β-adrenergic signaling activates inflammasome promoting pressure overload-induced cardiac fibrosis

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Introduction: Heart failure (HF) is an end-stage syndrome of all structural heart diseases accompanying the loss of myocardium and cardiac fibrosis. It has been reported that inflammasome plays a role in cardiac fibrosis. However, it is largely unknown how the inflammasome is activated during heart failure.

Methods: We established rat thoracic aorta constriction (TAC) model and measured inflammasome proteins in sham and TAC rat myocardium. Inflammasome proteins were also investigated in cultured cardiac fibroblasts with stimulation of norepinephrine.

Result: Our results showed that inflammasome was activated in cardiac fibroblasts of TAC rats. Stimulation of cultured cardiac fibroblasts with norepinephrine activated inflammasome in vitro, which was abrogated by inhibition of calcium channel and reactive oxygen species (ROS). Activation of inflammasome by norepinephrine promoted cardiac fibrosis, while inhibition of calcium channel/ROS/inflammasome abrogated this effect. Furthermore, blockade of β-adrenergic signaling with β-blocker suppressed inflammasome with promotion of heart function in TAC rats.

Conclusion: Our findings indicate that activation of inflammasome by β-adrenergic signaling promotes cardiac fibrosis. Therefore, modulation of inflammasome during HF may provide a novel strategy to treat this disease.