Lipopolysaccharide desensitizes monocytes-macrophages to CD40 ligand stimulation

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Date: 2007/10/25

Lipopolysaccharide (LPS), a major cell wall component of Gram-negative bacterial organisms, may stimulate many of the pathophysiological events within the patient during a septic episode (2). CD40 engagement in monocytes induces JAK3 phosphorylation and subsequent activation of transcription factors, suggesting that JAK3 may serve as a critical signal transducer after CD40 ligand (CD40L) stimulation (3). LPS reduced the responsiveness of monocyte-macrophages to CD40L, which can further suppress the production of cytokines such as interleukin-12 (IL-12) and tumour necrosis factor-α (TNF-α) (1). LPS is a potent trigger of prostaglandin E₂ (PGE₂) in monocytes and the interaction results in reduced activation of the JAK3. In this study, Sinistro et al. (4) reported that the cyclooxygenase (COX) inhibitor, indomethacin, can alter the suppressive effect of LPS on the response of monocytes to CD40L by interference with the production of PGE₂. This study provide a novel therapeutic strategy for septic immunosuppression.

References:
