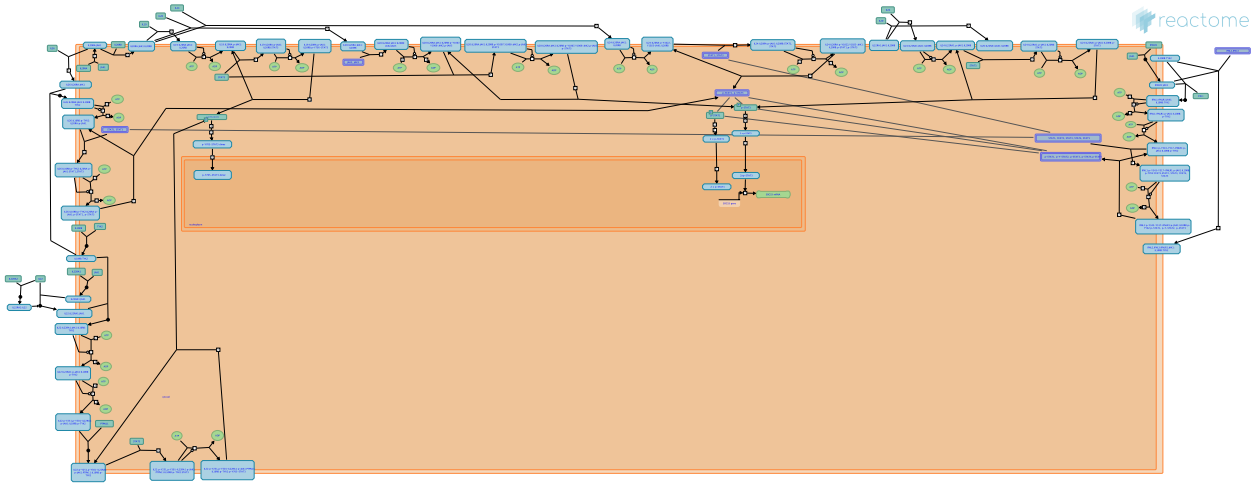
Interleukin-20 family signaling



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European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

25/09/2021

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. ↗

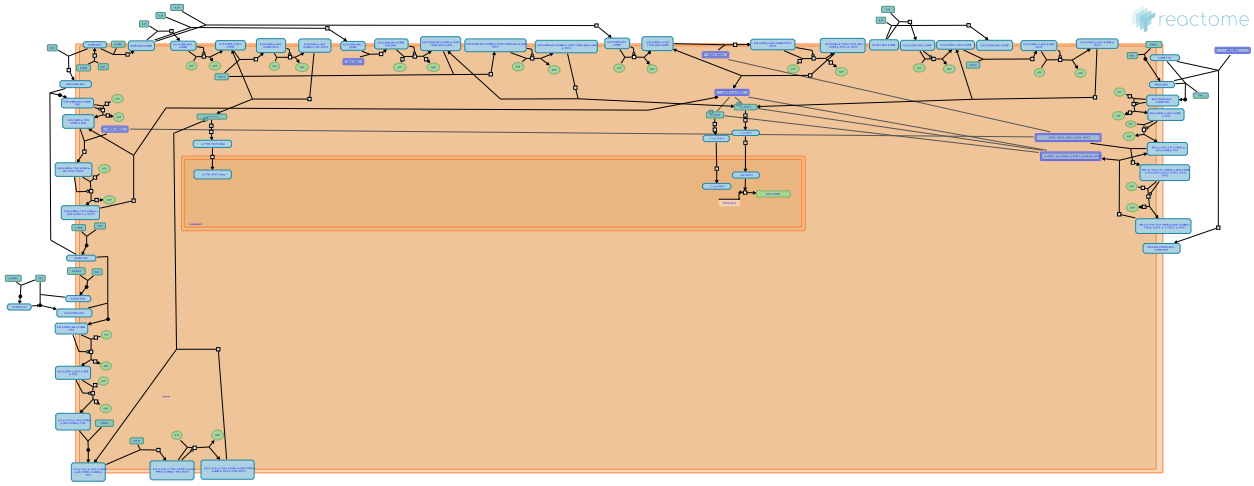
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Interleukin-20 family signaling ↗

Stable identifier: R-HSA-8854691



The interleukin 20 (IL20) subfamily comprises IL19, IL20, IL22, IL24 and IL26. They are members of the larger IL10 family, but have been grouped together based on their usage of common receptor subunits and similarities in their target cell profiles and biological functions. Members of the IL20 subfamily facilitate the communication between leukocytes and epithelial cells, thereby enhancing innate defence mechanisms and tissue repair processes at epithelial surfaces. Much of the understanding of this group of cytokines is based on IL22, which is the most studied member (Rutz et al. 2014, Akdis M et al. 2016, Longsdon et al. 2012).

Literature references

Akdis, M., Aab, A., Altunbulakli, C., Azkur, K., Costa, RA., Crameri, R. et al. (2016). Interleukins (from IL-1 to IL-38), interferons, transforming growth factor β, and TNF-α: Receptors, functions, and roles in diseases. *J. Allergy Clin. Immunol., 138*, 984-1010. ↗

Rutz, S., Wang, X., Ouyang, W. (2014). The IL-20 subfamily of cytokines--from host defence to tissue homeostasis. *Nat. Rev. Immunol., 14*, 783-95. ↗

Logsdon, NJ., Deshpande, A., Harris, BD., Rajashankar, KR., Walter, MR. (2012). Structural basis for receptor sharing and activation by interleukin-20 receptor-2 (IL-20R2) binding cytokines. *Proc. Natl. Acad. Sci. U.S.A., 109*, 12704-9. ↗

Editions

2014-06-04	Authored	Jupe, S.
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2016-01-28	Reviewed	Meldal, BH.
2017-11-15	Reviewed	Datta, SK.

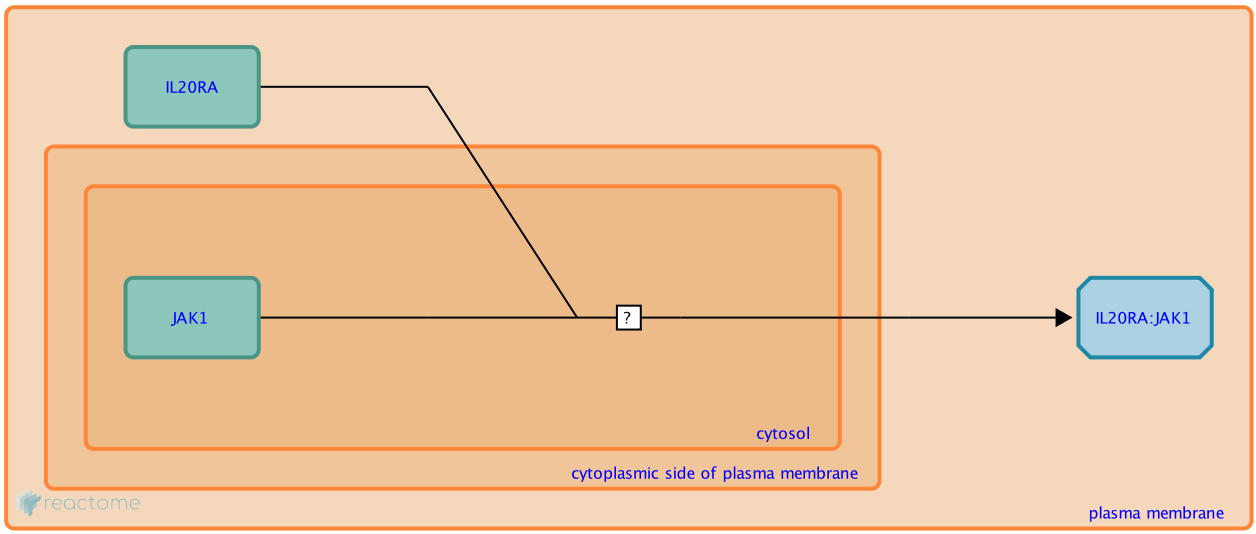
JAK1 binds IL20RA ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987039

Type: uncertain

Compartments: cytosol, plasma membrane



Tyrosine protein kinase JAK1 (JAK1) binds Interleukin-20 receptor subunit alpha (IL20RA). JAK1 coimmunoprecipitates with several class II receptor complexes including Interferon gamma receptor 1 (IFNGR1), Interferon alpha/beta receptor 2 (IFNAR2), Interferon lambda receptor 1 (IFNLR1), Interleukin-10 receptor subunit alpha (IL10RA), Interleukin-22 receptor subunit alpha 1 (IL22RA1) and Interleukin-20 receptor subunit alpha (IL20RA), leading to the suggestion that Class II receptors may have a common sequence motif for JAK recognition (Ferrao et al. 2016). This is a black box event because JAK1 binding to IL20RA is inferred from binding to related receptors and subsequent JAK/STAT signaling events (Ferrao et al 2016, Hann et al. 2006, Murakami et al. 1991).

Followed by: IL26 binds IL20RA:JAK1, IL20RA binds IL20RB

Literature references

Ferrao, R., Wallweber, HJ., Ho, H., Tam, C., Franke, Y., Quinn, J. et al. (2016). The Structural Basis for Class II Cytokine Receptor Recognition by JAK1. *Structure, 24*, 897-905. ↗

Haan, C., Kreis, S., Margue, C., Behrmann, I. (2006). Jaks and cytokine receptors--an intimate relationship. *Biochem. Pharmacol., 72*, 1538-46. ↗

Murakami, M., Narazaki, M., Hibi, M., Yawata, H., Yasukawa, K., Hamaguchi, M. et al. (1991). Critical cytoplasmic region of the interleukin 6 signal transducer gp130 is conserved in the cytokine receptor family. *Proc Natl Acad Sci U S A, 88*, 11349-53. ↗

Editions

2017-03-16	Authored	Duenas, C.
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2017-11-15	Reviewed	Datta, SK.

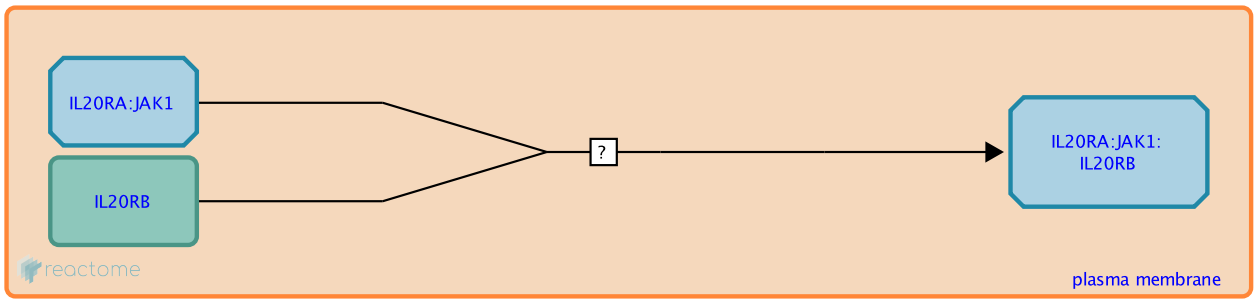
IL20RA binds IL20RB ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-448744

Type: uncertain

Compartments: plasma membrane, cytosol



Interleukin-20 receptor A (IL20RA) binds to Interleukin-20 receptor B (IL20RB) (Blumberg et al. 2001, Parrish-Novak et al. 2002, Logsdon et al. 2012, Rutz et al. 2014, Dumoutier et al. 2001).

This is a black box event because it is not clear whether the dimeric receptor can form in the absence of ligand.

Preceded by: JAK1 binds IL20RA

Followed by: IL20 binds IL20RA:JAK1:IL20RB, IL24 binds IL20RA:JAK1:IL20RB, IL19 binds IL20RA:JAK1:IL20RB

Literature references

Dumoutier, L., Leemans, C., Lejeune, D., Kotenko, SV., Renauld, JC. (2001). Cutting edge: STAT activation by IL-19, IL-20 and mda-7 through IL-20 receptor complexes of two types. *J Immunol, 167*, 3545-9. ↗

Blumberg, H., Conklin, D., Xu, WF., Grossmann, A., Brender, T., Carollo, S. et al. (2001). Interleukin 20: discovery, receptor identification, and role in epidermal function. *Cell, 104*, 9-19. ↗

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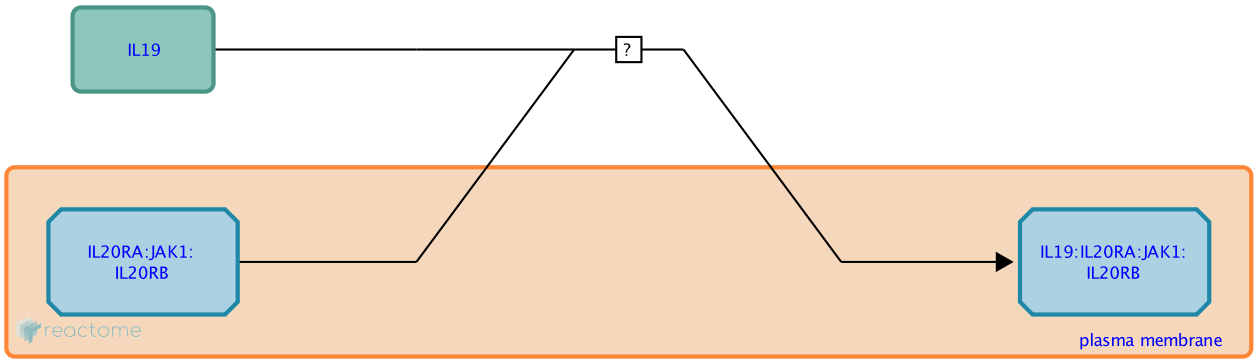
IL19 binds IL20RA:JAK1:IL20RB ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-448728

Type: uncertain

Compartments: extracellular region, plasma membrane, cytosol



Interleukin-19 (IL19) binds a heterodimeric receptor complex that consists of Interleukin-20 Receptor subunit alpha (IL20RA) associated with Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB).

