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Title

Role of IL-10-treated Dendritic Cells in Immunoregulatory Function via Induction of Tr1 Cells

Abstract

IL-10 has potent immunoregulatory effects on the maturation and antigen presenting function of dendritic cells (DCs). DCs are antigen-presenting cells that play a major role in induction of primary immune responses. Although underlying mechanisms have not been fully elucidated, tolerogenic DCs play critical roles in central tolerance and in the maintenance of peripheral tolerance in the steady state. We have utilized IL-10-treated bone marrow-derived DCs to analyze the capacity to induce regulatory T cells and maintain T cell tolerance. We show here that IL-10-treated DCs show reduced expression of CD40 and secrete IL-10 but not IL-12 in the response with LPS. IL-10-treated DCs induce antigen-specific unresponsiveness in naive and memory CD4⁺T cells. Naive CD4⁺T cells are skewed to T regulatory 1 (Tr1) cells by repeated priming with IL-10-treated DCs. Tr1 cells release immunoregulatory cytokines, such as IL-10 and TGF- β , and express CD25 and CTLA-4 by the antigen specific stimulation with DCs. Tr1 cells stimulated with immunogenic DCs inhibit CD4⁺T cell proliferation. Furthermore, Tr1 cells show the cytotoxic activity against immunogenic DCs in antigen dependent manner. These data indicate that IL-10-treated tolerogenic DCs are able to negatively regulate the CD4⁺T cell response for peripheral tolerance directly and also indirectly by induction of Tr1 cells, which effectively suppress to the adaptive immune response.