[gw22-e0703]

CALPAIN INDUCES TNFA EXPRESSION AND CARDIAC DYSFUNCTION BY IKB/NF-KB SYSTEM IN SEPTIC MICE

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10.1136/heartjnl-2011-300867.383

Objective In septic models, recent studies showed that both myocardial calpain activity and TNFα expression increased, and inhibition of calpain downregulated myocardial TNFα expression and improved cardiac dysfunction, however, the mechanism underlying the pathological process was unclear. Thus, in this study, we aim to explore the link between calpain activity and TNFα expression in septic mice.

Methods Male adult mice were injected by LPS (4 mg/kg, intraperitoneally) to induce sepsis, myocardial calpain activity, IκB/NF-κB signaling activation and TNFα expression in mRNA and protein levels were assessed, myocardial function was evaluated by Langdorff perfusion parameters.

Results In septic mice, myocardial calpain activity and expression of TNFα increased as expectedly, IκB α protein was found degradation, which results NF-κB activation, as indicating by NF-κB p65 phosphorylation, in septic mice. Calpain inhibitors, both calpain inhibitor-Ш and PD150606, prevented myocardial IκBαdegradation, inhibited NF-κB p65 phosphorylation, prevented NF-κB activation and TNFα mRNA expression, followed with improving myocardial function in septic mice.

Conclusion Myocardial calpain activity increases in septic mice, by modulating IκB/NF-κB pathway, calpain induces myocardial TNFα expression and myocardial dysfunction in septic mice.