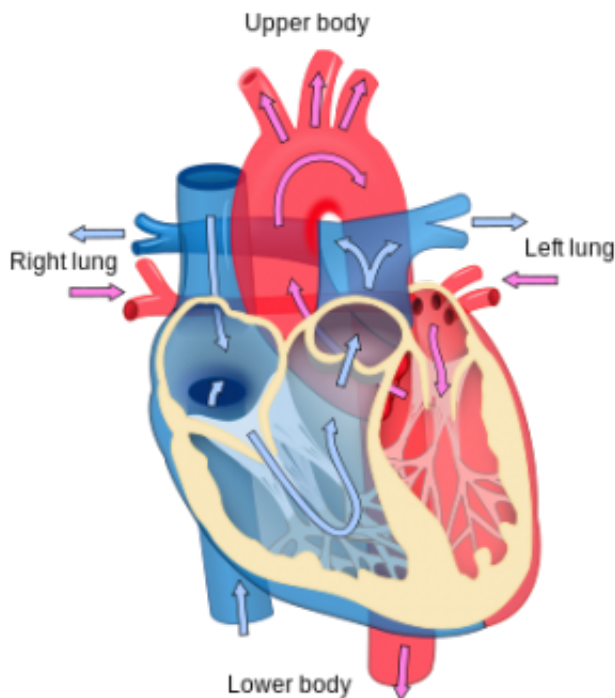


Calcium uptake by mitochondria makes heart beat harder in fight-or-flight response

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Heart diagram. Credit: Wikipedia

In a life-threatening situation, the heart beats faster and harder, invigorated by the fight-or-flight response, which instantaneously prepares a person to react or run. Now, a new study by researchers at Temple University School of Medicine (TUSM) shows that the uptick in heart muscle contractility that occurs under acute stress is driven by a flood of calcium into mitochondria—the cells' energy-producing

powerhouses.

Researchers have long known that calcium enters mitochondria in [heart muscle](#) cells, but the physiological role of that process was unclear. "The function of mitochondrial calcium uptake during stress generally was linked to the collapse of energy production and cell death," explained John W. Elrod, PhD, Assistant Professor of Pharmacology and at the Center for Translational Medicine at TUSM, and senior investigator on the new study, which appears June 25 in the journal *Cell Reports*.

"We show, however, that in periods of acute stress, increased calcium uptake by mitochondria in the heart functions in ways that are good and bad: during the fight-or-flight response, it provides the necessary energetic support for the heart, but during a heart attack, it leads to the death of large numbers of [heart cells](#)," Dr. Elrod said.

In the fight-or-flight response, the release of adrenaline activates numerous systems in the body to prepare for the perceived stress. A key aspect of this response is an increase in cardiac contractility. Adrenaline increases calcium cycling in the heart to drive contraction. That same calcium enters mitochondria through a channel known as the mitochondrial calcium uniporter (MCU). Dr. Elrod and colleagues at TUSM and Cincinnati Children's Hospital have been investigating MCU since its discovery in 2011, attempting to elucidate its function specifically in [heart muscle cells](#).

As part of their work, they knocked out, or removed, MCU from mitochondria in the hearts of adult mice. In doing so, they discovered that in mice lacking MCU, the heart failed to respond to adrenaline-receptor stimulation with isoproterenol—an adrenaline-like chemical that in high doses normally sends the heart into overdrive, mimicking aspects of the fight-or-flight response. Meanwhile, in mice lacking MCU that suffered heart attacks with ischemia (blockage of blood flow)

followed by reperfusion (the restoration of blood and oxygen supply), the loss of MCU was found to preserve heart tissue and increase cell survival. Without the channel, calcium was unable to enter mitochondria to trigger cell death.

"The effects were specific to [acute stress](#)," Dr. Elrod explained. "Under normal conditions, the loss of MCU appeared to have little to no impact on metabolic function in the heart."

The new findings complement work that is ongoing by researchers at Temple to better understand heart function and adrenergic (adrenaline-related) signaling in heart cells. In 2013, Madesh Muniswamy, PhD, Associate Professor of Biochemistry, Associate Professor at the Cardiovascular Research Center and Associate Professor at the Center for Translational Medicine at TUSM and a coauthor with Dr. Elrod on the new study, reported the discovery of MCUR1, a protein in the inner membrane of the mitochondrion that is essential to MCU-mediated [calcium uptake](#).

Dr. Elrod and colleagues plan to continue their investigations of MCU by next looking at its role in chronic stress, which is relevant to conditions such as heart failure and high blood pressure.

"We are also exploring other calcium handling pathways in [heart](#) cells and particularly how calcium escapes from mitochondria," Dr. Elrod noted. "Understanding how calcium exchange at the [mitochondria](#) is regulated may help target new therapies to preserve energy production in the cell but limit the [calcium](#) overload associated with cellular demise."

Provided by Temple University

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