Interleukin-20 receptor A (IL20RA) and Interleukin-20 receptor B (IL20RB) form a receptor complex for Interleukin-19 (IL19) (and Interleukin-20 (IL20) and Interleukin-24 (IL24)) (Gallagher et al. 2000, Blumberg et al. 2001, Parrish-Novak et al. 2002, Logsdon et al. 2012, Rutz et al. 2014, Pletnev et al. 2003).

This is a black box event because it is not clear whether the dimeric receptor can form in the absence of ligand.

Preceded by: IL20RA binds IL20RB

Followed by: IL19:IL20RA:JAK1:IL20RB phosphorylates JAK1

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Logsdon, NJ., Deshpande, A., Harris, BD., Rajashankar, KR., Walter, MR. (2012). Structural basis for receptor sharing and activation by interleukin-20 receptor-2 (IL-20R2) binding cytokines. *Proc. Natl. Acad. Sci. U.S.A., 109*, 12704-9. ↗

Gallagher, G., Dickensheets, H., Eskdale, J., Izotova, LS., Mirochnitchenko, OV., Peat, JD. et al. (2000). Cloning, expression and initial characterization of interleukin-19 (IL-19), a novel homologue of human interleukin-10 (IL-10) . *Genes Immun., 1*, 442-50. ↗

Pletnev, S., Magracheva, E., Kozlov, S., Tobin, G., Kotenko, SV., Wlodawer, A. et al. (2003). Characterization of the recombinant extracellular domains of human interleukin-20 receptors and their complexes with interleukin-19 and interleukin-20. *Biochemistry, 42*, 12617-24. ↗

Editions

2014-06-04	Authored	Jupe, S.
2016-01-28	Edited	Jupe, S.
2016-01-28	Reviewed	Meldal, BH.

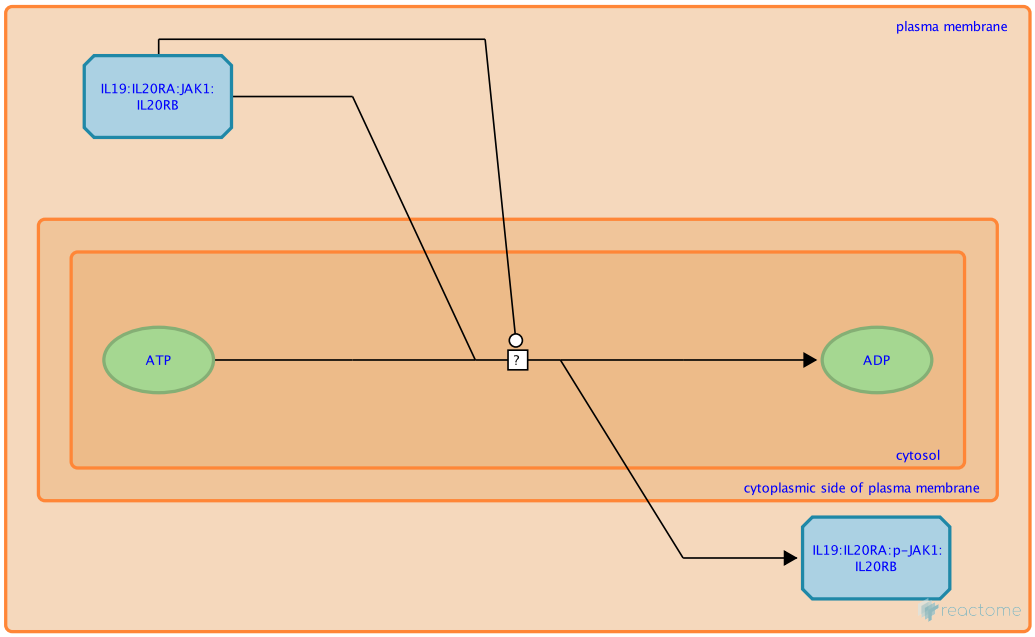
IL19:IL20RA:JAK1:IL20RB phosphorylates JAK1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987084

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine-protein kinase JAK1 (JAK1) is believed to be phosphorylated after Interleukin-19 (IL19)/IL19 receptor interaction. The IL19 receptor complex is identical to one of the two Interleukin-24 (IL24) receptors ((Dumoutier et al. 2001, Wang et al. 2002). IL24 can stimulate JAK1 phosphorylation in human colonic subepithelial myofibroblasts, where the components of both forms of the IL24 receptor are expresed (Andoh et al. 2009). Although it was not established that both forms of the IL24 receptor were involved in JAK1 phosphorylation, it has been demonstrated that the IL19 receptor when stimulated with IL19 and both forms of the IL24 receptor when stimulated with IL24 can activate STAT3 (Dumoutier et al. 2001, Wang et al. 2002). Based on the consensus understanding of JAK/STAT signaling, STAT3 activation is very likely to be preceded by JAK1 phosphorylation and it is therefore likely that both forms of the IL24 receptor, including the form that is also a receptor for IL19, lead to JAK1 phosphorylation. This reaction is a black box event because there is no experimental data confirming JAK1 phosphorylation in response to IL19.

Preceded by: IL19 binds IL20RA:JAK1:IL20RB

Followed by: IL19:IL20RA:p⊠JAK1:IL20RB binds STAT3

Literature references

Andoh, A., Shioya, M., Nishida, A., Bamba, S., Tsujikawa, T., Kim-Mitsuyama, S. et al. (2009). Expression of IL-24, an activator of the JAK1/STAT3/SOCS3 cascade, is enhanced in inflammatory bowel disease. *J. Immunol., 183*, 687-95 . ↗

Dumoutier, L., Leemans, C., Lejeune, D., Kotenko, SV., Renauld, JC. (2001). Cutting edge: STAT activation by IL-19, IL-20 and mda-7 through IL-20 receptor complexes of two types. *J Immunol, 167*, 3545-9. ↗

Wang, M., Tan, Z., Zhang, R., Kotenko, SV., Liang, P. (2002). Interleukin 24 (MDA-7/MOB-5) signals through two heterodimeric receptors, IL-22R1/IL-20R2 and IL-20R1/IL-20R2. *J. Biol. Chem., 277*, 7341-7. ↗

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2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

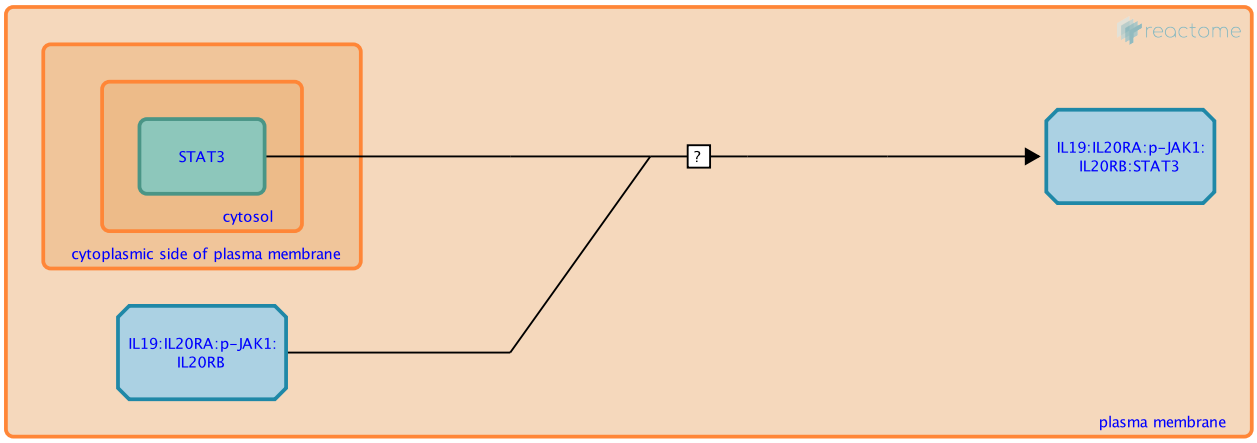
IL19:IL20RA:p□JAK1:IL20RB binds STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8982165

Type: uncertain

Compartments: plasma membrane, cytosol, extracellular region



Signal transducer and activator of transcription 3 (STAT3) is believed to bind the Interleukin-19 (IL19) /I-nterleukin-19 receptor complex. IL19 stimulates transient STAT3 phosphorylation and translocation from the cytoplasm to the nucleus (Dumoutier et al. 2001, Tian et al. 2008, Jain et al.2011). STAT3 binding is inferred to be a prerequisite for its phosphorylation from the signaling mechanism of the related interleukin-10 receptor, which is able to bind and phosphorylate STAT3 (Riley et al. 1999). The IL19 receptor complex consists of Interleukin-20 Receptor A (IL20RA) associated with Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor B (IL20RB). This is a black box event because binding of STAT3 after IL19 stimulus has not been demonstrated.

Preceded by: IL19:IL20RA:JAK1:IL20RB phosphorylates JAK1

Followed by: IL19:IL20RA:p-JAK1:IL20RB:STAT3 phosphorylates STAT3

Literature references

Jain, S., Gabunia, K., Kelemen, SE., Panetti, TS., Autieri, MV. (2011). The anti-inflammatory cytokine interleukin 19 is expressed by and angiogenic for human endothelial cells. *Arterioscler. Thromb. Vasc. Biol., 31*, 167-75. ↗

Tian, Y., Sommerville, LJ., Cuneo, A., Kelemen, SE., Autieri, MV. (2008). Expression and suppressive effects of interleukin-19 on vascular smooth muscle cell pathophysiology and development of intimal hyperplasia. *Am. J. Pathol., 173*, 901-9. ↗

Dumoutier, L., Leemans, C., Lejeune, D., Kotenko, SV., Renauld, JC. (2001). Cutting edge: STAT activation by IL-19, IL-20 and mda-7 through IL-20 receptor complexes of two types. *J Immunol, 167*, 3545-9. ↗

Editions

2017-03-16	Authored	Duenas, C.
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2017-11-15	Reviewed	Datta, SK.

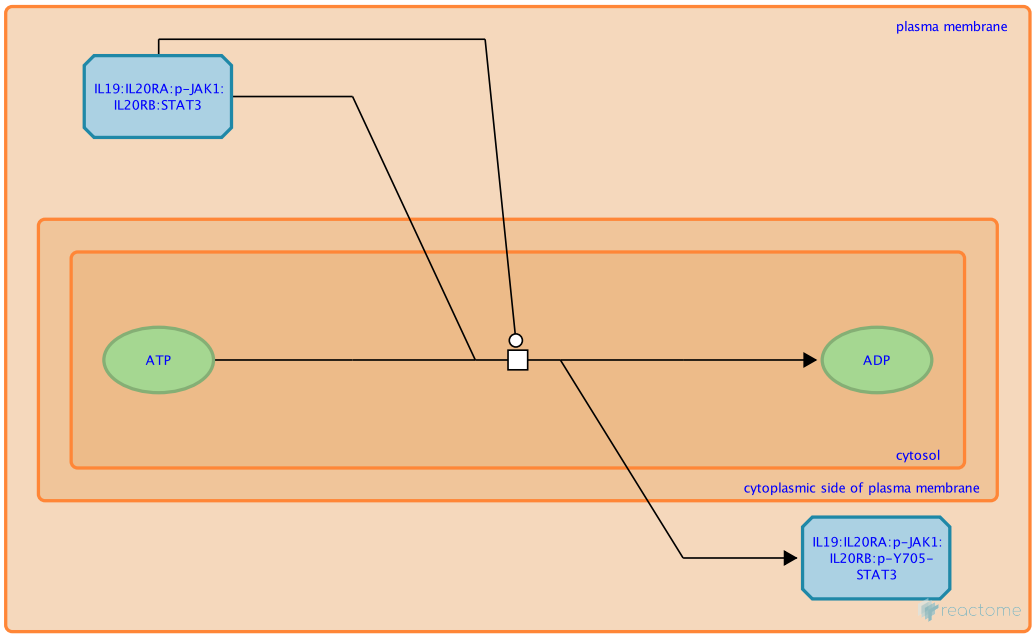
IL19:IL20RA:p-JAK1:IL20RB:STAT3 phosphorylates STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8982163

Type: transition

Compartments: cytosol, extracellular region, plasma membrane



Signal transducer and activator of transcription 3 (STAT3) is phosphorylated after Interleukin-19 (IL19) binds its receptor complex (Dumoutier et al. 2001, Tian et al. 2008, Jain et al.2011). The receptor complex consists of IL19, Interleukin-20 receptor subunit alpha (IL20RA), phosphorylated Tyrosine-protein kinase JAK1 (JAK1), Interleukin-20 receptor beta (IL20RB) and STAT3.

