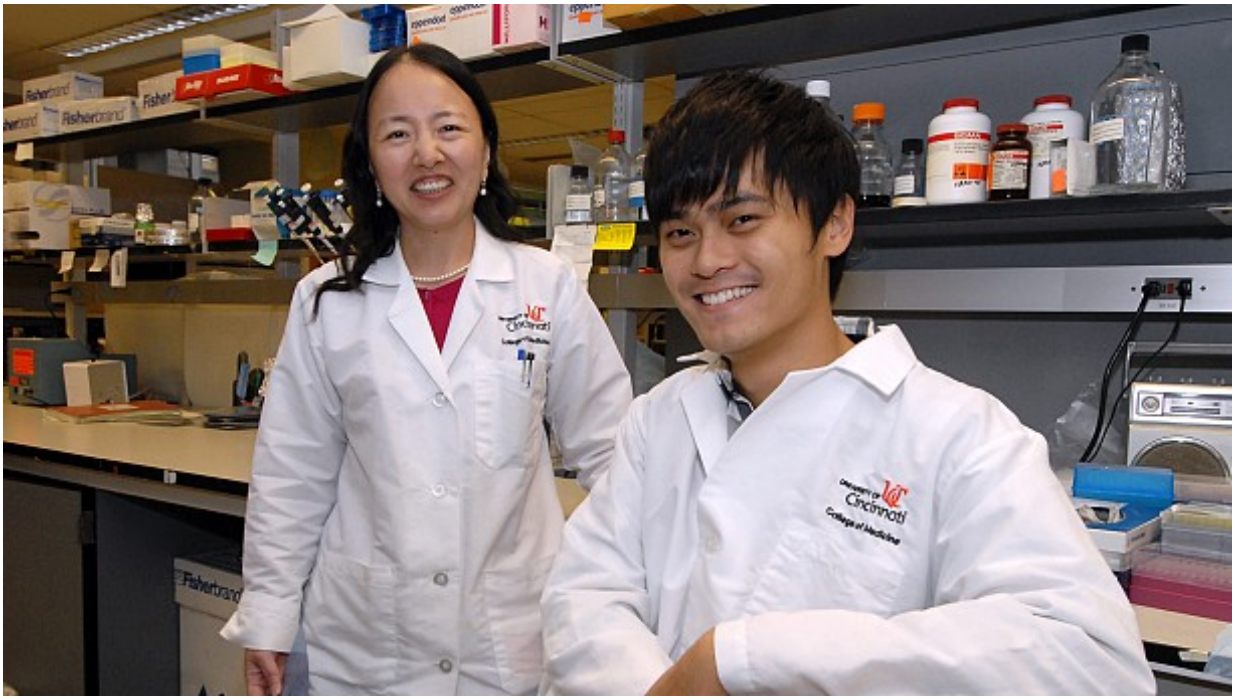

Wen Zhao, PhD, and Chi Keung Lam, PhD

University of Cincinnati (UC) researchers have observed levels of HAX-1, an anti-cell death protein, drop significantly in mice after a heart attack and during heart failure resulting in cardiac cells dying at a higher than normal rate.

HAX-1 regulates mitochondrial membrane integrity in the heart and

prevents the progression of cell death and damage to heart tissue, says Chi Keung Lam, PhD, a postdoctoral fellow working under the direction of Evangelia (Litsa) Kranias, PhD, Hanna Professor and director of cardiovascular biology in UC's Department of Pharmacology and Cell Biophysics.

HAX-1 is protective of cardiac cells during ischemia-reperfusion injury or damage to tissue caused by blood restriction. HAX-1 is an inhibitor of the mitochondrial permeability transition pore, promotes cell survival and works through recruitment of a chaperone protein called Hsp90 from cyclophilin-D, a major component of the pore, says Lam. Displacement of Hsp90 from cyclophilin-D leads to cyclophilin-D degradation and disruption of the pore opening and cell death.

The findings were published online this week in Proceedings in the National Academy of Sciences of the United States.

"If we can stimulate the function of this protein during or right before a heart attack we might be able to reduce the bad results of an episode," explains Lam, a lead author of the study. "Basically, what we have found is that this protein is inhibiting cell death through a pathway that is known to cause death."

Other investigators working with Lam and under the direction of Kranias include: Wen Zhao, PhD, former postdoctoral fellow at UC and also a lead author; Guan-Sheng Liu, PhD; Wen-Feng Cai, PhD; George Gardner, a PhD student; and George Adly.

"The opening of the mitochondrial permeability transition pore plays a key role in various diseases," says Lam. "This results in regulation of cell death in cancer, stroke and liver disease among many other conditions."

More information: C. K. Lam et al. HAX-1 regulates cyclophilin-D

levels and mitochondria permeability transition pore in the heart, *Proceedings of the National Academy of Sciences* (2015). DOI: 10.1073/pnas.1508760112