

## Regulation of IL-10 Production in Murine Bone Marrow Derived Dendritic Cells is Linked to Levels of B7-2 Expression.

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The role of B7-2 (CD86) as a positive costimulatory ligand capable of promoting the proliferation and survival of T cells in conjunction with TCR engagement has been well established. However, the ability of B7-2 to act as a signaling receptor with the capacity to regulate antigen presenting cell activity remains unclear. In order to examine this question, antisense oligomers designed to mask the AUG start site were used to inhibit the de novo expression of B7-2 protein in either LPS or anti-CD40 treated bone marrow derived dendritic cells (DCs). Using this conventional antisense approach it was observed that B7-2 expression was significantly inhibited compared to untreated or scrambled sequence oligomer treated DCs. Surprisingly, the level of B7-1 (CD80) was also diminished even though the region of B7-2 targeted by the antisense shares little homology with the B7-1 sequence. Intracellular cytokine staining of the B7-2 antisense treated DCs revealed that the decrease in B7-1 expression may be due, in part, to an autocrine effect of IL-10. A unique antisense approach using oligomers targeting either splice-donor or splice-acceptor sequences was employed to systematically eliminate the expression of different exons within B7-2. Using this method, the putative IL-10 regulatory activity was mapped to an intracellular domain of B7-2. Although the B7-2 polypeptide does not possess intrinsic receptor signaling capabilities these findings suggest that it is linked to a regulatory pathway involved in controlling cytokine expression.