

**The role of CC-chemokine-receptor-4 in the murine abdominal sepsis model CASP**

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Aim of the study is to define the role of chemokines and especially of the CC-chemokine-receptor-4 during the course of abdominal sepsis. Thereby, potential targets for immunomodulatory treatment strategies should be identified.

Intraabdominal infection due to anastomosis insufficiency after major abdominal surgery remains a life threatening condition. Despite extensive scientific effort, immunomodulatory therapy regimens failed to improve the outcome of abdominal sepsis in patients.

It is widely accepted, that leucocyte recruitment and trafficking is crucial for the initiation and mediation of the host's immune response against an intraabdominal septic focus. Chemokines are a superfamily of small proteins involved both in routine leukocyte trafficking and in the activation and recruitment of specific cell populations to sites of inflammation and infection. CC-chemokine-receptor-(CCR-)4, a high affinity receptor for the CC chemokines thymus-and-activation-regulated chemokine (TARC) and macrophage-derived chemokine (MDC), is expressed in the thymus and spleen, and also by peripheral blood T cells, macrophages, platelets, and basophils. Analysis of peritoneal lavage cells from CCR4-deficient mice revealed a significant decrease in the F4/80<sup>+</sup> cell population suggesting a defect in the ability of the CCR4<sup>-/-</sup> macrophages to be retained in the peritoneal cavity. Thus, the impact of CCR4-deficiency in the murine Colon-Ascendens-Stent-Peritonitis (CASP) model is addressed in the current study. CASP is an experimental sepsis model resembling closely to the clinical course of sepsis due to intestinal leakage as a stent is surgically inserted in the ascending colon to establish a persistent connection from the luminal site to the peritoneal cavity. In this model, early and sustained induction of chemokines and infiltration of various organs by inflammatory cells could be demonstrated. First results reveal a significantly increased susceptibility of CCR4-deficient mice to CASP surgery as compared to the controls. The further and detailed characterization of the phenotype is continued presently...