

Gene Section

Mini Review

IL3RA (Interleukin-3 Receptor alpha)

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Identity

Other names: CD123

HGNC (Hugo): IL3RA

Location: Xp22.3; Yp13.3

DNA/RNA

Description

The gene encoding interleukin-3 receptor is located in the pseudoautosomal region (PAR) at the end of the short arm of the X and Y chromosomes. The IL-3R alpha chain gene contains twelve exons and eleven introns that span an area of approximately 40 Kb. It is positioned near (190 Kbp) to the gene encoding for GM-CSFR alpha chain. Both the IL-3R alpha and GM-CSFR alpha genes display a similar structural organization, suggesting a common evolutionary origin for both genes.

Protein

Description

The IL-3R alpha gene encodes a type I transmembrane protein of 41.3 kDa. The IL-3R alpha precursor chain protein is composed by 378 amino acids. Cleavage of the 18 amino acid signal peptide yields a mature polypeptide chain of 360 amino acids, containing a 288 amino acid extracellular domain involved in IL-3 binding, a 20 amino acid transmembrane domain and a short cytoplasmic tail of 52 amino acids. The extracellular domain is composed by two regions: a N-terminal region of about 100 amino acids, whose sequence exhibits a great similarity to equivalent regions of the GM-CSF and IL-5 receptor alpha-chains; a region, proximal to the transmembrane

domain, that contains four conserved cysteine residues and a WSXWS motif, common to other members of this cytokine receptor family. The ligand binding domain consists of about 200 amino acid residue cytokine receptor motifs (CRMs) made up of two Ig-like folding domains. The IL-3R alpha chain is highly glycosylated: six potential N-glycosylation sites have been detected in the extracellular domain. Due to the high glycosylation, the natural IL-3R alpha protein exhibits a MW of about 70 kDa. N-glycosylation is necessary for both ligand binding and receptor signaling. The IL-3R alpha cytoplasmic tail contains a short proline motif, similar to box 1 of the IL-3R beta common chain.

Expression

At the level of the hematopoietic system IL-3R alpha expression was described on bone marrow CD34+ cells (including primitive multipotential and committed progenitors), granulocytes, monocytes/macrophages, megakaryocytes and B-lymphocytes. Although the IL-3R alpha is expressed on the large majority of progenitor cells, it does not seem to be expressed on the stem cell fraction. The large majority of CD34+ cells possess IL-3R alpha, but its expression is lost during the initial steps of erythroid differentiation, while its expression is maintained up to terminal stages of granulo-monocytic differentiation. The IL-3R alpha is also a distinctive marker of the "lymphoid" dendritic cells present in peripheral blood. IL-3R alpha expression has also been described in several cell types outside the hemopoietic system, including endothelial cells, fibroblasts and smooth muscle cells.

Localisation

Functional mature IL-3R alpha is located at the level of the plasma membrane where it forms a molecular complex with the IL-3R beta chain.

Function

IL-3R alpha function can be defined by the activity of its ligand interleukin-3. IL-3 is a multipotent cytokine that promotes the development of hemopoietic progenitors into cells of the erythroid, myeloid and lymphoid lineages. In in vitro colony forming assays IL-3 supports the colony formation by virtually all types of hemopoietic progenitors, including CFU-GEMM, CFU-GM, CFU-G, CFU-M, CFU-Mk, CFU-E and BFU-E.

Mutations

Note

No mutations of the IL-3Ra gene have been reported in hematological and non hematological human malignancies. Elevated IL-3Ra expression has been reported in about 45% of patients with acute myeloid leukemia and in 40% of patients with acute B lymphoid leukemia. An high IL-3Ra expression has been reported also in hairy cell leukemia.

References

Itoh N, Yonehara S, Schreurs J, Gorman DM, Maruyama K, Ishii A, Yahara I, Arai K, Miyajima A. Cloning of an interleukin-3 receptor gene: a member of a distinct receptor gene family. *Science*. 1990 Jan 19;247(4940):324-7

Kitamura T, Sato N, Arai K, Miyajima A. Expression cloning of the human IL-3 receptor cDNA reveals a shared beta subunit for the human IL-3 and GM-CSF receptors. *Cell*. 1991 Sep 20;66(6):1165-74

Kremer E, Baker E, D'Andrea RJ, Slim R, Phillips H, Moretti PA, Lopez AF, Petit C, Vadas MA, Sutherland GR. A cytokine receptor gene cluster in the X-Y pseudoautosomal region? *Blood*. 1993 Jul 1;82(1):22-8

