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CALPAIN INDUCES TNF α EXPRESSION AND CARDIAC DYSFUNCTION BY I κ B/NF- κ B SYSTEM IN SEPTIC MICE

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Objective In septic models, recent studies showed that both myocardial calpain activity and TNF α expression increased, and inhibition of calpain downregulated myocardial TNF α 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 TNF α expression in septic mice.

Methods Male adult mice were injected by LPS (4 mg/kg, intraperitoneally) to induce sepsis, myocardial calpain activity, I κ B/NF- κ B signaling activation and TNF α 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 TNF α increased as expectedly, I κ B α protein was found degradation, which results NF- κ B activation, as indicating by NF- κ B p65 phosphorylation, in septic mice. Calpain inhibitors, both calpain inhibitor-III and PD150606, prevented myocardial I κ B α degradation, inhibited NF- κ B p65 phosphorylation, prevented NF- κ B activation and TNF α mRNA expression, followed with improving myocardial function in septic mice.

Conclusion Myocardial calpain activity increases in septic mice, by modulating I κ B/NF- κ B pathway, calpain induces myocardial TNF α expression and myocardial dysfunction in septic mice.