IL-4-mediated fine tuning of IL-12p70 production by human DC

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IL-4 is expressed at high levels in allergic diseases and dominates the early phases of multiple acquired immune responses. However, the precise role of IL-4 during early inflammation and its impact on the differentiation of newly recruited DC precursors remains elusive. In order to characterize the impact of IL-4 on the differentiation of human DC, we investigated the role of IL-4 on the differentiation of monocytes into DC. Human DC were differentiated from peripheral blood precursors under either low or high concentrations of IL-4. We analyzed their cytokine profile and capacity to polarize T-cell differentiation. Concentrations of 5 (low) and 50 (high) ng/mL IL-4 induced two distinct types of DC. DC differentiated under low-dose IL-4 (5 ng/mL) produced almost no IL-12p70, and primed naïve CD4+ T cells allowing IL-4 secretion and Th2 induction. In contrast, DC generated under high concentrations of IL-4 (50 ng/mL) produced large amounts of IL-12p70, low IL-10 and primed naïve CD4+ T cells to become Th1 cells. Thus, we demonstrate that the Th2 cell cytokine IL-4 decisively determines the phenotype of ongoing immune responses by orchestrating the functional phenotype of newly immigrating DC precursors.

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