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(54) Title: T-CELL SELECTIVE INTERLEUKIN-4 AGONISTS

(57) Abstract

The invention is directed to human IL-4 muteins numbered in accordance with wild-type IL-4 having T-cell activating activity, but having reduced endothelial cell activating activity. In particular, the invention is related to human IL-4 muteins wherein the surface-exposed residues of the D helix of the wild-type IL-4 are mutated whereby the resulting mutein causes T-cell proliferation, and causes reduced IL-6 secretion from HUVECs, relative to wild-type IL-4. This invention realizes a less toxic IL-4 mutant that allows greater therapeutic use of this interleukin. Further, the invention is directed to IL-4 muteins having single, double and triple mutations represented by the designators R121A, R121D, R121E, R121F, R121H, R121I, R121K, R121N, R121P, R121T, R121W; Y124A, Y124Q, Y124R, Y124S, Y124T; Y124A/S125A, T13D/R121E; and R121T/E122F/Y124Q, when numbered in accordance with wild-type IL-4 (His=1). The invention also includes polynucleotides coding for the muteins of the invention, vectors containing the polynucleotides, transformed host cells, pharmaceutical compositions comprising the muteins, and therapeutic methods of treatment.

