Expression of type I interferon by splenic macrophages suppresses adaptive immunity during sepsis.

Abstract:

Early during Gram-negative sepsis, excessive release of pro-inflammatory cytokines can cause septic shock that is often followed by a state of immune paralysis characterized by the failure to mount adaptive immunity towards secondary microbial infections. Especially, the early mechanisms responsible for such immune hypo-responsiveness are unclear. Here, we show that TLR4 is the key immune sensing receptor to initiate paralysis of T-cell immunity after bacterial sepsis. Downstream of TLR4, signalling through TRIF but not MyD88 impaired the development of specific T-cell immunity against secondary infections. We identified type I interferon (IFN) released from splenic macrophages as the critical factor causing T-cell immune paralysis. Early during sepsis, type I IFN acted selectively on dendritic cells (DCs) by impairing antigen presentation and secretion of pro-inflammatory cytokines. Our results reveal a novel immune regulatory role for type I IFN in the initiation of septic immune paralysis, which is distinct from its well-known immune stimulatory effects. Moreover, we identify potential molecular targets...
for therapeutic intervention to overcome impairment of T-cell immunity after sepsis.

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