Abdominal sepsis due to secondary fecal peritonitis following anastomosis insufficiency is a rare but life threatening complication of colorectal surgery. The induction of IFN-gamma by IL-12 is believed to play a key role in sepsis as it promotes antibacterial effector mechanisms such as oxidative burst or nitric oxide induction. The impact of gene deficiency for IL-12 (IL-12p40 KO), oxidative burst (p47(phox) KO), or NO induction (iNOS KO) on the outcome of fecal peritonitis was characterized using the murine Colon Ascendens Stent Peritonitis model (CASP). In the IL-12p40 KO model, 3 and 12 h after surgery, serum cytokine levels of IL-1beta, TNF, IL-18, and IL-10 were analyzed. Expression of IL-1beta, IL-10, IP-10, and MIP-1alpha was measured in lung and liver by RNAse Protection Assay. IL-12p40 and iNOS-deficient mice exhibited a significantly higher susceptibility to CASP as compared to the controls, whereas no significant difference was observed in p47(phox) KO mice. Absence of IL-12 resulted in delayed expression of proinflammatory cytokines and chemokines in both the liver and the lung, and was associated with significant reduction of IL-1beta levels in the serum 12 h after CASP. IL-12 and iNOS possess protective functions in fecal murine peritonitis. Surprisingly, no significant contribution of oxidative burst to the immune response was observed. Overall, these findings suggest that IL-12
deficiency causes a profound delay of the immune response after polymicrobial challenge resulting in significantly increased susceptibility in the CASP model.