

IL21 binds IL21R:JAK1

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 90

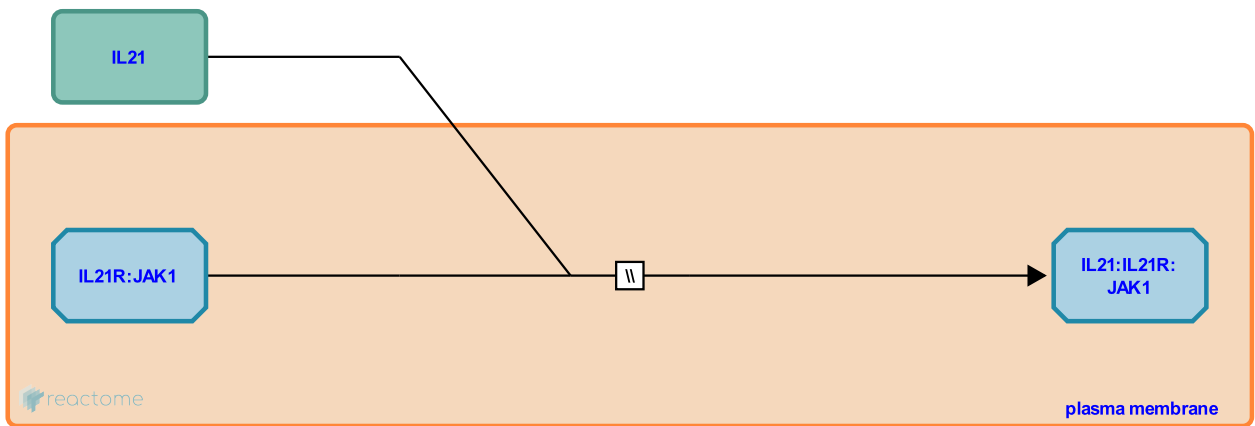
This document contains 1 reaction ([see Table of Contents](#))

IL21 binds IL21R:JAK1 ↗

Stable identifier: R-HSA-9005980

Type: omitted

Compartments: extracellular region, plasma membrane



Interleukin-21 (IL21) is a pleiotropic cytokine with four alpha-helical bundles. It is produced primarily by natural killer T cells, T follicular helper cells and TH17 cells, with lower levels of production by numerous other populations of lymphohaematopoietic cells (Spolski & Leonard 2014). IL21 binds Interleukin-21 receptor (IL21R, NILR) and Cytokine receptor common subunit gamma (IL2RG, GammaC).

IL21R has significant homology with the class I cytokine receptors Interleukin-2 receptor subunit beta (IL2RB) and Interleukin-4 receptor subunit alpha (IL4R) and was predicted to similarly form a complex with IL2RG. IL21R dimers can weakly bind and signal in response to IL21 but IL21 generates a much stronger response when IL21R is combined with IL2RG, which is required for a fully signaling capable IL21 receptor complex (Ozaki et al. 2000, Asao et al. 2001, Habib et al. 2002). IL21R can bind Janus kinase 1 (JAK1) (Ozaki et al. 2000) but IL2RG is required for IL21 induced signaling (Asao et al. 2001). The heteromeric IL21 receptor complex can activate JAK1, JAK3, Signal transducer and activator of transcription 1 (STAT1), STAT3, STAT4 and STAT5, depending on the cell type. In cultured T-cells IL21 induced phosphorylation of JAK1, JAK3, STAT1, STAT3 and weakly STAT5 (Asao et al. 2001). In primary CD4+ T cells IL21 induced the phosphorylation of STAT1 and STAT3 but not STAT5, whereas IL2 induced the phosphorylation of STAT5 and STAT1 but not STA3 (Bennet et al. 2003). IL21 stimulation of primary splenic B cells and the pro-B-cell line Ba-F3 induced the activation of JAK1, JAK3 and STAT5 (Habib et al. 2002). In primary human NK cells or the NK cell line NK-92, IL21 induced the activation of STAT1, STAT3, and STAT4 but not STAT5 (Strengell et al. 2002, 2003). IL21 activated STAT1 and STAT3 in human monocyte-derived macrophages (Valli res & Girard 2017). This is a black-box event because the pre-association of IL21R with JAK1 is inferred from the constitutive association of JAKs with other interleukin receptor subunits such as IL2R.

Literature references

Kikly, K., Michalovich, D., Young, PR., Ozaki, K., Leonard, WJ. (2000). Cloning of a type I cytokine receptor most related to the IL-2 receptor beta chain. *Proc. Natl. Acad. Sci. U.S.A.*, 97, 11439-44. ↗

Editions

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