Preceded by: IL19:IL20RA:p□JAK1:IL20RB binds STAT3

Followed by: p□Y705-STAT3 dissociates from IL19:IL20RA:p-JAK1:IL20RB

Literature references

Tian, Y., Sommerville, LJ., Cuneo, A., Kelemen, SE., Autieri, MV. (2008). Expression and suppressive effects of interleukin-19 on vascular smooth muscle cell pathophysiology and development of intimal hyperplasia. *Am. J. Pathol., 173*, 901-9. ↗

Dumoutier, L., Leemans, C., Lejeune, D., Kotenko, SV., Renauld, JC. (2001). Cutting edge: STAT activation by IL-19, IL-20 and mda-7 through IL-20 receptor complexes of two types. *J Immunol, 167*, 3545-9. ↗

Jain, S., Gabunia, K., Kelemen, SE., Panetti, TS., Autieri, MV. (2011). The anti-inflammatory cytokine interleukin 19 is expressed by and angiogenic for human endothelial cells. *Arterioscler. Thromb. Vasc. Biol., 31*, 167-75. ↗

Editions

2017-03-16	Authored	Duenas, C.
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2017-11-15	Reviewed	Datta, SK.

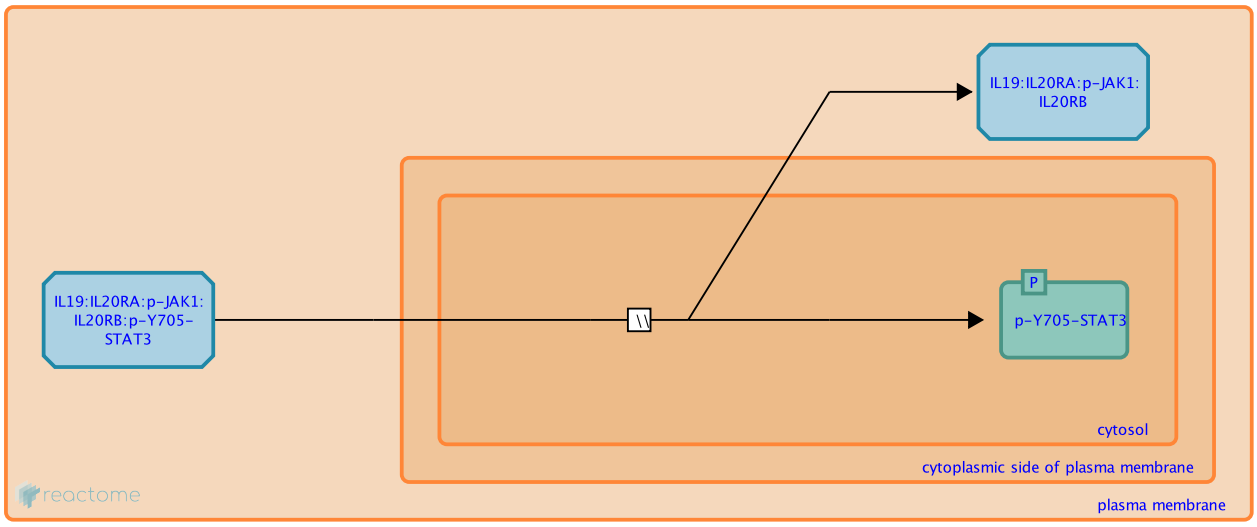
p□Y705-STAT3 dissociates from IL19:IL20RA:p-JAK1:IL20RB ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8982162

Type: omitted

Compartments: cytosol, extracellular region, plasma membrane



Signal transducer and activator of transcription 3 (STAT3) is believed to dissociate from the Interleukin-19 (IL19) receptor complex after phosphorylation. The Interleukin-19 receptor complex is formed by Interleukin-20 receptor A (IL20RA) associated with Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor B (IL20RB). This is a black box event because dissociation of STAT3 from the IL19 receptor is inferred from IL-19 induced changed in STA3 regulated gene expression (Tian et al. 2008).

Preceded by: IL19:IL20RA:p-JAK1:IL20RB:STAT3 phosphorylates STAT3

Followed by: p-Y705-STAT3 dimerizes

Literature references

Tian, Y., Sommerville, LJ., Cuneo, A., Kelemen, SE., Autieri, MV. (2008). Expression and suppressive effects of interleukin-19 on vascular smooth muscle cell pathophysiology and development of intimal hyperplasia. *Am. J. Pathol., 173*, 901-9. ↗

Editions

2017-03-16	Authored	Duenas, C.
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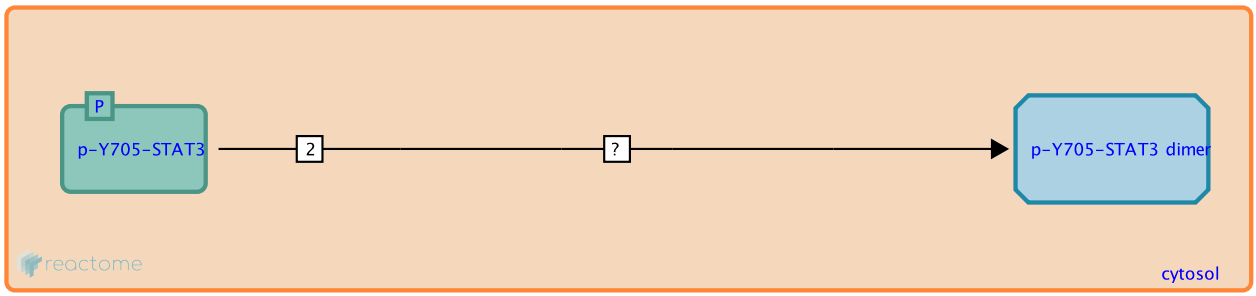
p-Y705-STAT3 dimerizes ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-6784765

Type: uncertain

Compartments: cytosol



Phosphorylated Signal transducer and activator of transcription 3 (STAT3) dimerizes after dissociating from the interleukin-19 (IL19) receptor complex (Akira et al. 1994) or Interleukin-22 (IL22) receptor complex (Lagos-Quintana et al. 2003, Sestito et al. 2011).

According to the classical model, phosphorylated Signal transducer and activator of transcription (STAT) monomers associate in an active dimer form, which is stabilized by the reciprocal interactions between a phosphorylated tyrosine residue of one and the SH2 domain of the other monomer (Shuai et al. 1994). These dimers then translocate to the nucleus (Akira et al. 1994). Recently an increasing number of studies have demonstrated the existence of STAT dimers in unstimulated cell states and the capability of STATs to exert biological functions independently of phosphorylation (Braunstein et al. 2003, Li et al. 2008, Santos & Costas-Pereira 2011). As phosphorylation of STATs is not unequivocally required for its subsequent translocation to the nucleus, this event is shown as an uncertain process.

Preceded by: p□Y705-STAT3 dissociates from IL19:IL20RA:p-JAK1:IL20RB, p-Y705-STAT3 dissociates from IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:IL10RB:p-TYK2:p-Y705-STAT3

Followed by: p-Y705-STAT3 dimer translocates from cytosol to nucleoplasm

Literature references

Shuai, K., Horvath, CM., Huang, LH., Qureshi, SA., Cowburn, D., Darnell JE, Jr. (1994). Interferon activation of the transcription factor Stat91 involves dimerization through SH2-phosphotyrosyl peptide interactions. *Cell, 76*, 821-8 . ↗

Braunstein, J., Brutsaert, S., Olson, R., Schindler, C. (2003). STATs dimerize in the absence of phosphorylation. *J. Biol. Chem., 278*, 34133-40. ↗

Lagos-Quintana, M., Rauhut, R., Meyer, J., Borkhardt, A., Tuschl, T. (2003). New microRNAs from mouse and human . *RNA, 9*, 175-9. ↗

Akira, S., Nishio, Y., Inoue, M., Wang, XJ., Wei, S., Matsusaka, T. et al. (1994). Molecular cloning of APRF, a novel IFN-stimulated gene factor 3 p91-related transcription factor involved in the gp130-mediated signaling pathway. *Cell, 77*, 63-71. ↗

Editions

2015-06-17	Authored	Jupe, S.
2016-09-05	Reviewed	Meldal, BH.
2016-11-14	Edited	Jupe, S.

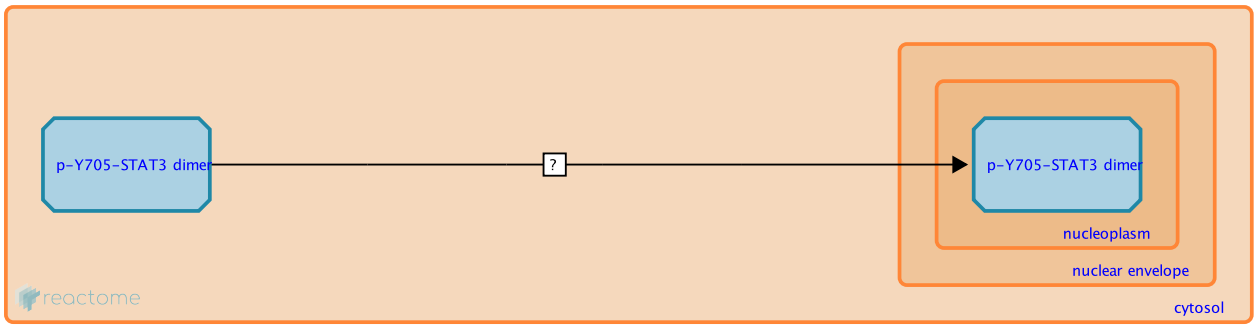
p-Y705-STAT3 dimer translocates from cytosol to nucleoplasm ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-6784763

Type: uncertain

Compartments: cytosol, nucleoplasm



The classical model of JAK-STAT signaling suggests that phosphorylated Signal transducer and activator of transcription 3 (STAT3) translocates to the nucleus (Akira et al. 1994) where it binds DNA to mediate the effects of Interleukin-10 (IL10) on expression of cytokines, soluble mediators and cell surface molecules by cells of myeloid origin, with important consequences for their ability to activate and sustain immune and inflammatory responses. STAT3 is able to shuttle freely between the cytoplasm and the nucleus, independent of tyrosine phosphorylation (Liu et al. 2005, Li 2008, Reich 2013). Binding of unphosphorylated STAT3 to DNA has been reported (Nkansah et al. 2013). As it is not clear what triggers nuclear accumulation of STAT3 in response to IL10 this event is shown as an uncertain process.

Preceded by: p-Y705-STAT3 dimerizes

Literature references

Akira, S., Nishio, Y., Inoue, M., Wang, XJ., Wei, S., Matsusaka, T. et al. (1994). Molecular cloning of APRF, a novel IFN-stimulated gene factor 3 p91-related transcription factor involved in the gp130-mediated signaling pathway. *Cell, 77*, 63-71. ↗

Liu, L., McBride, KM., Reich, NC. (2005). STAT3 nuclear import is independent of tyrosine phosphorylation and mediated by importin-alpha3. *Proc. Natl. Acad. Sci. U.S.A., 102*, 8150-5. ↗

Lagos-Quintana, M., Rauhut, R., Meyer, J., Borkhardt, A., Tuschl, T. (2003). New microRNAs from mouse and human . *RNA, 9*, 175-9. ↗

Editions

2015-06-17	Authored	Jupe, S.
2016-09-05	Reviewed	Meldal, BH.
2016-11-14	Edited	Jupe, S.

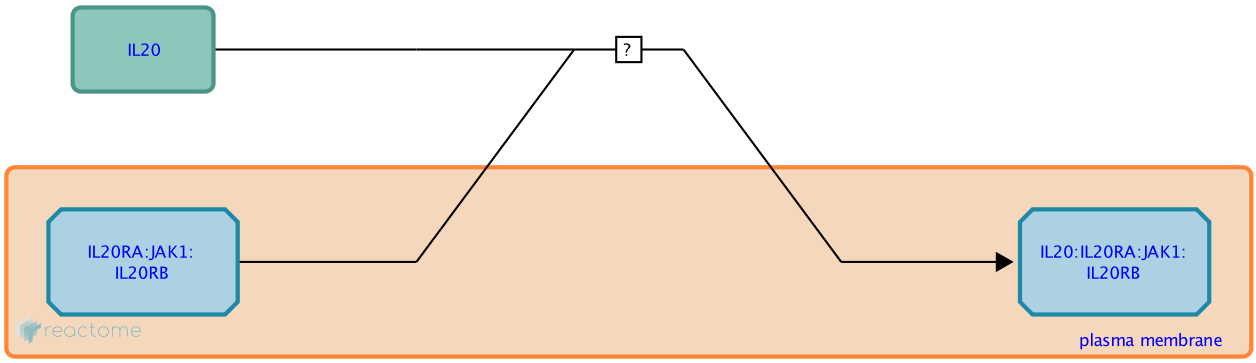
IL20 binds IL20RA:JAK1:IL20RB ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987015

Type: uncertain

Compartments: extracellular region, plasma membrane, cytosol



Interleukin-20 (IL20) binds a heterodimeric receptor complex that consists of Interleukin-20 receptor subunit alpha (IL20RA), which is associated with Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB) (Blumberg et al. 2001, Parrish-Novak et al. 2002, Logsdon et al. 2012, Rutz et al. 2014). Interleukin-20 receptor A (IL20RA) and Interleukin-20 receptor B (IL20RB) form a receptor complex for Interleukin-20 (IL20), Interleukin-19 (IL19) and Interleukin-24 (IL24) (Blumberg et al. 2001, Parrish-Novak et al. 2002, Logsdon et al. 2012, Rutz et al. 2014). IL20 can also bind a receptor complex that consists of Interleukin-22 receptor subunit alpha-1 (IL22RA1) and IL20RB (Kolumam et al. 2017). As it is not clear whether the dimeric receptor can form in the absence of ligand, formation of the receptor dimer is represented here as an uncertain black box event.

