

# Study identifies protein essential for normal heart function

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A study by researchers at Skaggs School of Pharmacy and Pharmaceutical Sciences and the Department of Pharmacology at the University of California, San Diego, shows that a protein called MCL-1, which promotes cell survival, is essential for normal heart function.

Their study, published in the June 15 online issue of the journal *Genes & Development*, found that deletion of the gene encoding MCL-1 in adult mouse hearts led to rapid [heart](#) failure within two weeks, and death within a month.

MCL-1 (myeloid cell leukemia-1) is an anti-apoptotic [protein](#), meaning that it prevents or delays the death of a cell. It is also a member of the BCL-2 family of proteins that regulate mitochondria – the cell's power producers – and [cell death](#). Aberrant expression of anti-apoptotic BCL-2 family members is one of the defining features of cancer cells, and is strongly associated with resistance to current therapies. Thus, these proteins are currently major targets in the development of new therapies for patients with cancer.

But, while MCL-1 is up regulated in a number of human cancers, contributing to the overgrowth of cancer cells, it is found at high levels in normal heart tissue. Additionally, the researchers found that autophagy – a process which deals with mitochondrial maintenance and is normally induced by myocardial stress – was impaired in mice with MCL-1 deficient hearts.

In summary, the study demonstrated that the loss of MCL-1 led to rapid dysfunction of mitochondria, impaired autophagy and heart failure, even in the absence of cardiac stress.

"Cardiac injury, such as a heart attack, causes levels of MCL-1 to drop in the heart, and this process may increase cardiac cell death," said Åsa B. Gustafsson, PhD, an associate professor at UCSD Skaggs School of Pharmacy and [Pharmaceutical Sciences](#). "Therefore, preserving normal levels of this protein in cardiac tissue could reduce damage after a heart attack and prevent progression to heart failure."

By compromising both autophagy and mitochondrial function, MCL-1 inhibitors are likely to affect the cells' energy supply. "Our findings raise concerns about the potential cardiac toxicity of drugs that block MCL-1 – drugs that have entered clinical trials because they increase cancer cell death," said the study's first author, Robert L. Thomas.

Provided by University of California - San Diego

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