Galectin-3-centered paracrine network mediates cardiac inflammation and fibrosis upon β-adrenergic insult

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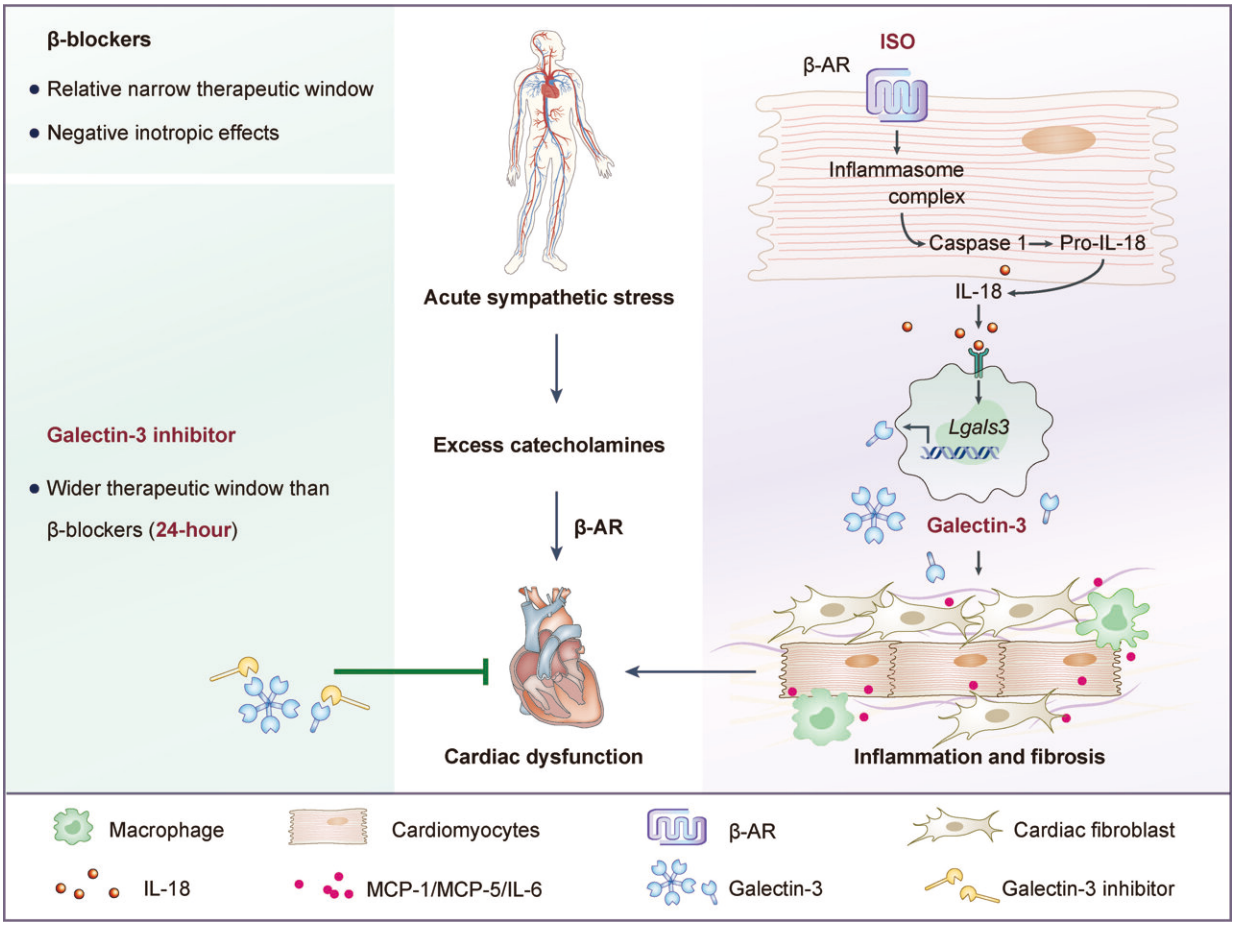

Galectin-3 upregulated both in patients and mice upon acute sympathetic overactivation. IL-18/galectin-3 axis mediates the cardiac inflammatory injuries induced by acute β-adrenergic receptor activation. Galectin-3 inhibitor, but not a β-blocker, treatment one day after β-AR insult can successfully block cardiac

inflammatory injuries upon acute β-adrenergic receptor overactivation. Credit: Science China Press

In a study led by Dr. Han Xiao (Department of cardiology and institute of vascular medicine, Peking university third hospital), researchers found that rapid over-activation of β-adrenergic receptors (β-AR) following acute stress initiates cardiac inflammation and injury. However, the process of inflammation cascades has not been fully illustrated.

Using bioinformatics analysis, the research team discovered galectin-3 as a potential significant downstream effector of β-AR and IL-18 activation. In the heart of mice treated with β-AR agonist (isoproterenol), galectin-3 expression was upregulated markedly later than IL-18 activation.

The serum level of galectin-3 was positively correlated with norepinephrine or IL-18 in ACS (acute coronary syndrome) patients. ISO-induced galectin-3 upregulation was attenuated in Il18-/- mice. It was further revealed that cardiomyocyte-derived IL-18 induced galectin-3 expression in macrophages following ISO treatment.

Moreover, galectin-3 deficiency suppressed ISO-induced cardiac inflammation and fibrosis without blocking ISO-induced IL-18 increase. Treatment with a galectin-3 inhibitor, but not a β-blocker, one day after ISO treatment effectively attenuated cardiac inflammation and fibrosis.

This study demonstrates that following acute sympathetic activation, galectin-3 was upregulated in macrophages by cardiomyocyte-derived IL-18 and subsequently promoted cardiac inflammation cascades leading to fibrosis. Galectin-3 inhibitor effectively blocks cardiac injury one day

after β-AR insult. Galectin-3 mediated cardiac inflammatory amplification and is a potential therapeutic target for cardiac diseases involving β-adrenergic toxicity.

The paper is published in the journal *Science China Life Sciences*.

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