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Titel des Beitrags: Murine TLR2 expression analysis and systemic antagonism by usage of specific monoclonal antibodies.

Abstract: Cellular recognition of immuno-stimulatory microbial products alarming the host immune system upon infection, as well as endogenous molecular patterns representing perturbation of regular homeostasis such as through necrosis of host cells is mediated by innate pattern recognition receptors to which toll-like receptors (TLRs) belong. A variety of agonists has been attributed to TLR2. We raised monoclonal antibodies (mAbs) toward the murine TLR2 extracellular domain (mT2ECD) in order to analyze murine TLR2 expression. Murine macrophages were stained TLR2-specifically with distinct mAbs as shown by flow cytometry, immuno precipitation, and immuno-cytochemical analysis. TLR2-specific murine macrophage activation was inhibited through pre-incubation with a mAb mT2.4 while another mTLR2-specific mAb mT2.7 did not affect cell activation through TLR2. Plasmon resonance based analysis showed inhibition of lipopeptide binding to mT2ECD if complex formation with mT2.4 preceded binding analysis. Systemic induction of IL-6, IL-12p40, and GROalpha/KC release to the serum upon lipopeptide challenge of mice was inhibited by systemic administration of mT2.4. Furthermore, 120 mg/kg of mT2.4 protected mice from lethal shock-like syndrome in an experimental low-dose model of septic shock. This result validates blockage of cell surface TLR2 for inhibition of
immune cell over-activation upon microbial challenge.