Preceded by: IL20RA binds IL20RB

Followed by: IL20:IL20RA:JAK1:IL20RB binds JAK2,JAK3

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Logsdon, NJ., Deshpande, A., Harris, BD., Rajashankar, KR., Walter, MR. (2012). Structural basis for receptor sharing and activation by interleukin-20 receptor-2 (IL-20R2) binding cytokines. *Proc. Natl. Acad. Sci. U.S.A., 109*, 12704-9. ↗

Blumberg, H., Conklin, D., Xu, WF., Grossmann, A., Brender, T., Carollo, S. et al. (2001). Interleukin 20: discovery, receptor identification, and role in epidermal function. *Cell, 104*, 9-19. ↗

Editions

2014-06-04	Authored	Jupe, S.
2016-01-28	Edited	Jupe, S.
2016-01-28	Reviewed	Meldal, BH.

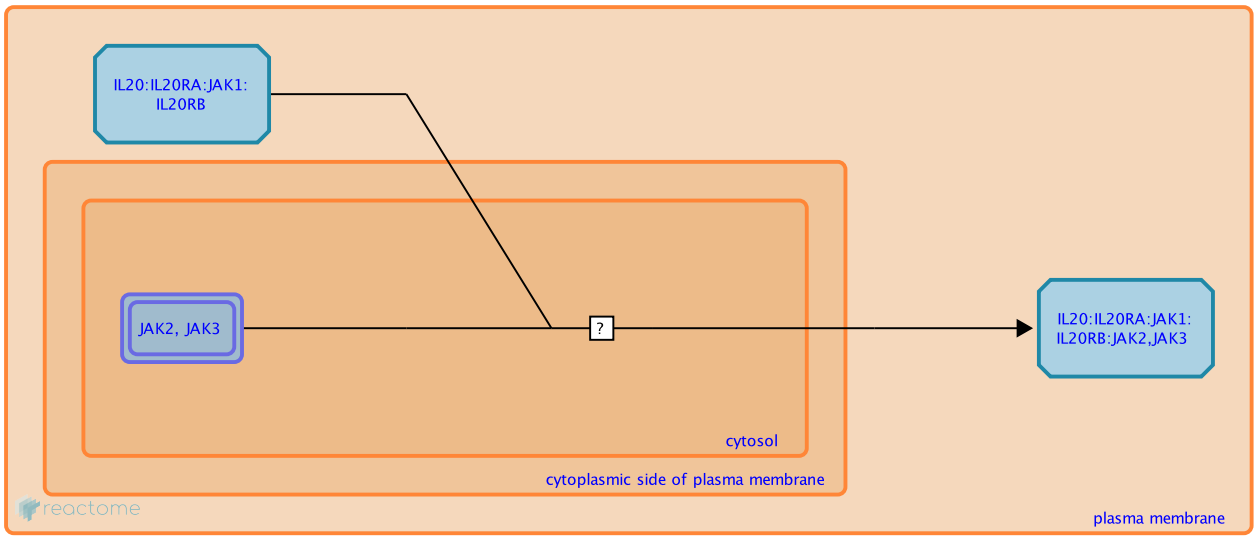
IL20:IL20RA:JAK1:IL20RB binds JAK2,JAK3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987220

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine-protein kinase JAK2 (JAK2) or Tyrosine-protein kinase JAK3 (JAK3) are believed to bind the complex formed by Interleukin-20 (IL20), Interleukin-20 Receptor subunit alpha (IL20RA), which is associated with Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB). JAK2 was phosphorylated in response to IL20 in porcine aorta endothelial cells (Tritsaris et al. 2007). JAK2 and JAK3 were phosphorylated after IL20 stimulation of human 253J bladder cancer cells (Lee et al. 2012).

This is a black box event since it is unclear whether JAK2/3 are constitutively associated or bind to the receptor after IL20 stimulation.

Preceded by: IL20 binds IL20RA:JAK1:IL20RB

Followed by: IL20:IL20RA:JAK1:IL20RB:JAK2,JAK3 phosphorylates JAK2,JAK3

Literature references

Tritsaris, K., Myren, M., Ditlev, SB., Hübschmann, MV., van der Blom, I., Hansen, AJ. et al. (2007). IL-20 is an arteriogenic cytokine that remodels collateral networks and improves functions of ischemic hind limbs. *Proc. Natl. Acad. Sci. U.S.A., 104*, 15364-9. ↗

Lee, SJ., Lee, EJ., Kim, SK., Jeong, P., Cho, YH., Yun, SJ. et al. (2012). Identification of pro-inflammatory cytokines associated with muscle invasive bladder cancer; the roles of IL-5, IL-20, and IL-28A. *PLoS ONE, 7*, e40267. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

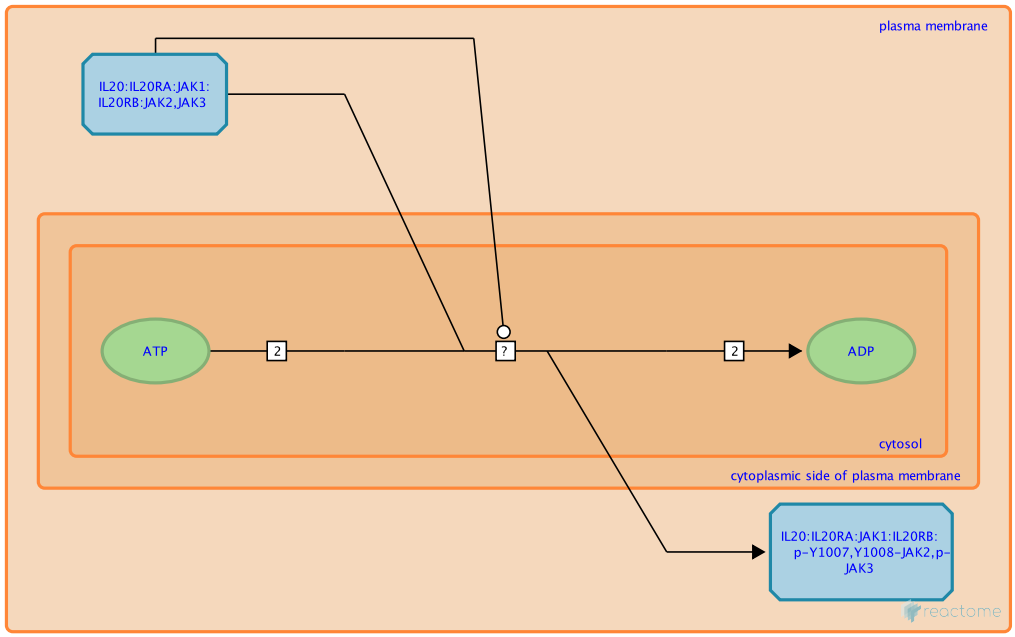
IL20:IL20RA:JAK1:IL20RB:JAK2,JAK3 phosphorylates JAK2,JAK3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987179

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine-protein kinase JAK2 (JAK2) or Tyrosine-protein kinase JAK3 (JAK3) are phosphorylated after the binding of Interleukin-20 (IL20) to a heterodimeric receptor complex formed by Interleukin-20 receptor subunit alpha (IL20RA) associated with Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB).

JAK2 is phosphorylated at Tyr-1007/1008 (Tritsaris et al. 2007). JAK3 is also phosphorylated (Lee et al. 2012).

This is a black box event because it is unclear whether JAK2 and JAK3 are phosphorylated simultaneously or sequentially during IL20 stimulation.

Preceded by: IL20:IL20RA:JAK1:IL20RB binds JAK2,JAK3

Followed by: IL20:IL20RA:JAK1:IL20RB:p□JAK2,p□JAK3 binds STAT3

Literature references

Tritsaris, K., Myren, M., Ditlev, SB., Hübschmann, MV., van der Blom, I., Hansen, AJ. et al. (2007). IL-20 is an arteriogenic cytokine that remodels collateral networks and improves functions of ischemic hind limbs. *Proc. Natl. Acad. Sci. U.S.A., 104*, 15364-9. ↗

Lee, SJ., Lee, EJ., Kim, SK., Jeong, P., Cho, YH., Yun, SJ. et al. (2012). Identification of pro-inflammatory cytokines associated with muscle invasive bladder cancer; the roles of IL-5, IL-20, and IL-28A. *PLoS ONE, 7*, e40267. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

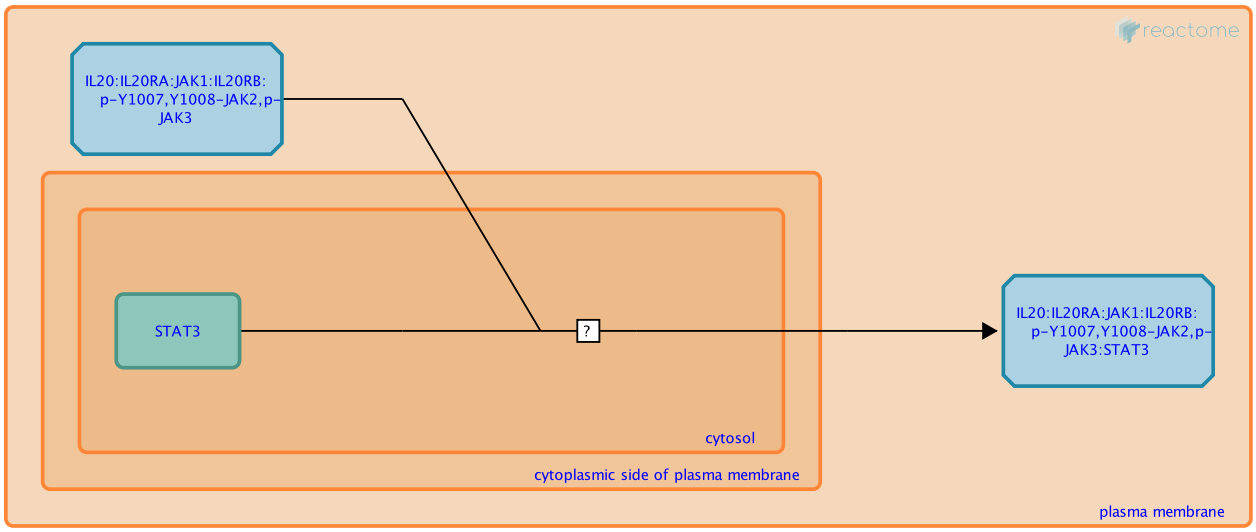
IL20:IL20RA:JAK1:IL20RB:p□JAK2,p□JAK3 binds STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987104

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Signal transducer and activator of transcription 3 (STAT3)and STAT5 are believed to bind the receptor complex following the phosphorylation of JAK2 and JAK3 within the IL20:IL20RA receptor complex, because Interleukin-20 (IL20) stimulation leads to STAT3 nuclear translocation (Blumberg et al. 2001, Parrish-Novak et a. 2002)). Phosphorylation of STAT5 at Tyr-694 has been observed in response to IL20 but it is not clear which IL20 receptor was involved (Tritsaris et al. 2007). This is a black box event because there is no direct evidence of STAT3 or STAT5 binding, which is inferred to be a prerequisite for STAT phosphorylation in response to IL20.

