

NLM AIDSLINE

IL-10 inhibits nuclear factor-kappa B/Rel nuclear activity in CD3-stimulated human peripheral T lymphocytes.

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IL-10 markedly reduces nuclear factor (NF)-kappa B/Rel nuclear activity induced in PBMC by stimulation with the anti-CD3 mAb OKT3. The inhibition is exerted specifically on the NF-kappa B/Rel activation induced by mAb OKT3, and not that produced by PMA. As judged by supershifting the DNA-protein complexes with Abs recognizing specific components of the NF-kappa B/Rel protein family, the p50/p65 (Rel A) heterodimeric form of NF-kappa B is primarily affected. The maximal effect is observed at the IL-10 concentration of 20 U/ml. IL-10 inhibitory activity is exerted on T lymphocytes and is mediated by monocytes. Indeed, monocytes pretreated with IL-10 are able to inhibit NF-kappa B nuclear activity in purified T lymphocytes stimulated with OKT3. Soluble factors do not appear to be involved in the mechanism of inhibition. On the other hand, the up-regulation of CD80 Ag, found on monocytes obtained from PBMC incubated with OKT3, is not detected after addition of IL-10, and the anti-CD28 mAb CLB-CD28/1 restores the NF-kappa B/Rel nuclear activity in IL-10-inhibited lymphocytes. Therefore, the NF-kappa B/Rel inhibition might be ascribed to a lack of cooperation between accessory cells and T lymphocytes, resulting from down-regulation of a costimulatory molecule, such as CD80, produced by IL-10 on activated monocytes. Our results demonstrate that IL-10 can inhibit the induction of NF-kappa B/Rel nuclear activity in CD3-stimulated T lymphocytes. Since inappropriate activation of kappa B-driven genes has a physiopathologic role in a number of diseases, such as HIV infection, our findings support the possibility of using this cytokine to suppress an undesirable activation of these transcription factors.

Antigens, CD3/*IMMUNOLOGY Base Sequence Dose-Response Relationship, Immunologic Down-Regulation (Physiology)/IMMUNOLOGY Human Interleukin-10/*PHARMACOLOGY Leukocytes, Mononuclear/DRUG EFFECTS/IMMUNOLOGY/METABOLISM *Lymphocyte Transformation/DRUG EFFECTS Molecular Sequence Data Monocytes/IMMUNOLOGY Muromonab-CD3/PHARMACOLOGY NF-kappa B/*ANTAGONISTS & INHIB/BIOSYNTHESIS Support, Non-U.S. Gov't T-Lymphocytes/DRUG EFFECTS/IMMUNOLOGY/*METABOLISM Tetradecanoylphorbol Acetate/PHARMACOLOGY JOURNAL ARTICLE

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