

IL-10 regulates plasmacytoid dendritic cell response to CpG-containing immunostimulatory sequences

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There is strong evidence to support a major role for CpG motif-containing oligodeoxynucleotides in the induction of Th1 response. Immunostimulatory sequences (ISS) are short oligonucleotides containing such unmethylated CpG dinucleotides that stimulate innate immune responses through Toll-like receptor-9 on B cells and plasmacytoid dendritic cell precursors (PDC). The anti-inflammatory cytokine IL-10 is predicted to be a potent inhibitor of many of the activities described for ISS, and this may impact the use of ISS in disease states characterized by elevated IL-10. As the activities of ISS on PDC are central to many clinical applications of ISS, we have studied the effects of IL-10 on PDC stimulation by three distinct classes of ISS. IL-10 inhibited cytokine production and survival of ISS-activated PDC, IL-12 induction was much more sensitive to inhibition than IFN- α induction. Within the PDC population there are cells that respond to ISS by producing either IL-12 or IFN- α , but not both cytokines. IL-12 producing PDC require costimulation through CD40 and appear more mature than IFN- α -producing PDC. The three distinct classes of ISS differed with respect to induction of PDC maturation and T cell priming capacity. IL-10 regulated PDC activation, but did not inhibit the subsequent T cell priming ability of PDC already activated by ISS.