

Gene Section

Review

IL22 (interleukin 22)

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Identity

Other names: IL-21, IL-22, IL-D110, IL-TIF, IL21, ILTIF, MGC79382, MGC79384, TIFIL-23, TIFa, zcyto18

HGNC (Hugo): IL22

Location: 12q15

DNA/RNA

Description

The gene spans a region of 5.2 kb and the coding part is divided into five exons.

Transcription

Only one type of transcript has been described. The 540-nucleotide transcript encodes a protein of 179 amino acid residues. The first and last exons are partially untranslated.

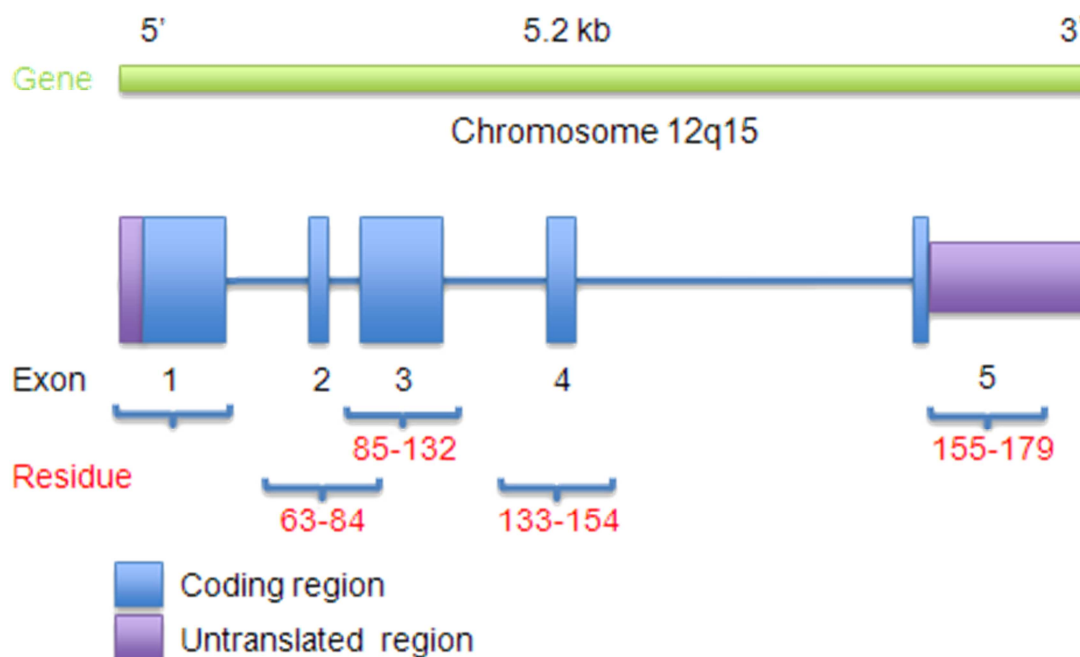
Pseudogene

None described so far.

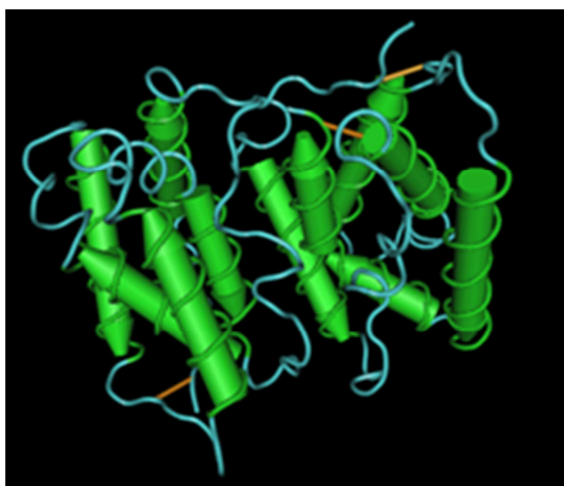
Protein

Description

IL-22 is a cytokine composed of 179 residues.



Representation of the IL22 gene organization. Interleukin 22 gene and RNA structure.



Crystal structure of IL-22 at 2.6 Å resolution. Adapted from PDB (access number: 1YKB).

Expression

Interleukin 22 (IL-22) is a cytokine that was originally labeled IL-10-related T-cell-derived inducible factor. IL-22 belongs to a family of IL-10-related proteins that includes IL-19, IL-20, IL-24/MDA-7, IL-26/AK155, IL-28 and IL-29. IL-22 production is inducible by IL-9 in T-lymphocytes and is known to exert its function by binding to a heterodimeric receptor complex composed of IL-22R1 and IL-10R2. However, more recently, it has been shown that IL-22 can bind the homodimeric receptor composed of the IL-22RA1 chain. IL-22 is normally produced by natural killer cells and Th-17 T cells, a functional distinct population of human helper T cells recently identified as an important source of IL-22.

Localisation

IL-22 is a secreted protein.

