IL7R gene

interleukin 7 receptor

Normal Function

The *IL7R* gene provides instructions for making a protein called interleukin 7 (IL-7) receptor alpha chain. This protein is one piece of both the IL-7 receptor and the thymic stromal lymphopoietin (TSLP) receptor. These receptors are embedded in the cell membrane of immune system cells. The IL-7 receptor is found in B cells and T cells as well as the early blood-forming cells that give rise to them. The TSLP receptor is found in several types of immune cells, including B cells, T cells, monocytes, and dendritic cells. These cells identify foreign substances and defend the body against infection and disease.

At the cell surface, the IL-7 receptor interacts with a protein called IL-7. IL-7 is a cytokine, which is a protein that regulates the activity of immune system cells. The receptor and cytokine fit together like a lock and its key, triggering a series of chemical signals inside the cell. In early blood-forming cells, signaling through the IL-7 receptor ensures the development of mature B cells and T cells. IL-7 receptor signaling also stimulates the later growth and division (proliferation) and survival of these cells.

Similarly, the TSLP receptor interacts with the cytokine TSLP. Attachment of TSLP to its receptor triggers a set of signals that support proliferation and maturation of a variety of immune system cells.

Health Conditions Related to Genetic Changes

Multiple sclerosis

A common variation of the *IL-7R* gene increases the risk of developing multiple sclerosis. This condition affects the brain and spinal cord (central nervous system), causing muscle weakness, poor coordination, numbness, and a variety of other health problems. The genetic variation involved in multiple sclerosis affects a single protein building block (amino acid) in the IL-7 receptor alpha chain, specifying the amino acid isoleucine at position 244 instead of the amino acid threonine (written as Thr244Ile). The IL-7 receptor that contains this version of the alpha chain is not embedded in the cell surface but is instead found inside the cell. It is not clear if this alpha chain variant affects the TSLP receptor.

Because the *IL7R* gene is involved in regulation of the immune system, changes in it might be involved in the autoimmune response and inflammation that damage nerves and the protective coating surrounding them (the myelin sheath), leading to the signs and symptoms of multiple sclerosis. (Autoimmunity occurs when the immune system malfunctions and attacks the body's own tissues and organs, in this case tissues of

the nervous system.) However, it is unclear exactly what role the *IL-7R* gene variant plays in development of multiple sclerosis. It is likely that a combination of genetic and environmental factors is involved.

Omenn syndrome

Other disorders

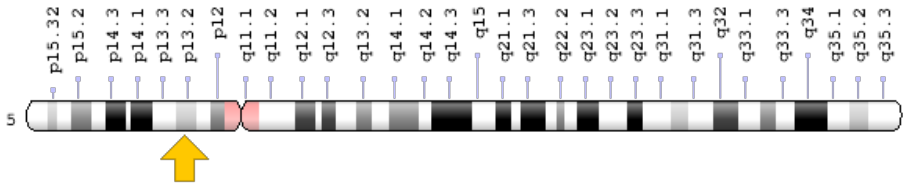
Mutations in the *IL7R* gene can cause a form of severe combined immunodeficiency (SCID), in which affected individuals have decreased immune function and are prone to recurrent and persistent infections. Affected individuals with *IL7R* gene mutations have few or no T cells but normal numbers of B cells and another type of immune cell called NK cells. This form of the condition is called $T^-B^+NK^+$ SCID. Many *IL7R* gene mutations that cause SCID prevent the production of the IL-7 receptor alpha chain, which impairs IL-7 receptor and TSLP receptor signaling. Without this signaling, development of T cells is disrupted. A lack of T cells reduces the immune system's ability to fight infections, leading to recurrent infections in people with $T^-B^+NK^+$ SCID.

Mutations in the *IL7R* gene can also cause cancers of blood-forming cells, specifically B-cell acute lymphoblastic leukemia (ALL), which is characterized by elevated numbers of B cells in the blood, and T-cell ALL, characterized by elevated numbers of T cells. The mutations associated with these cancers lead to an altered IL-7 receptor alpha chain. With this alteration, signaling pathways like those triggered by the IL-7 receptor or the TSLP receptor are constantly turned on (constitutively active) even without cytokine interaction. Constant signaling increases proliferation and survival of B cells or T cells, leading to ALL.

