Changes in the PD-1 and PD-L1 expressions of splenic dendritic cells in multiple-organ dysfunction syndrome mice and their significance


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Received June 25, 2013
Accepted July 2, 2014
Published September 26, 2014
DOI http://dx.doi.org/10.4238/2014.September.26.4

ABSTRACT. The aim of this study was to evaluate the expression of surface molecules in splenic dendritic cells (DC) in multiple-organ dysfunction syndrome (MODS) mice and their effects on the immunosuppression of sepsis and MODS. One hundred thirty C57BL/6 mice were divided into 7 groups: 6, 12, 24, 48 h, 5-7 days, 10-12 days, and the normal control group. The sepsis-MODS mouse model was established by zymosan injection into the peritoneal cavity. Histopathological changes in the spleen were evaluated by hematoxylin and eosin (HE) staining. After enrichment with BD IMag, the expressions of PD-1, PD-L1, MHC-II (I-A^b), and CD86 in splenic DCs were examined by flow cytometry, and their relationship with sepsis development and MODS was analyzed. The histological structures of the spleen were damaged in the 24-, 48-h, and 10-12-day groups. PD-L1 expression increased 6 h after zymosan injection, decreased to normal levels at 24 and 48 h, and increased at 5-7 days, peaking at 10-12 days. The change in PD-1 expression roughly
paralleled that of PD-L1. MHC-II and CD86 increased at 6 and 12 h, and dropped to normal levels at 10-12 days. In the early stage of injury, splenic DCs were mainly activated, whereas in the later stage, the expressions of the negative co-stimulatory molecules, PD-L1 and PD-1, were upregulated, similar to tolerogenic DCs. Splenic DCs might suppress the stimulation of T lymphocytes in MODS mice through the PD-L1/PD-1 pathway, which would induce immunosuppression and the pathogenesis of MODS.

**Key words:** Multiple organ failure; Dendritic cells; PD-1/PD-L1; Spleen