Function

IL-22 exerts its biological effects through the IL-22 receptor/signaling complex, which expression is largely restricted to epithelial cells. Activation of this complex leads to the activation of various cellular signaling pathways, with the JAK/STAT and MAPK pathways being the best characterized. IL-22, as a Th1 cytokine, has been shown to play important roles in mediating inflammation and the wound healing process.

Mutations

Note

No mutation has been reported thus far.

Implicated in

ALK-positive anaplastic large cell lymphoma (ALK+ALCL)

Disease

Anaplastic lymphoma kinase (ALK)-positive anaplastic large-cell lymphoma (ALCL), or ALK+ALCL, is a

specific type of non-Hodgkin lymphoma characterized by the T/null-cell immunophenotype, consistent expression of CD30 and reciprocal chromosomal translocations involving the ALK gene. In most cases, the chromosomal translocation is that of the t(2;5)(p23;q35) type, which leads to the juxtaposition of the nucleophosmin (NPM) gene at 5q35 to the ALK gene at 2p23. Mounting evidence suggests that the resulting oncogenic fusion protein, NPM-ALK, plays crucial roles in the pathogenesis of these tumors. Patients with ALK+ALCL are typically treated with combination chemotherapy containing doxorubicin. ALK+ALCL represents the second most common pediatric lymphoid cancer. The prognosis of pediatric patients is far better than that of adult patients.

Dien Bard et al. have shown that IL-22 secreted by ALK+ALCL lymphoma cells stimulates STAT3 activation and the growth of these cells. Blocking the IL-22 signaling pathway using an IL-22-neutralizing antibody has been shown to significantly decrease the growth of ALK+ALCL cells in-vitro.

Cytogenetics

t(2;5)(p23;q35) in most ALK+ALCL patients; other translocation variants have been described.

Hybrid/Mutated gene

NPM-ALK

Abnormal protein

NPM-ALK

ALK negative anaplastic large cell lymphoma (ALK-ALCL)

Disease

ALK-ALCL is a subtype of ALCL characterized by a strong and homogeneous expression of CD30. These cells don't express the ALK protein. ALK-ALCL has a less favourable prognosis than ALK+ALCL. Patients with ALK-ALCL are usually older than in ALK+ALCL, 58 versus 34 years, and present a male predominance. Patients are treated with standard CHOP (cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone) chemotherapy. By subtractive genomic hybridization, Lamant et al. have identified that IL-22 transcript is over-expressed in ALK-ALCL when compared to ALK+ALCL. However, the authors did not investigate the biological significance of this observation.

Lung cancer

Disease

There are two major types of lung cancer. The non-small cell lung cancer (NSCLC) is the most common type of lung cancer and is divided into three major subtypes: squamous cell carcinoma, adenocarcinoma and large cell carcinoma. Small cell lung cancer represents the second type of lung cancer and is also subdivided in three different subgroups: small cell carcinoma, mixed small cell/large cell and combined small cell carcinoma. More than 90% of lung cancers in

men, and at least 70% in women are directly caused by cigarette smoking. Treatment is dependent on the lung cancer type and may involve surgery, radiation therapy and chemotherapy. The overall survival after 5 years for men and women is less than 20%. Evidence from both in vivo and in vitro experiments implicates IL-22 as a player in the development of non-small cell lung carcinoma (NSCLC) (Zhang et al., 2008). The authors have demonstrated that NSCLC patients have high levels of IL-22 protein in their serum when compared to normal individuals. Moreover, in NSCLC cells exogenous addition of recombinant IL-22 cytokine induces pro-survival pathways, including STAT3 signaling, and increase cell proliferation. They have also showed that IL-22 protects cancer cells from serum starvation and chemotherapeutic drug-induced apoptosis. In a xenograft model of NSCLC they have showed that down-regulation of IL-22 production significantly decreases the volume of the lung tumors.

Vitiligo

Disease

Vitiligo is characterized by the loss skin pigmentation. It's a multifactorial and polygenic disease. There are two forms of vitiligo, the segmental and the non-segmental form that are related to the pattern of the lesion. The disease affects both men and women. Vitiligo has been associated with autoimmune and inflammatory disorders, but the exact origin and causes are unknown. There is no cure for vitiligo to date, but treatment is available to slow down the depigmentation. In a recent study by Rätsep et al., it has been demonstrated that IL-22 mRNA and protein levels are associated with the disease. The authors have suggested that IL-22 may induce the inflammation process at the origin of the destruction of the melanocyte leading to skin depigmentation.

Psoriasis

Note

Recently, Ma et al. have demonstrated in a mouse model of psoriasis, that IL-22 is a key player in the development of this disease. Antibodies that neutralized IL-22 were found to prevent the development of psoriasis-like disease, reducing thickening of the skin, inflammatory infiltrates, and expression of Th17 cytokines. On the other hand, injection of IL-22 into the skin of normal mice induced the expression of genes associated with the development of psoriasis-like lesions. These data have revealed a new and promising approach for the treatment of psoriasis by antagonizing IL-22 activity.

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