Chromosomal Location

Cytogenetic Location: 5p13.2, which is the short (p) arm of chromosome 5 at position 13.2

Molecular Location: base pairs 35,856,891 to 35,879,603 on chromosome 5 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CD127
- CD127 antigen
- CDW127
- IL-7 receptor subunit alpha
- IL-7R-alpha
- IL-7R subunit alpha
- IL-7RA
- IL7RA
- IL7RA_HUMAN
- ILRA
- interleukin 7 receptor alpha chain
- interleukin 7 receptor isoform H5-6
- interleukin-7 receptor subunit alpha
- interleukin-7 receptor subunit alpha precursor

Additional Information & Resources

Educational Resources

- Holland-Frei Cancer Medicine (sixth edition, 2003): Interleukin-7
  https://www.ncbi.nlm.nih.gov/books/NBK13387/
- Immunobiology: The Immune System in Health and Disease (fifth edition, 2001): Generation of Lymphocytes In Bone Marrow and Thymus
  https://www.ncbi.nlm.nih.gov/books/NBK27123/
- National Cancer Institute: General Information about Childhood Acute Lymphoblastic Leukemia
  https://www.cancer.gov/types/leukemia/patient/child-all-treatment-pdq

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28IL7R%5BTIAB%5D%29+OR+%28interleukin+7+receptor%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- INTERLEUKIN 7 RECEPTOR
  http://omim.org/entry/146661

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/IL7RID51090ch5p13.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=IL7R%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:6024
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3575
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3575
- UniProt
  https://www.uniprot.org/uniprot/P16871

Sources for This Summary

- Akashi K, Kondo M, Weissman IL. Role of interleukin-7 in T-cell development from hematopoietic stem cells. Immunol Rev. 1998 Oct;165:13-28. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9850848
- Corfe SA, Paige CJ. The many roles of IL-7 in B cell development; mediator of survival, proliferation and differentiation. Semin Immunol. 2012 Jun;24(3):198-208. doi: 10.1016/j.smim.2012.02.001. Epub 2012 Mar 14. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22421572
- Giliani S, Mori L, de Saint Basile G, Le Deist F, Rodriguez-Perez C, Forino C, Mazzolari E, Dupuis S, Elhasid R, Kessel A, Galambrun C, Gil J, Fischer A, Etzioni A, Notarangelo LD. Interleukin-7 receptor alpha (IL-7Ralpha) deficiency: cellular and molecular bases. Analysis of clinical, immunological, and molecular features in 16 novel patients. Immunol Rev. 2005 Feb;203: 110-26. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15661025
- Gregory SG, Schmidt S, Seth P, Oksenberg JR, Hart J, Prokop A, Caillier SJ, Ban M, Goris A, Barcellos LF, Lincoln R, McCauley JL, Sawcer SJ, Compston DA, Dubois B, Hauser SL, Garcia-Blanco MA, Pericak-Vance MA, Haines JL; Multiple Sclerosis Genetics Group. Interleukin 7 receptor alpha chain (IL7R) shows allelic and functional association with multiple sclerosis. Nat Genet. 2007 Sep;39(9):1083-91. Epub 2007 Jul 29.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17660817
- He R, Geha RS. Thymic stromal lymphopoietin. Ann N Y Acad Sci. 2010 Jan;1183:13-24. doi: 10.1111/j.1749-6632.2009.05128.x. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20146705
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2895428/

- OMIM: INTERLEUKIN 7 RECEPTOR
  http://omim.org/entry/146661
- Lundmark F, Duvefelt K, Iacobaeus E, Kockum I, Wallström E, Khademi M, Oturai A, Ryder LP, Saarela J, Harbo HF, Celius EG, Salter H, Olsson T, Hillert J. Variation in interleukin 7 receptor alpha chain (IL7R) influences risk of multiple sclerosis. Nat Genet. 2007 Sep;39(9):1108-13. Epub 2007 Jul 29.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17660816
- Puel A, Ziegler SF, Buckley RH, Leonard WJ. Defective IL7R expression in T(-)B(+)NK(+) severe combined immunodeficiency. Nat Genet. 1998 Dec;20(4):394-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9843216
- Shochat C, Tal N, Bandapalli OR, Palmi C, Ganmore I, te Kronnie G, Cario G, Cazzaniga G, Kulozik AE, Stanulla M, Schrappe M, Biondi A, Basso G, Bercovich D, Muckenthaler MU, Izraeli S. Gain-of-function mutations in interleukin-7 receptor-α (IL7R) in childhood acute lymphoblastic leukemias. J Exp Med. 2011 May 9;208(5):901-8. doi: 10.1084/jem.20110580. Epub 2011 May 2. Erratum in: J Exp Med. 2011 May 9;208(5):preceding 901. J Exp Med. 2011 Jun 6;208(6):1333.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21536738
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3092356/
- Zenatti PP, Ribeiro D, Li W, Zuurbier L, Silva MC, Paganin M, Tritapoe J, Hixon JA, Silveira AB, Cardoso BA, Sarmento LM, Correia N, Toribio ML, Kobarg J, Horstmann M, Pieters R, Brandalise SR, Ferrando AA, Meijerink JP, Durum SK, Yunes JA, Barata JT. Oncogenic IL7R gain-of-function mutations in childhood T-cell acute lymphoblastic leukemia. Nat Genet. 2011 Sep 4;43(10):932-9. doi: 10.1038/ng.924.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21892159

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