

Title (en)

MUTEINS OF INTERLEUKIN 4 SHOWING LOW-AFFINITY AND SHORT-TERM INTERACTION WITH THE COMMON γ (g) CHAIN

Title (de)

INTERLEUKIN-4 MUTEINE MIT NIEDRIGEN AFFINITÄT UND EINER KURZZEIT-WECHSELWIRKUNG MIT DER GAMMA C-KETTE

Title (fr)

MUTEINES D'INTERLEUKINE 4 PRESENTANT UNE INTERACTION A FAIBLE AFFINITE ET A COURT TERME AVEC LA CHAÎNE γ (g) COMMUNE

Publication

EP 1023446 A1 20000802 (EN)

Application

EP 98951511 A 19981012

Priority

- EP 98951511 A 19981012
- EP 9806448 W 19981012
- EP 97118219 A 19971021

Abstract (en)

[origin: EP0911401A1] Human IL-4 (IL-4), one of the small 4-helix-bundle cytokines, uses the specific IL-4 receptor α chain together with a promiscuous subunit, the common gamma chain (γ c) for transmembrane signaling. The ligand-binding properties of γ c, which are presently poorly understood, were analysed by biosensor techniques employing recombinant ectodomains gamex (γ c) and IL4-BP (α) of the receptor chains. The formation and decay of a ternary complex between solute gamex and IL-4 liganded IL4-BP could be established to exhibit a low affinity ($K_d = 3 \mu\text{M}$) as well as a short half life $t_{1/2} = 7\text{s}$. This binding affinity resulted to the major part from the interaction of gamex with IL-4 and not from a direct contact of IL4-BP and gamex, since the binary complex between solute gamex and immobilized IL-4 showed an only 50fold greater K_d of $150 \mu\text{M}$. The IL-4 residues involved in gamex binding were identified by means of an alanine-scanning mutational approach. A functional gamex binding IL-4 epitope is proposed comprising I11, N15, and Y124 as major determinants. Even IL-4 variants which bind gamex 300fold weaker than IL-4 with a dissociation half life $t_{1/2}$ of less than 1s, retained a substantial T-cell proliferative activity. These findings suggest that low affinity gamma c binding and short half lives of the heterodimeric α/γ c receptor complex are sufficient for initiating IL-4 dependent signal transduction.

IPC 1-7

C12N 15/24; **C12N 1/21**; **C07K 14/54**

IPC 8 full level

C12N 15/09 (2006.01); **C07K 14/54** (2006.01); **C12N 1/15** (2006.01); **C12N 1/19** (2006.01); **C12N 1/21** (2006.01); **C12N 5/10** (2006.01); **C12N 15/24** (2006.01); **C12P 21/00** (2006.01)

CPC (source: EP)

C07K 14/5406 (2013.01)

Citation (search report)

See references of WO 9920765A1

Designated contracting state (EPC)

DE ES FR GB IT

DOCDB simple family (publication)

EP 0911401 A1 19990428; AR 016147 A1 20010620; AU 9749598 A 19990510; EP 1023446 A1 20000802; JP 2001520040 A 20011030; WO 9920765 A1 19990429; ZA 989540 B 19990422

DOCDB simple family (application)

EP 97118219 A 19971021; AR P980105234 A 19981020; AU 9749598 A 19981012; EP 9806448 W 19981012; EP 98951511 A 19981012; JP 2000517085 A 19981012; ZA 989540 A 19981020