Preceded by: IL20:IL20RA:JAK1:IL20RB:JAK2,JAK3 phosphorylates JAK2,JAK3

Followed by: IL20:IL20RA:JAK1:IL20RB:p-JAK3,p-JAK2:STAT3 phosphorylates STAT3

Literature references

Blumberg, H., Conklin, D., Xu, WF., Grossmann, A., Brender, T., Carollo, S. et al. (2001). Interleukin 20: discovery, receptor identification, and role in epidermal function. *Cell, 104*, 9-19. ↗

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

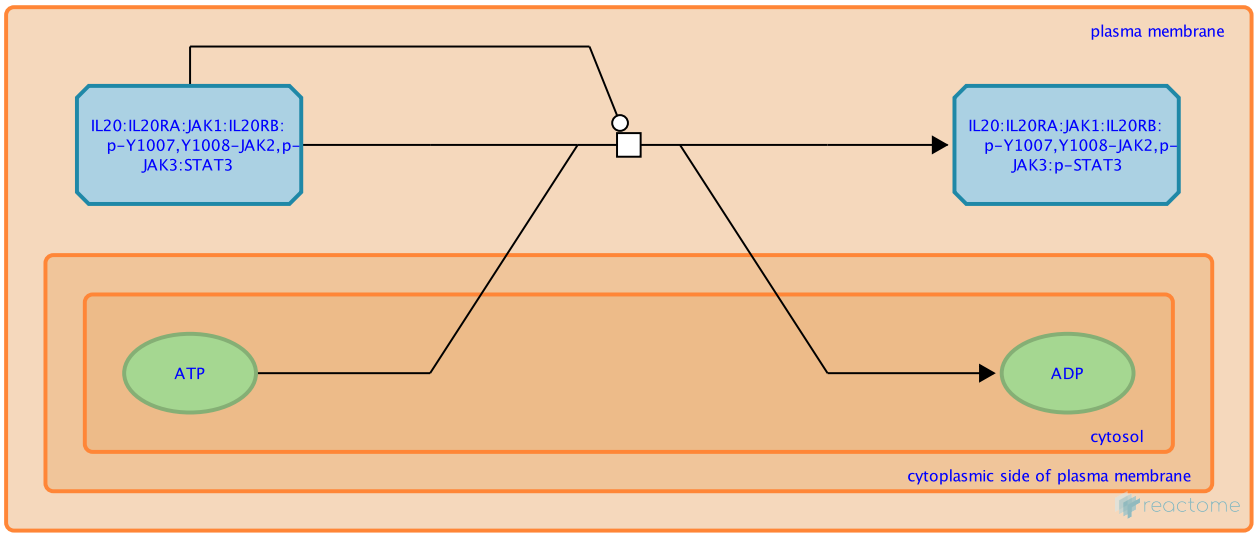
IL20:IL20RA:JAK1:IL20RB:p-JAK3,p-JAK2:STAT3 phosphorylates STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987141

Type: transition

Compartments: plasma membrane, cytosol, extracellular region



Signal transducer and activator of transcription 5A and 5B (STAT5A, STAT5B) is phosphorylated after binding the Interleukin-20 (IL20) receptor complex, which consist of IL20, Interleukin-20 receptor subunit alpha (IL20RA), phosphorylated Tyrosine-protein kinase JAK1 (JAK1), Interleukin-20 receptor subunit beta (IL20RB), phosphorylated Tyrosine-protein kinase JAK2 (JAK2), Tyrosine-protein kinase JAK3 (JAK3) and STAT5. After IL20 stimulation STAT5 is phosphorylated at Tyr-694 (Tritsaris et al. 2007). It is not clear which kinase subunit of the receptor complex is responsible for STAT5 phosphorylation.

Preceded by: IL20:IL20RA:JAK1:IL20RB:p-JAK2,p-JAK3 binds STAT3

Followed by: p-STAT3 dissociates from IL20:IL20RA:JAK1:IL20RB:p-Y1007,Y1008-JAK2,p-JAK3

Literature references

Tritsaris, K., Myren, M., Ditlev, SB., Hübschmann, MV., van der Blom, I., Hansen, AJ. et al. (2007). IL-20 is an arteriogenic cytokine that remodels collateral networks and improves functions of ischemic hind limbs. *Proc. Natl. Acad. Sci. U.S.A., 104*, 15364-9. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

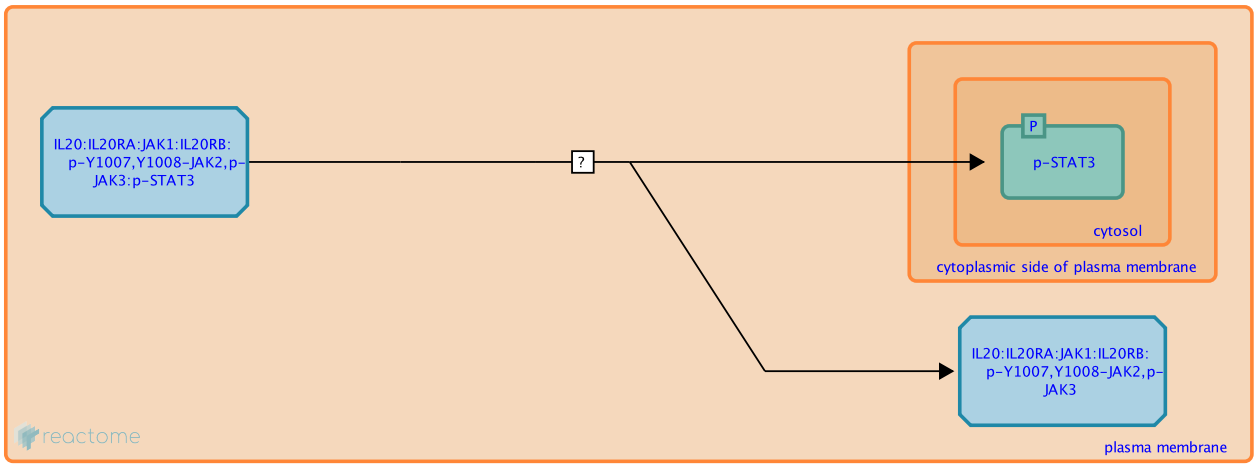
p-STAT3 dissociates from IL20:IL20RA:JAK1:IL20RB:p-Y1007,Y1008-JAK2,p-JAK3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987156

Type: uncertain

Compartments: plasma membrane, cytosol, extracellular region



Phosphorylated Signal transducer and activator of transcription 5A or 5B (STAT5) dissociates from the Interleukin-20 (IL20) receptor complex (Tristaris et al. 2007). This is a black box event because dissociation is inferred from the signalling events of other Interleukins where phosphorylated STATs translocate to the nucleus, as with Interleukin-3 (Hirose et al. 2014).

Preceded by: IL20:IL20RA:JAK1:IL20RB:p-JAK3,p-JAK2:STAT3 phosphorylates STAT3

Followed by: p-STAT3 dimerizes

Literature references

Tritsaris, K., Myren, M., Ditlev, SB., Hübschmann, MV., van der Blom, I., Hansen, AJ. et al. (2007). IL-20 is an arteriogenic cytokine that remodels collateral networks and improves functions of ischemic hind limbs. *Proc. Natl. Acad. Sci. U.S.A., 104*, 15364-9. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

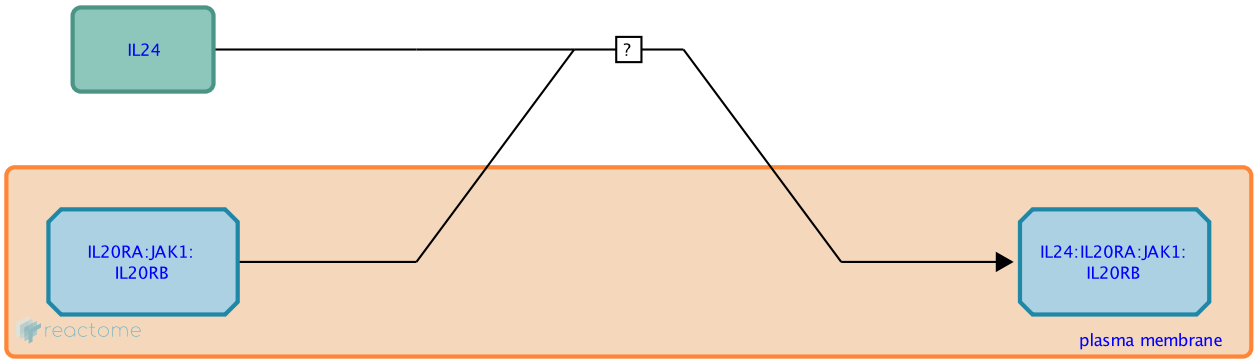
IL24 binds IL20RA:JAK1:IL20RB ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8986972

Type: uncertain

Compartments: extracellular region, plasma membrane, cytosol



Interleukin-24 (IL24) binds a receptor complex containing Interleukin-20 Receptor subunit alpha (IL20RA) associated with Tyrosine-protein kinase JAK1 (JAK1) (Andoh et al. 2009, Logsdon et al. 2012) and Interleukin-20 receptor subunit beta (IL20RB) (Parrish Novak et al.1998). Furthermore IL24 can also bind Interleukin-22 receptor subunit alpha-1 (IL22RA1) and IL20RB (Wang et al. 2002) to form a ligand receptor complex.

As it is not clear whether the receptor complex can form in the absence of ligand, formation of the receptor dimer is represented here as an uncertain event.

Preceded by: IL20RA binds IL20RB

Followed by: JAK1 in IL24:IL20RA:JAK1:IL20RB is phosphorylated

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Logsdon, NJ., Deshpande, A., Harris, BD., Rajashankar, KR., Walter, MR. (2012). Structural basis for receptor sharing and activation by interleukin-20 receptor-2 (IL-20R2) binding cytokines. *Proc. Natl. Acad. Sci. U.S.A., 109*, 12704-9. ↗

Wang, M., Tan, Z., Zhang, R., Kotenko, SV., Liang, P. (2002). Interleukin 24 (MDA-7/MOB-5) signals through two heterodimeric receptors, IL-22R1/IL-20R2 and IL-20R1/IL-20R2. *J. Biol. Chem., 277*, 7341-7. ↗

Editions

2014-06-04	Authored	Jupe, S.
2016-01-28	Edited	Jupe, S.
2016-01-28	Reviewed	Meldal, BH.

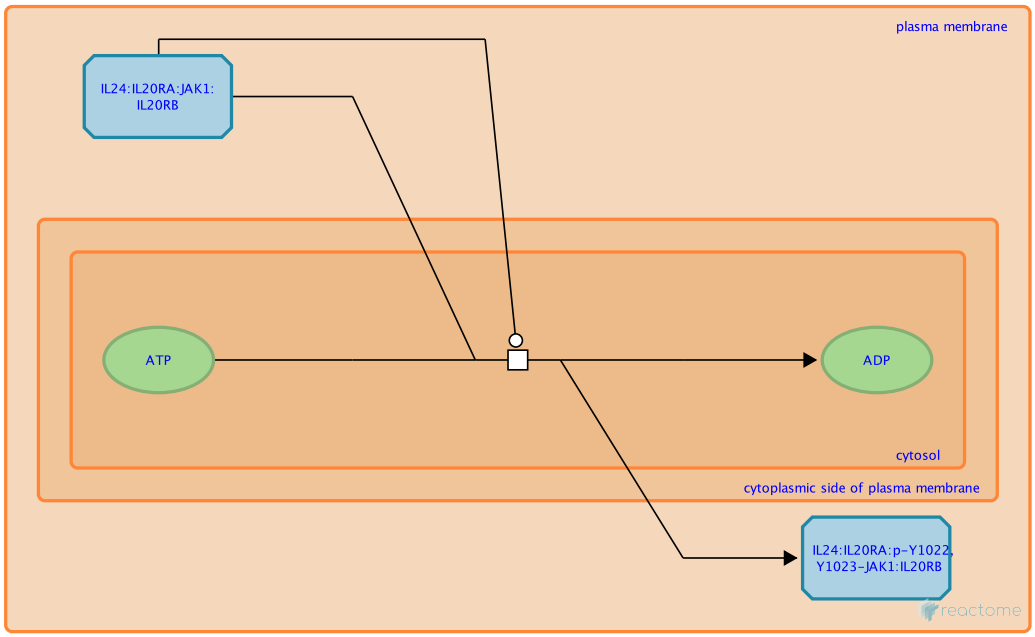
JAK1 in IL24:IL20RA:JAK1:IL20RB is phosphorylated ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987129

Type: transition

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine-protein kinase JAK1 (JAK1) is phosphorylated after Interleukin-24 (IL24) ligand interaction with its receptor. There are two IL24 receptors. One consists of Interleukin-20 receptor subunit alpha (IL20RA), Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB), the other uses nterleukin-22 receptor subunit alpha-1 (IL22RA1) instead of IL20RA (Dumoutier et al. 2001, Wang et al. 2002). IL24 can stimulate JAK1 phosphorylation in human colonic subepithelial myofibroblasts, where the components of both forms of the IL24 receptor are expresed (Andoh et al. 2009). It has been demonstrated that both forms of the IL24 receptor can activate STAT3 (Dumoutier et al. 2001, Wang et al. 2002). Based on the consensus understanding of JAK/STAT signaling, STAT3 activation is very likely to be preceded by JAK1 phosphorylation and it is therefore likely that JAK1 is phosphorylated in both forms of the IL24 receptor.

This is a black box event because it has not been established that both forms of the IL24 receptor are involved in JAK1 phosphorylation.

