A synthetic peptide homologous to IL-10 functional domain induces monocyte differentiation to TGF-?+ tolerogenic dendritic cells

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We have previously demonstrated that IT9302, a nonameric peptide homologous to the C-terminal domain of human IL-10, mimics several effects of the cytokine including down-regulation of the antigen presentation machinery and increased sensitivity of tumor cells to NK-mediated lysis. In the present report, we have explored a potential therapeutic utility for IT9302 related to the ex vivo production of tolerogenic dendritic cells (DCs). Our results indicate that IT9302 impedes human monocyte response to differentiation factors and reduces antigen presentation and co-stimulatory capacity by DCs. Additionally, peptide-treated DCs show impaired capacity to stimulate T-cell proliferation and IFN-? production. IT9302 exerts its effect through mechanisms, in part, distinct from IL-10, involving STAT3 inactivation and NF-?B intracellular pathway. IT9302-treated DCs display increased expression of membrane-associated TGF-?, linked to a more effective induction of foxp3+

regulatory T cells. These