Increased inflammation and lethality of Dusp1-/- mice in polymicrobial peritonitis models.

Abstract:
The mitogen-activated protein kinase phosphatase Dusp1 (also known as MKP-1) is essential for control of the inflammatory response to systemic challenge with the lipopolysaccharide of Gram-negative bacteria. Here, we have investigated the consequences of Dusp1-deficiency in colon ascendens stent peritonitis (CASP) and caecal ligation and puncture (CLP), two mouse models of septic peritonitis. Following CASP, Dusp1(-/-) mice had increased serum levels of CCL4, interleukin-10 (IL-10) and IL-6, with differences from wild-type mice being dependent on severity of sepsis. These cytokines, along with inducible nitric oxide synthase messenger RNA, were also expressed at higher levels in spleen and liver. Similar over-production of these cytokines was detected in the CLP model, with even larger differences from wild-type mice. Despite the increased inflammatory response, bacterial clearance was impaired in Dusp1(-/-) mice subjected to CASP and CLP. Dusp1(-/-) mice suffered increased lethality in both peritonitis models. Together our data indicate that exaggerated inflammatory responses to gut bacteria introduced into the peritoneum in the absence of Dusp1 do not help to control bacterial replication but are detrimental for the host.