Interleukin-12 antagonist activity of mouse interleukin-12 p40 homodimer in vitro and in vivo


Mo(p40)2 is a potent IL-12 antagonist that interacts strongly with the beta 1 subunit of the IL-12R to block binding of moIL-12 to the high-affinity mouse IL-12R. Mo(p40)2, alone or in synergy with the 2B5 mAb specific for the moIL-12 heterodimer, blocked IL-12-induced responses in vitro, Mo(p40)2 was thus used alone or with 2B5 mAb to examine the role of IL-12 in vivo, Mo(p40)2 caused a dose-dependent inhibition of both the rise in serum IFN-gamma levels in mice injected with endotoxin and the Th1-like response to immunization with KLH. Treatment with mo(p40)2 plus 2B5 anti-moIL-12 mAb also suppressed DTH responses to methylated bovine serum albumin but not specific allogeneic CTL responses in vivo. In each of these models, responses seen in mice treated with mo(p40)2 +/- 2B5 anti-moIL-12 mAb were similar to those observed in IL-12 knockout mice. Thus, mo(p40)2 can act as a potent IL-12 antagonist in vivo, as well as in vitro, and is currently being used to investigate the role of IL-12 in the pathogenesis of some Th1-associated autoimmune disorders in mice.

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