Beclin-1 controls caspase-4 inflammasome activation and pyroptosis after myocardial injury

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Video Byte

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Abstract

Reperfusion of heart tissue with blood after interruption of the blood supply (ischemia) often contributes to inflammation and cell death, including a specific form of cell death called pyroptosis, which can be regulated by the protein caspase-4. The protein beclin-1 is involved in an intracellular degradation process called autophagy that can limit cell death. However, whether beclin-1 limits caspase-4-mediated pyroptosis after heart reperfusion injury remains unclear. To find out, a recent study examined the effects of beclin-1 overexpression in mouse hearts and cultured human heart cells subjected to ischemia/reperfusion. Ischemia/reperfusion increased caspase-4 activity and the expression of the pyroptosis protein gasdermin D. In contrast, beclin-1 overexpression decreased caspase-4 activity, gasdermin D expression, and the levels of the inflammation molecule IL-1 β . Beclin-1 overexpression also promoted autophagy in the mouse hearts and human cells, and it increased mouse survival and reduced the extent of tissue damage after ischemia/reperfusion. Although the roles of other cell death pathways need to be clarified, the results show that beclin-1-driven autophagy suppresses caspase-4-mediated pyroptosis, which may help protect small blood vessels from injury after ischemia/reperfusion and that inducing beclin-1 signaling may help limit heart reperfusion-induced injury.