HHS Public Access

Author manuscript

Sci Transl Med. Author manuscript; available in PMC 2019 February 28.

Published in final edited form as:

Sci Transl Med. 2018 May 30; 10(443): . doi:10.1126/scitranslmed.aau0462.

Cardioprotective effects of autophagy: Eat your heart out, heart failure!

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Abstract

Activation of autophagy improves post-infarction myocardial function in mice.

Autophagy is an evolutionarily conserved intracellular process that mediates organelle turnover, protein degradation, and recycling of superfluous, aging, or damaged cytoplasmic components in response to diverse stimuli, including cellular stress, ischemic injury, proteotoxicity, infection, and nutrient starvation. The functional role of autophagy in the pathophysiology of cardiovascular disorders has not been fully established, and its beneficial or detrimental effects remain quite controversial.

Sciarretta and collaborators elegantly demonstrate that an efficient autophagic response allows cardiomyocytes to cope with ischemic injury. Using an established model (ligation of the left anterior descending coronary artery in mice), they provided compelling evidence that the natural, nonreducing sugar trehalose (also known as mycose or tremalose, which consists of two molecules of glucose) activates autophagy and reverses the adverse structural remodeling of the heart following myocardial infarction, markedly attenuating cardiac dysfunction. These favorable effects were not observed in *beclin 1*$^{+/-}$ heterozygous mice, which are insensitive to autophagy inducers, thereby confirming that the beneficial effects of trehalose occur via the activation of autophagy. Trehalose had previously been shown to protect cells from oxidative stress and thermal shock, although the underlying mechanisms had not been clarified. Here, the authors proved that trehalose—administered intraperitoneally for the first 48 hours after infarction and then in the drinking water for four weeks—significantly improved mitochondrial quality control, reduced the accumulation of damaged organelles by promoting mitophagy, and enhanced lysosomal function.

Authors of this study had previously identified several fundamental pathways underlying autophagic fluxes in the heart. The present findings explain the beneficial role of autophagy in post-ischemic heart disease. However, the molecular mechanisms by which trehalose induces autophagy have not been fully elucidated. Nevertheless, these preclinical results have translational potential, providing a novel therapeutic strategy for patients at risk of developing heart failure following myocardial infarction.

Acknowledgments

GS is supported by the NIH: R00DK107895

Highlighted Article

1. Sciarretta S, Yee D, Nagarajan N, Bianchi F, Saito T, Valenti V, Tong M, Del Re DP, Vecchione C, Schirone L, Forte M, Rubattu S, Shirakabe A, Boppana VS, Volpe M, Frati G, Zhai P, Sadoshima J. Trehalose-induced activation of autophagy improves cardiac remodeling after myocardial infarction. J Am Coll Cardiol. 2018; 71:1999–2010. [PubMed: 29724354]