Preceded by: IL24 binds IL20RA:JAK1:IL20RB

Followed by: IL24:p-IL20RA:p-JAK1:IL20RB binds STAT1,STAT3

Literature references

Andoh, A., Shioya, M., Nishida, A., Bamba, S., Tsujikawa, T., Kim-Mitsuyama, S. et al. (2009). Expression of IL-24, an activator of the JAK1/STAT3/SOCS3 cascade, is enhanced in inflammatory bowel disease. *J. Immunol., 183*, 687-95 . ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

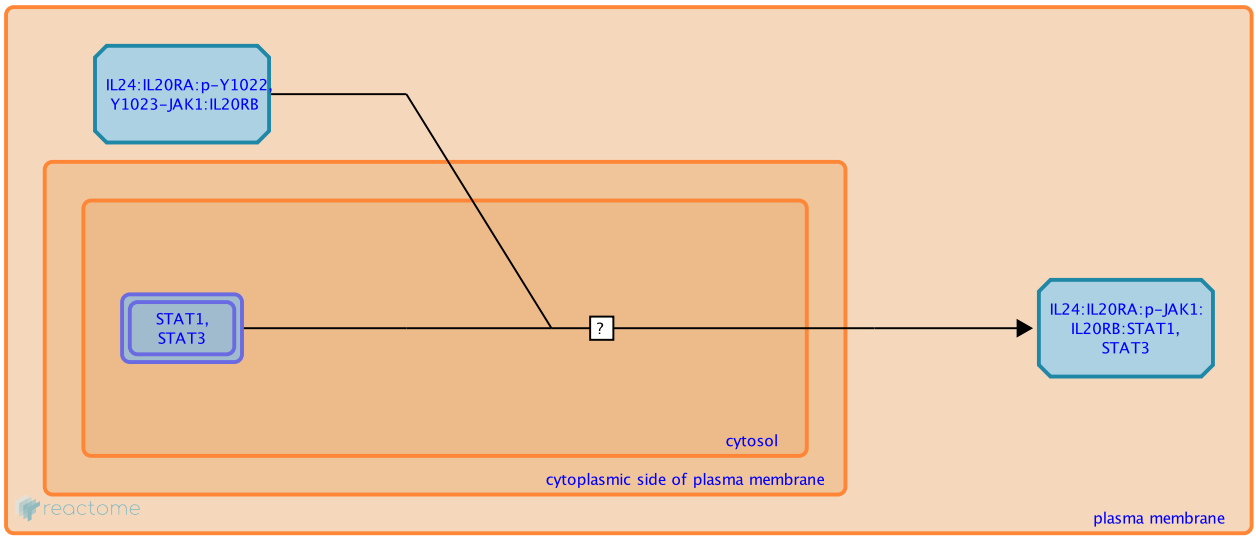
IL24:p-IL20RA:p-JAK1:IL20RB binds STAT1,STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987097

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Signal transducer and activator of transcription 1 alpha/beta (STAT1) and Signal transducer and activator of transcription 3 (STAT3) are believed to bind the Interleukin-24 (IL24) receptor complex (Wang et al. 2002, Andoh et al. 2009, Parrish-Novak et al. 1998, Li et al. 2013). This is a black box event because STAT3 binding is inferred from other interleukin receptor ligand interactions where STAT3 activation is followed by a transient interaction with the receptor complex e.g.Interleukin-10 receptor (Weber-Nordt et al. 1996).

Preceded by: JAK1 in IL24:IL20RA:JAK1:IL20RB is phosphorylated

Followed by: IL24:IL20RA:p-JAK1:IL20RB:STAT1,STAT3 phosphorylates STAT1 or STAT3

Literature references

Sainz-Perez, A., Gary-Gouy, H., Gaudin, F., Maarof, G., Marfaing-Koka, A., de Revel, T. et al. (2008). IL-24 induces apoptosis of chronic lymphocytic leukemia B cells engaged into the cell cycle through dephosphorylation of STAT3 and stabilization of p53 expression. *J. Immunol., 181*, 6051-60. ↗

Andoh, A., Shioya, M., Nishida, A., Bamba, S., Tsujikawa, T., Kim-Mitsuyama, S. et al. (2009). Expression of IL-24, an activator of the JAK1/STAT3/SOCS3 cascade, is enhanced in inflammatory bowel disease. *J. Immunol., 183*, 687-95 . ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

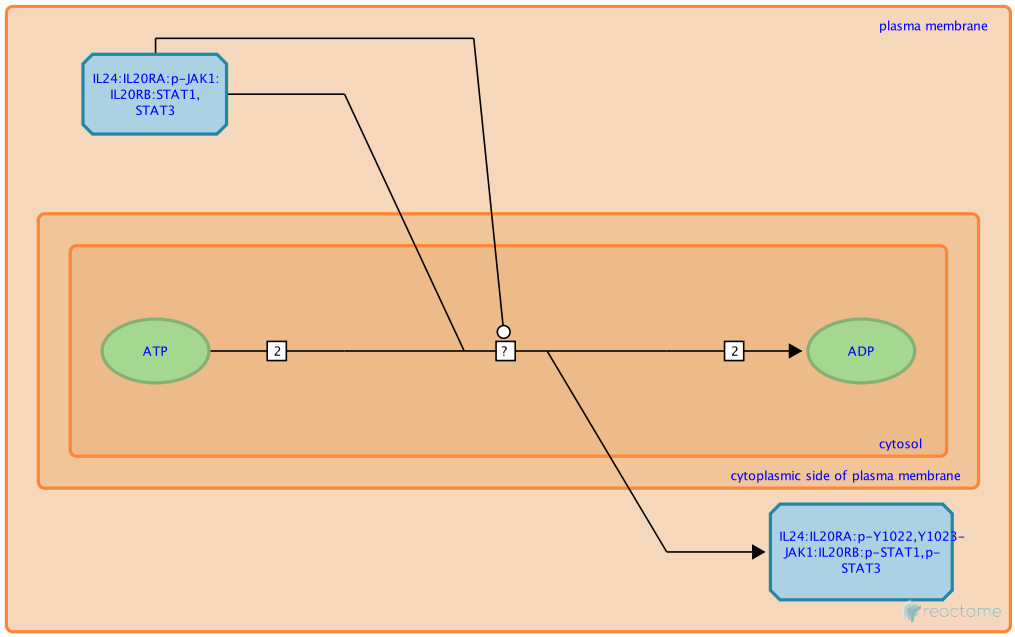
IL24:IL20RA:p-JAK1:IL20RB:STAT1,STAT3 phosphorylates STAT1 or STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987150

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Signal transducer and activator of transcription 1 alpha/beta (STAT1) and Signal transducer and activator of transcription 3 (STAT3) are believed to be phosphorylated after binding the Interleukin-24 (IL24) receptor complex (Parrish Novak et al. 1998, Andoh et al. 2009, Wang et al. 2002). This complex consists of IL24 ligand, phosphorylated Interleukin-20 receptor subunit alpha (IL20RA), phosphorylated Tyrosine-protein kinase JAK1 (JAK1), Interleukin-20 receptor subunit beta (IL20RB) and STAT1 or STAT3 .

This is a black box event because STAT binding is inferred to precede STAT phosphorylation.

Preceded by: IL24:p-IL20RA:p-JAK1:IL20RB binds STAT1,STAT3

Followed by: p-STAT1,p-STAT3 dissociate from IL24:IL20RA:p-Y1022,Y1023-JAK1:IL20RB:p-STAT1, p-STAT3

Literature references

Sainz-Perez, A., Gary-Gouy, H., Gaudin, F., Maarof, G., Marfaing-Koka, A., de Revel, T. et al. (2008). IL-24 induces apoptosis of chronic lymphocytic leukemia B cells engaged into the cell cycle through dephosphorylation of STAT3 and stabilization of p53 expression. *J. Immunol., 181*, 6051-60. ↗

Andoh, A., Shioya, M., Nishida, A., Bamba, S., Tsujikawa, T., Kim-Mitsuyama, S. et al. (2009). Expression of IL-24, an activator of the JAK1/STAT3/SOCS3 cascade, is enhanced in inflammatory bowel disease. *J. Immunol., 183*, 687-95 . ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

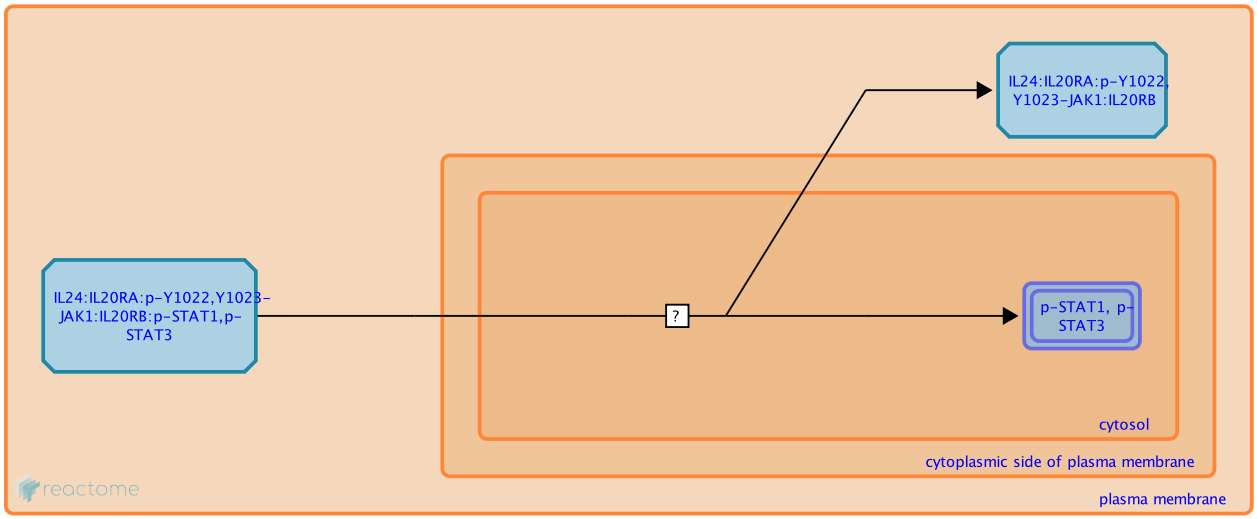
p-STAT1,p-STAT3 dissociate from IL24:IL20RA:p-Y1022,Y1023-JAK1:IL20RB:p-STAT1, p-STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987270

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Phosphorylated Signal transducer and activator of transcription 3 (STAT3) and Signal transducer and activator of transcription 1 alpha/beta (STAT1) dissociate from the Interleukin-24 (IL24) receptor complex (Wang et al. 2002). This complex is formed by IL24 ligand, phosphorylated Interleukin-20 receptor subunit alpha (IL20RA), phosphorylated Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB) (Parrish-Novak et al. 2007). This is a black box event because dissociation is inferred to occur to allow STAT dimerization and translocation to the nucleus, as is the case for STAT3 activation by the Interleukin-10 receptor (Niemand et al. 2003).

Preceded by: IL24:IL20RA:p-JAK1:IL20RB:STAT1,STAT3 phosphorylates STAT1 or STAT3

Followed by: p-STAT1 dimerizes, p-STAT3 dimerizes

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

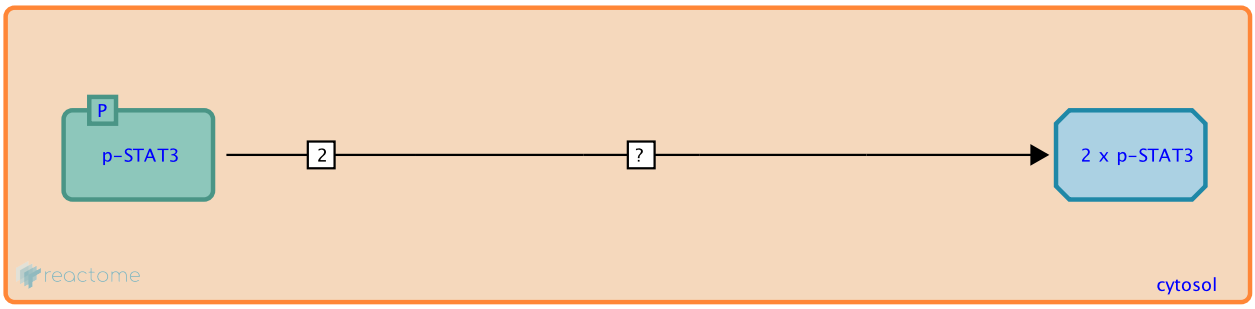
p-STAT3 dimerizes ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987214

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Phosphorylated Signal transducer and activator of transcription 3 (STAT3) is believed to dimerize after it dissociates from the Interleukin-24 (IL24) receptor complex.

This is a black box event because dimerization is inferred from STAT3 dimerization in response to interleukin-10 (Niemand et al. 2003) and the observed translocation of STAT3 to the nucleus in response to IL24 (Parrish-Novak et al. 2002). In several other cytokine signalling cascades a phosphorylated dimer is necessary for binding to DNA and gene transcription (Park et al. 2000).

