Phospho-Tyr705 of STAT3 regulates inflammation and coagulation during sepsis

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Video Byte

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Abstract

Sepsis – life-threatening organ dysfunction caused by infection – is a major cause of death in intensive care units. Inflammation and coagulation are known to build off of each other to contribute to sepsis pathogenesis. Unfortunately, the detailed mechanisms behind signaling in sepsis are incompletely understood. In a new study, researchers evaluated signaling pathways using human cell lines and a mouse model of sepsis. They found that inhibiting phosphorylation of the Tyr705 site on STAT3 (pY-STAT3) reduced inflammation. In septic mice, pY-STAT3 inhibition reduced proinflammatory factors, coagulation, lung injury, and vascular leakage, improving the sepsis survival rate. Inhibiting pY-STAT3 decreased LPS-induced cytokine production by macrophages, protecting pulmonary endothelial cells from damage, and procoagulant factors were downregulated by pY-STAT3 inhibition. Although further studies are needed to translate these findings to the clinic, the results suggest pY-STAT3 inhibitors may have a therapeutic role in modulating the inflammatory response and defective coagulation, protecting patients from harm during sepsis.