Inhibition of interleukin-22 attenuates bacterial load and organ failure during acute polymicrobial sepsis.

Interleukin-22 (IL-22) is a recently discovered proinflammatory cytokine, structurally related to IL-10. Since IL-22 is induced by lipopolysaccharide in vivo, we studied the role of IL-22 in a model of polymicrobial peritonitis. Quantitative real-time reverse transcription-PCR analysis showed marked induction of IL-22 and IL-22 receptor in spleen and kidney during the course of sepsis. The biological activity of IL-22 is modulated by IL-22-binding protein (IL-22BP), which is considered a natural antagonist of IL-22. To further analyze the role of IL-22 during septic peritonitis, mice were treated with recombinant IL-22BP generated as Fc gamma 2a fusion protein. IL-22BP-Fc completely blocked IL-22-induced STAT3 activation in hepatocytes in vitro. Treatment of mice with IL-22BP-Fc 4 h before sepsis induction led to enhanced accumulation of neutrophils and mononuclear phagocytes and a reduced bacterial load at the site of infection. In addition, IL-22 blockade led to an enhanced bacterial clearance in liver and kidney and reduced kidney injury. These results imply an important proinflammatory role of IL-22 during septic peritonitis, contributing to bacterial spread and organ failure. IL-22 therefore appears to play an important role in the regulation of inflammatory processes in vivo.