Milatovich A, Kitamura T, Miyajima A, Francke U. Gene for the alpha-subunit of the human interleukin-3 receptor (IL3RA) localized to the X-Y pseudoautosomal region. *Am J Hum Genet*. 1993 Nov;53(5):1146-53

Kosugi H, Nakagawa Y, Hotta T, Saito H, Miyajima A, Arai K, Yokota T. Structure of the gene encoding the alpha subunit of the human interleukin 3 receptor. *Biochem Biophys Res Commun*. 1995 Mar 8;208(1):360-7

Stomski FC, Sun Q, Bagley CJ, Woodcock J, Goodall G, Andrews RK, Berndt MC, Lopez AF. Human interleukin-3 (IL-3) induces disulfide-linked IL-3 receptor alpha- and beta-chain heterodimerization, which is required for receptor activation but not high-affinity binding. *Mol Cell Biol*. 1996 Jun;16(6):3035-46

Klein BK, Feng Y, McWherter CA, Hood WF, Paik K, McKearn JP. The receptor binding site of human interleukin-3 defined by mutagenesis and molecular modeling. *J Biol Chem*. 1997 Sep 5;272(36):22630-41

Guthridge MA, Stomski FC, Barry EF, Winnall W, Woodcock JM, McClure BJ, Dottore M, Berndt MC, Lopez AF. Site-specific serine phosphorylation of the IL-3 receptor is required for hemopoietic cell survival. *Mol Cell*. 2000 Jul;6(1):99-108

Jordan CT, Upchurch D, Szilvassy SJ, Guzman ML, Howard DS, Pettigrew AL, Meyerrose T, Rossi R, Grimes B, Rizzieri DA, Luger SM, Phillips GL. The interleukin-3 receptor alpha chain is a unique marker for human acute myelogenous leukemia stem cells. *Leukemia*. 2000 Oct;14(10):1777-84

Militi S, Riccioni R, Parolini I, Sposi NM, Samoggia P, Pelosi E, Testa U, Peschle C. Expression of interleukin 3 and granulocyte-macrophage colony-stimulating factor receptor common chain betac, betaIT in normal haematopoiesis: lineage specificity and proliferation-independent induction. *Br J Haematol*. 2000 Nov;111(2):441-51

Carr PD, Gustin SE, Church AP, Murphy JM, Ford SC, Mann DA, Woltring DM, Walker I, Ollis DL, Young IG. Structure of the complete extracellular domain of the common beta subunit of the human GM-CSF, IL-3, and IL-5 receptors reveals a novel dimer configuration. *Cell*. 2001 Jan 26;104(2):291-300

Muñoz L, Nomdedéu JF, López O, Carnicer MJ, Bellido M, Aventin A, Brunet S, Sierra J. Interleukin-3 receptor alpha chain (CD123) is widely expressed in hematologic malignancies. *Haematologica*. 2001 Dec;86(12):1261-9

Evans CA, Ariffin S, Pierce A, Whetton AD. Identification of primary structural features that define the differential actions of IL-3 and GM-CSF receptors. *Blood*. 2002 Nov 1;100(9):3164-74

Testa U, Riccioni R, Militi S, Coccia E, Stellacci E, Samoggia P, Latagliata R, Mariani G, Rossini A, Battistini A, Lo-Coco F, Peschle C. Elevated expression of IL-3Ralpha in acute myelogenous leukemia is associated with enhanced blast proliferation, increased cellularity, and poor prognosis. *Blood*. 2002 Oct 15;100(8):2980-8

Akagawa E, Muto A, Arai K, Watanabe S. Analysis of the 5' promoters for human IL-3 and GM-CSF receptor alpha genes. *Biochem Biophys Res Commun*. 2003 Jan 10;300(2):600-8

Wong S, McLaughlin J, Cheng D, Shannon K, Robb L, Witte ON. IL-3 receptor signaling is dispensable for BCR-ABL-induced myeloproliferative disease. *Proc Natl Acad Sci U S A*. 2003 Sep 30;100(20):11630-5

Barreda DR, Hanington PC, Belosevic M. Regulation of myeloid development and function by colony stimulating factors. *Dev Comp Immunol*. 2004 May 3;28(5):509-54

Riccioni R, Rossini A, Calabrò L, Diverio D, Pasquini L, Lococo F, Peschle C, Testa U. Immunophenotypic features of acute myeloid leukemias overexpressing the interleukin 3 receptor alpha chain. *Leuk Lymphoma*. 2004 Aug;45(8):1511-7

Testa U, Riccioni R, Diverio D, Rossini A, Lo Coco F, Peschle C. Interleukin-3 receptor in acute leukemia. *Leukemia*. 2004 Feb;18(2):219-26

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