Impact of NKT Cells and LFA-1 on Liver Regeneration under Subseptic Conditions.

Activation of the immune system in terms of subseptic conditions during liver regeneration is of paramount clinical importance. However, little is known about molecular mechanisms and their mediators that control hepatocyte proliferation. We sought to determine the functional role of immune cells, especially NKT cells, in response to partial hepatectomy (PH), and to uncover the impact of the integrin lymphocyte function-associated antigen-1 (LFA-1) on liver regeneration in a septic setting. Wild-type (WT) and LFA-1-/- mice underwent a 2/3 PH and low-dose lipopolysaccharide (LPS) application. Hepatocyte proliferation, immune cell infiltration, and cytokine profile in the liver parenchyma were determined. Low-dose LPS application after PH results in a significant delay of liver regeneration between 48h and 72h, which is associated with a reduced number of CD3+ cells within the regenerating liver. In absence of LFA-1, an impaired regenerative capacity was observed under low-dose LPS application. Analysis of different leukocyte subpopulations showed less CD3+NK1.1+ NKT cells in the liver parenchyma of LFA-1-/- mice after PH and LPS application compared to WT controls, while CD3-NK1.1+ NK cells markedly
increased. Concordantly with this observation, lower levels of NKT cell related cytokines IL-12 and IL-23 were expressed in the regenerating liver of LFA-1-/- mice, while the expression of NK cell-associated CCL5 and IL-10 was increased compared to WT mice. A subseptic situation negatively alters hepatocyte proliferation. Within this scenario, we suggest an important impact of NKT cells and postulate a critical function for LFA-1 during processes of liver regeneration.