Preceded by: p-STAT1,p-STAT3 dissociate from IL24:IL20RA:p-Y1022,Y1023-JAK1:IL20RB:p-STAT1, p-STAT3, p-STAT3 dissociates from IL20:IL20RA:JAK1:IL20RB:p-Y1007,Y1008-JAK2,p-JAK3, p-STAT3 dissociates from IL24:IL22RA1:p□JAK1:IL20RB:p□STAT3, p-STAT1 and p-STAT3 dissociates from IL26:IL10RB:p-TYK2:IL20RA:p-JAK1, p-STAT1, p-Y-STAT2, p-STAT3, p-STAT4, p-STAT5 dissociates from IFNL1:p-Y343,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2:p-STAT1,p-STAT2,p-STAT3,p-STAT4,p-STAT5

Followed by: p-STAT3 dimer translocates from cytosol to nucleoplasm

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

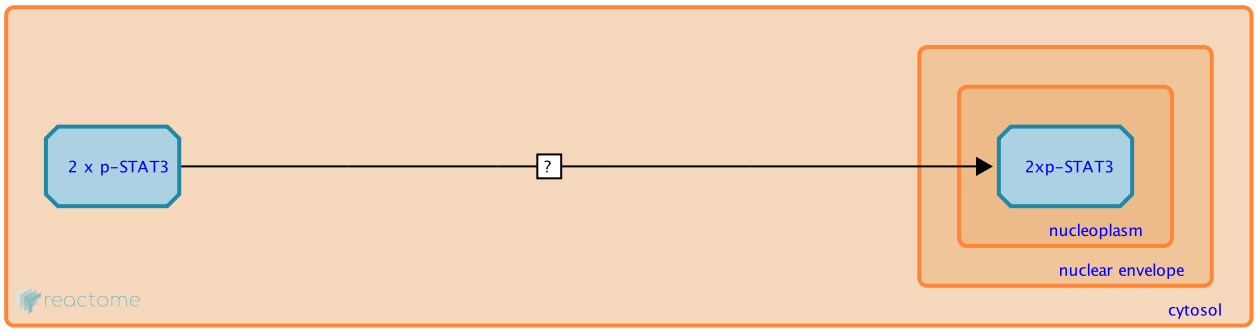
p-STAT3 dimer translocates from cytosol to nucleoplasm ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987052

Type: uncertain

Compartments: cytosol, nucleoplasm



Phosphorylated Signal transducer and activator of transcription 3 (STAT3) dimer translocates from the cytosol to the nucleoplasm after Interleukin-24 (IL24) stimulus (in BHK570 cells). Signal transducer and activator of transcription 1 alpha/beta (STAT1) was also translocated but only at high Interleukin-20 (IL20) doses (Parrish-Novak et al. 2002).

This is a black box event because the mechanism of translocation is not fully represented and may not require STAT3 dimer formation, but it can be inferred from the pattern of other Interleukins as IL10 signaling cascade (Niemand et al. 2003).

Preceded by: p-STAT3 dimerizes

Followed by: Expression of SOCS3

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

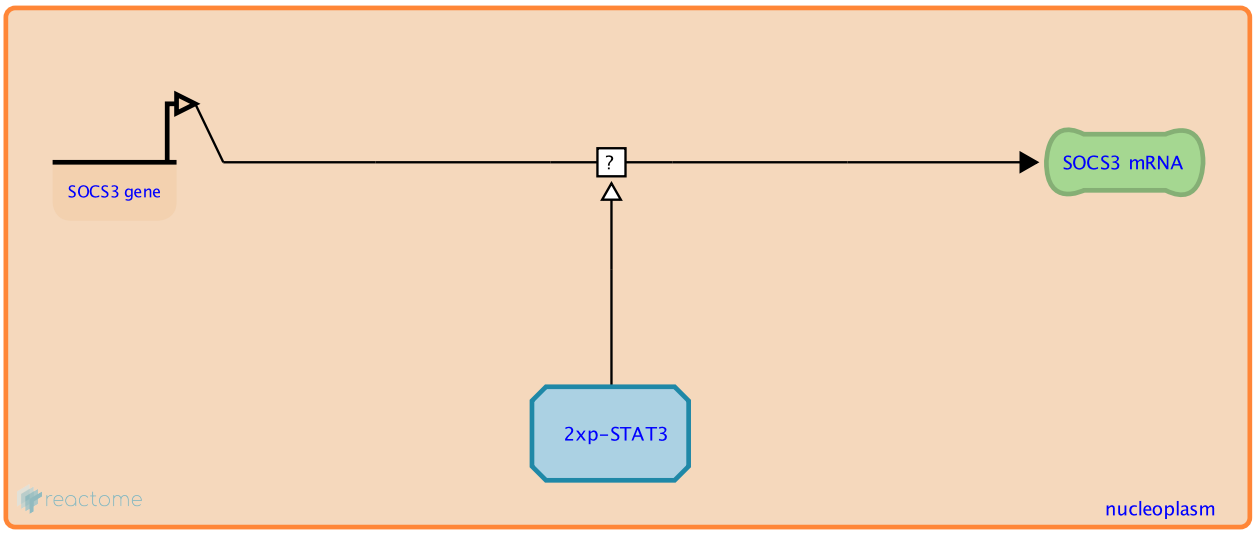
Expression of SOCS3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-9005340

Type: uncertain

Compartments: nucleoplasm



Overexpression and production of Suppressor of cytokine signaling 3 (SOCS3) has been reported after Interleukin 24 (IL24) stimulus (Andoh et al. 2009, Uto-Konomi et al. 2012).

This is a black box event since details about the binding to DNA, transcription and translation are omitted.

Preceded by: p-STAT3 dimer translocates from cytosol to nucleoplasm

Literature references

Andoh, A., Shioya, M., Nishida, A., Bamba, S., Tsujikawa, T., Kim-Mitsuyama, S. et al. (2009). Expression of IL-24, an activator of the JAK1/STAT3/SOCS3 cascade, is enhanced in inflammatory bowel disease. *J. Immunol., 183*, 687-95 . ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

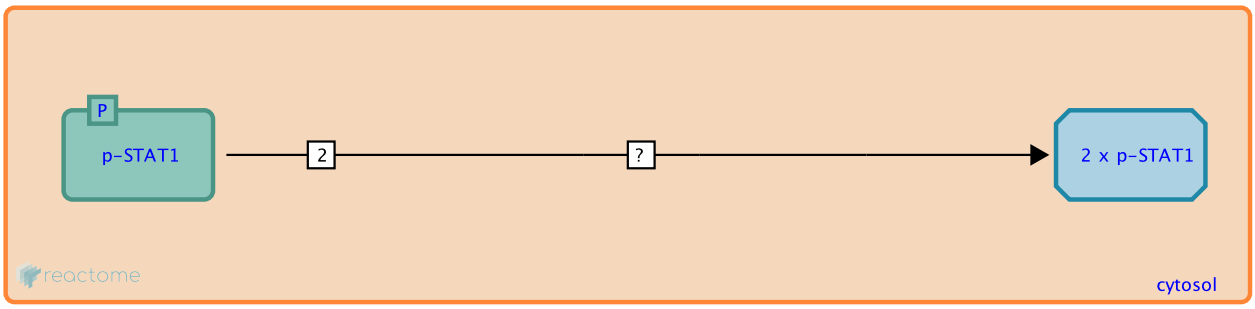
p-STAT1 dimerizes ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987007

Type: uncertain

Compartments: cytosol



Signal transducer and activator of transcription 1alpha/beta (STAT1) is believed to dimerize after it dissociates from the Interleukin-24 (IL24) receptor complex. This is a black box event because dimerization is inferred from STAT1 dimerization in response to Interferon gamma (IFNG) (Wehinger et al. 1996) and the observed translocation of STAT1 to the nucleus in response to IL24 (Parrish-Novak et al. 2002).

Preceded by: p-STAT1,p-STAT3 dissociate from IL24:IL20RA:p-Y1022,Y1023-JAK1:IL20RB:p-STAT1, p-STAT3, p-STAT1 and p-STAT3 dissociates from IL26:IL10RB:p-TYK2:IL20RA:p-JAK1, p-STAT1, p-Y-STAT2, p-STAT3, p-STAT4, p-STAT5 dissociates from IFNL1:p-Y343,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2:p-STAT1,p-STAT2,p-STAT3,p-STAT4,p-STAT5

Followed by: p-STAT1 dimer translocates from the cytosol to the nucleoplasm

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Wehinger, J., Gouilleux, F., Groner, B., Finke, J., Mertelsmann, R., Weber-Nordt, RM. (1996). IL-10 induces DNA binding activity of three STAT proteins (Stat1, Stat3, and Stat5) and their distinct combinatorial assembly in the promoters of selected genes. *FEBS Lett., 394*, 365-70. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

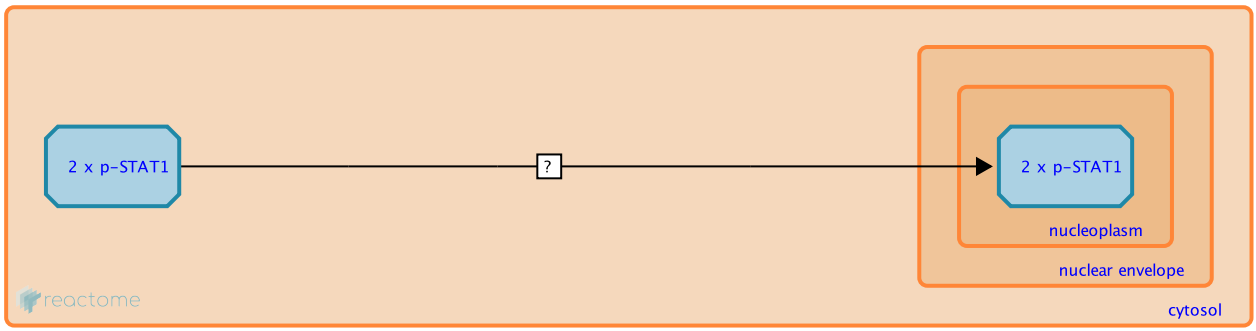
p-STAT1 dimer translocates from the cytosol to the nucleoplasm ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987218

Type: uncertain

Compartments: cytosol, nucleoplasm



Signal transducer and activator of transcription 1 alpha/beta (STAT1) dimer translocates from the cytosol to the nucleus after Interleukin-24 stimulus (IL24) (in BHK cells bearing IL 20RA/IL 20RB) (Parrish Novak et al. 2007). This is a black box event because the mechanism by which this event occurs (diffusion, transport) is unknown (Darnell 1997).

Preceded by: p-STAT1 dimerizes

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Editions

2017-03-16	Authored	Duenas, C.
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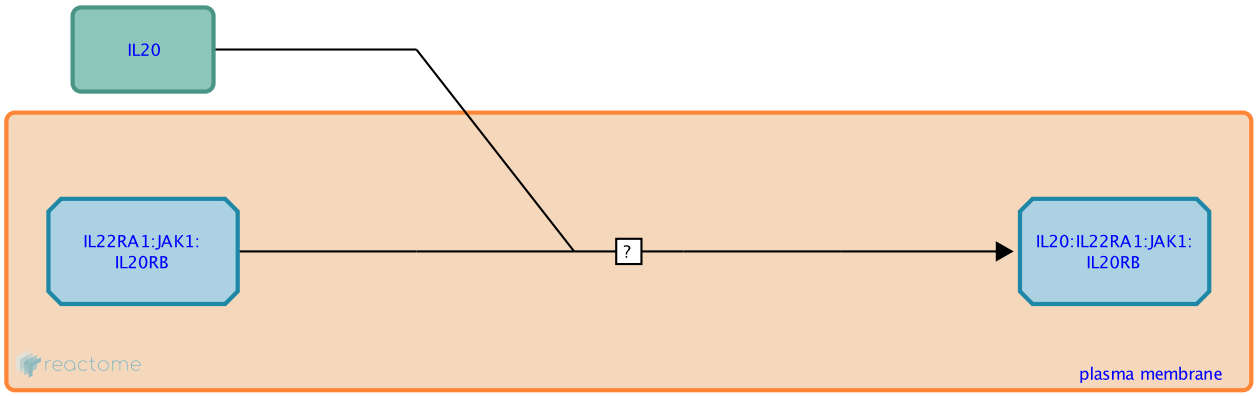
IL20 binds to IL22RA1:JAK1:IL20RB ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-9009227

Type: uncertain

Compartments: plasma membrane, extracellular region, cytosol



Interleukin-20 (IL20) (and Interleukin-24 (IL24)) can activate a complex that consists of Interleukin-22 receptor subunit alpha-1 (IL22RA1), which is associated with Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor B (IL20RB) (Dumoutier et al. 2001, Parrish-Novak et al. 2002). As it is not clear whether the receptor can form in the absence of ligand, association of the ligand with the receptor trimer is represented here as an uncertain event.

