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Letter to the Editor

Decreased ATP production during mitochondrial calcium uniporter inhibition enhances autophagy and mitophagy to provide cardioprotection in cardiac failure

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Dear Editor,

The previous study by Su and Ge et al. [1] firstly showed that mitochondrial calcium uniporter (MCU) inhibition enhanced autophagy and mitophagy to provide cardioprotective effects in patients with pressure overload-induced heart failure.

However, the mechanism underlying enhanced autophagy and mitophagy is not clear in this study. Here we hypothesized that decreased ATP production during mitochondrial calcium uniporter inhibition enhances autophagy and mitophagy to provide cardioprotection in cardiac failure. The following possible mechanisms are considered:

First of all, MCU is responsible for mitochondrial calcium uptake, whose inhibition decreases calcium concentrations in the mitochondria. As calcium plays a critical role in regulating mitochondrial energy generation in cardiomyocytes, accordingly, low calcium intake inhibits mitochondrial ATP synthesis. Particularly, a decline in the ATP level induces activation of AMPK, causing phosphorylation and inhibition of mTORC1, which suppresses autophagy initiation via directly phosphorylating and inactivating mATG13 [2]. In addition, downregulation of ATP concentrations via prevention of F0F1-ATPase biogenesis also triggers mitophagy [3]. Substantial researches have reported that autophagy and mitophagy serve as a defense against cardiac failure [4,5].

In conclusion, reduced ATP production may play an essential role in MCU inhibition-associated autophagy and mitophagy. If so, it will further deepen our understanding of the mechanism of cardioprotective effects by MCU inhibition, which could serve as a novel therapeutic target in cardiac failure treatment.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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