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Titel des Beitrags: Attenuated pathogenesis of polymicrobial peritonitis in mice after TLR2 agonist pre-treatment involves ST2 up-regulation.

Abstract: The innate immune system uses Toll-like receptors (TLRs) to activate and instruct immune responses against microbial pathogens. Administration of TLR agonists to mice induces a state of hyporesponsiveness, or tolerance, characterized by reduced cytokine production upon subsequent second challenge. The present study examined the effects of pre-treatment of mice with TLR2-dependent stimuli on the host defense against acute polymicrobial infection. Immune priming of mice with macrophage-activating lipopeptide-2 (MALP-2) 4 days prior to infection greatly improves survival and bacterial clearance in a model of polymicrobial septic peritonitis which is associated with enhanced accumulation of effector neutrophils in the peritoneal cavity. Further, the systemic and local production of both myeloid differentiation factor 88 (MyD88)-dependently and MyD88-independently produced cytokines was substantially diminished, but not completely absent, in TLR2-treated mice. While pre-treatment with MALP-2 does not involve differential expression of TLR and IL-1R-associated kinase proteins, ST2, a negative regulator of TLR signaling, was up-regulated after treatment of mice with either MALP-2 or N-alpha-palmitoyl-S-[2,3-bis(palmityloxy)-(2RS)-propyl]-L-cysteine.
Therefore, ST2 may be a mechanism, among others, to attenuate the sepsis-induced cytokine burst. Thus, these results suggest that immune protection in mice after pre-treatment with TLR2-dependent stimuli involves the induction of enhanced pathogen defense by neutrophils. In addition, up-regulation of ST2 could contribute to the diminished cytokine production.