学 位 論 文 の 要 旨

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主論文の題名

Differential Roles of Dendritic Cells in Expanding CD4 T Cells in Sepsis

主論文の要旨

Sepsis is a systemically dysregulated inflammatory syndrome, in which dendritic cells (DCs) play a critical role in coordinating aberrant immunity. The aim of this study is to shed light on the differential roles played by systemic versus mucosal DCs in regulating immune responses in sepsis. We identified a differential impact of the systemic and mucosal DCs on proliferating allogenic T lymphocytes (CD4 T cells) in a mouse model of sepsis. Despite the fact that the frequency of CD4 T cells was reduced in septic mice, septic mesenteric lymph node (MLN) DCs proved superior to septic spleen (SP) DCs in expanding allogeneic CD4 T cells. Moreover, septic MLN DCs markedly augmented the surface expression of Major Histocompatibility Complex class II (MHC-II) and Cluster of differentiation 40 (CD 40), as well as the messaging of interleukin-1ß (IL-1ß). Interestingly, IL-1ß-treated CD4 T cells expanded in a dose-dependent manner, suggesting that this cytokine acts as a key mediator of MLN DCs in promoting septic inflammation. Thus, mucosal and systemic DCs were found to be functionally different in the way CD4 T cells respond during sepsis. Our study provides a molecular basis for the differential nature of DCs activity in acute phase of sepsis, depending on location; potentially inducing septic inflammation or immune-paralysis.