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

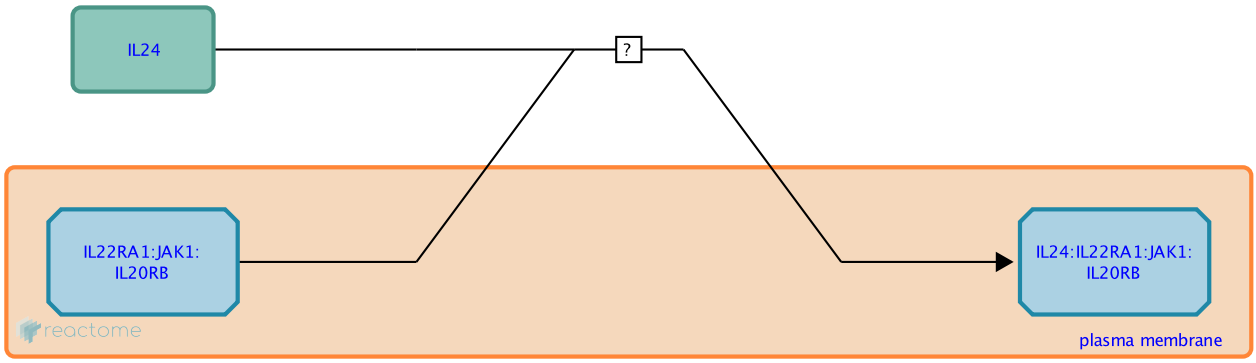
IL24 binds to IL22RA1:JAK1:IL20RB ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-448708

Type: uncertain

Compartments: extracellular region, plasma membrane, cytosol



Interleukin-24 (IL24) (and Interleukin-20 (IL20)) can activate a complex that consists of Interleukin-22 receptor subunit alpha-1 (IL22RA1), which is associated with Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor B (IL20RB) (Dumoutier et al. 2001, Parrish-Novak et al. 2002). As it is not clear whether the receptor can form in the absence of ligand, association of the ligand with the receptor trimer is represented here as an uncertain event.

Followed by: IL24:IL22RA1:JAK1:IL20RB phosphorylates JAK1

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Editions

2014-06-04	Authored	Jupe, S.
2016-01-28	Edited	Jupe, S.
2016-01-28	Reviewed	Meldal, BH.

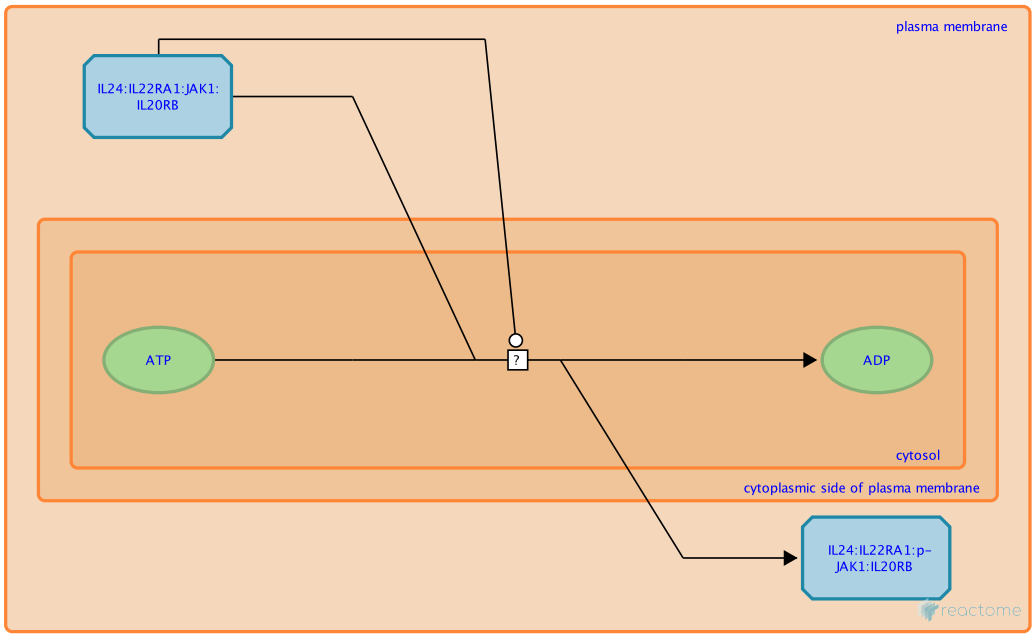
IL24:IL22RA1:JAK1:IL20RB phosphorylates JAK1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987012

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine-protein kinase JAK1 (JAK1) is phosphorylated after Interleukin-24 (IL24) ligand interaction with its receptor. There are two IL24 receptors. One consists of Interleukin-20 receptor subunit alpha (IL20RA), Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB), the other, represented in this event, uses interleukin-22 receptor subunit alpha-1 (IL22RA1) instead of IL20RA (Dumoutier et al. 2001, Wang et al. 2002). IL22RA1 can bind JAK1 (Ferrao et al. 2016). IL24 can stimulate JAK1 phosphorylation in human colonic subepithelial myofibroblasts, where the components of both forms of the IL24 receptor are expressed (Andoh et al. 2009). It has been demonstrated that both forms of the IL24 receptor can activate STAT3 (Dumoutier et al. 2001, Wang et al. 2002). Based on the consensus understanding of JAK/STAT signaling, STAT3 activation is very likely to be preceded by JAK1 phosphorylation and it is therefore likely that JAK1 is phosphorylated in both forms of the IL24 receptor. This is a black box event because it has not been established that both forms of the IL24 receptor are involved in JAK1 phosphorylation.

Preceded by: IL24 binds to IL22RA1:JAK1:IL20RB

Followed by: IL24:IL22RA1:p-JAK1:IL20RB binds STAT3

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Andoh, A., Shioya, M., Nishida, A., Bamba, S., Tsujikawa, T., Kim-Mitsuyama, S. et al. (2009). Expression of IL-24, an activator of the JAK1/STAT3/SOCS3 cascade, is enhanced in inflammatory bowel disease. *J. Immunol., 183*, 687-95 . ↗

Wang, M., Tan, Z., Zhang, R., Kotenko, SV., Liang, P. (2002). Interleukin 24 (MDA-7/MOB-5) signals through two heterodimeric receptors, IL-22R1/IL-20R2 and IL-20R1/IL-20R2. *J. Biol. Chem., 277*, 7341-7. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

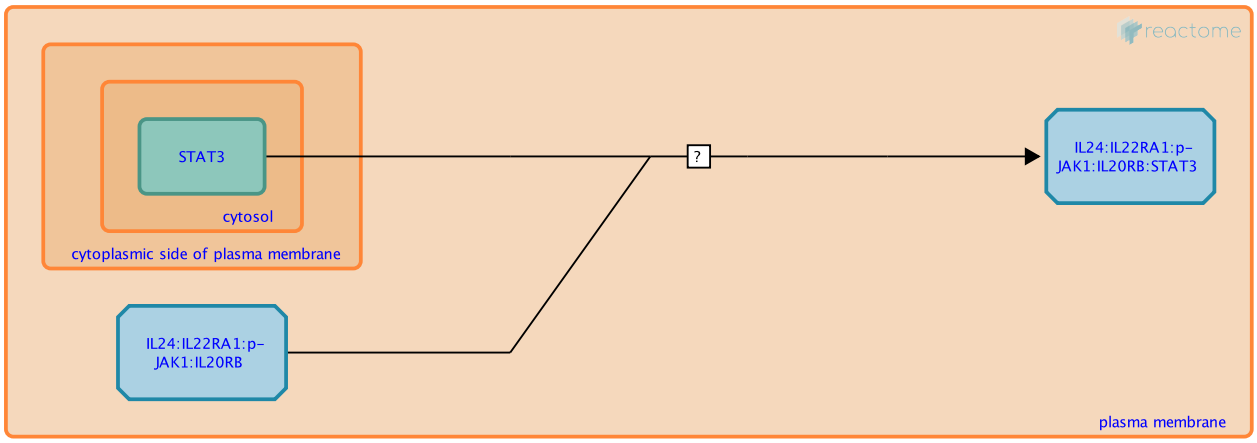
IL24:IL22RA1:p-JAK1:IL20RB binds STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987063

Type: uncertain

Compartments: plasma membrane, cytosol, extracellular region



Signal transducer and activator of transcription 3 (STAT3) is believed to bind the Interleukin-24 (IL24) receptor complex (Parrish Novak et al. 2002, Wang et al. 2002, Andoh et al. 2009). There are two forms of the IL24 receptor. The receptor complex represented here consists of IL24, Interleukin 22 receptor subunit alpha 1 (IL22RA1), phosphorylated Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB). Both forms of the IL24 receptor can activate STAT3 (Dumoutier et al. 2001, Wang et al. 2002). Based on the consensus understanding of JAK/STAT signaling, STAT3 activation is very likely to be preceded by STAT3 binding to the IL24 receptor.

This is a black box event because STAT3 binding is inferred as a prerequisite for STAT3 phosphorylation, based on STAT3 binding by the related IL10 receptor (Riley et al. 1999).

Preceded by: IL24:IL22RA1:JAK1:IL20RB phosphorylates JAK1

Followed by: IL24:IL22RA1:p-JAK1:IL20RB:STAT3 phosphorylates STAT3

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Wang, M., Tan, Z., Zhang, R., Kotenko, SV., Liang, P. (2002). Interleukin 24 (MDA-7/MOB-5) signals through two heterodimeric receptors, IL-22R1/IL-20R2 and IL-20R1/IL-20R2. *J. Biol. Chem., 277*, 7341-7. ↗

Andoh, A., Shioya, M., Nishida, A., Bamba, S., Tsujikawa, T., Kim-Mitsuyama, S. et al. (2009). Expression of IL-24, an activator of the JAK1/STAT3/SOCS3 cascade, is enhanced in inflammatory bowel disease. *J. Immunol., 183*, 687-95 . ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

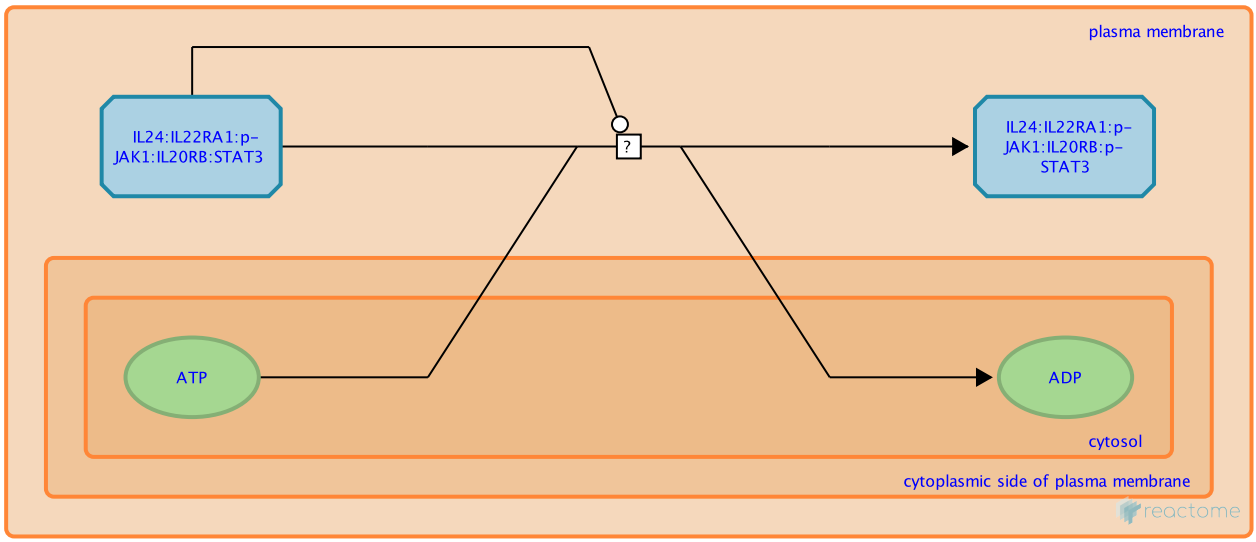
IL24:IL22RA1:p-JAK1:IL20RB:STAT3 phosphorylates STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987096

Type: uncertain

Compartments: plasma membrane, cytosol, extracellular region



Signal transducer and activator of transcription 3 (STAT3) is phosphorylated after binding to Interleukin-24 (IL24) activated receptor complex. This activated receptor complex is formed by IL24 ligand, Interleukin-22 receptor subunit alpha-1 (IL22RA1), phosphorylated Tyrosine-protein kinase JAK1 (JAK1) and Interleukin-20 receptor subunit beta (IL20RB) (Parrish-Novak et al. 2002, Wang et al. 2002, Dumoutier et al. 2001).

This is a black box event since the identity of the phosphorylated residues in STAT3 is unknown.

Preceded by: IL24:IL22RA1:p-JAK1:IL20RB binds STAT3

Followed by: p-STAT3 dissociates from IL24:IL22RA1:p□JAK1:IL20RB:p□STAT3

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23. ↗

Wang, M., Tan, Z., Zhang, R., Kotenko, SV., Liang, P. (2002). Interleukin 24 (MDA-7/MOB-5) signals through two heterodimeric receptors, IL-22R1/IL-20R2 and IL-20R1/IL-20R2. *J. Biol. Chem., 277*, 7341-7. ↗

Dumoutier, L., Leemans, C., Lejeune, D., Kotenko, SV., Renauld, JC. (2001). Cutting edge: STAT activation by IL-19, IL-20 and mda-7 through IL-20 receptor complexes of two types. *J Immunol, 167*, 3545-9. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

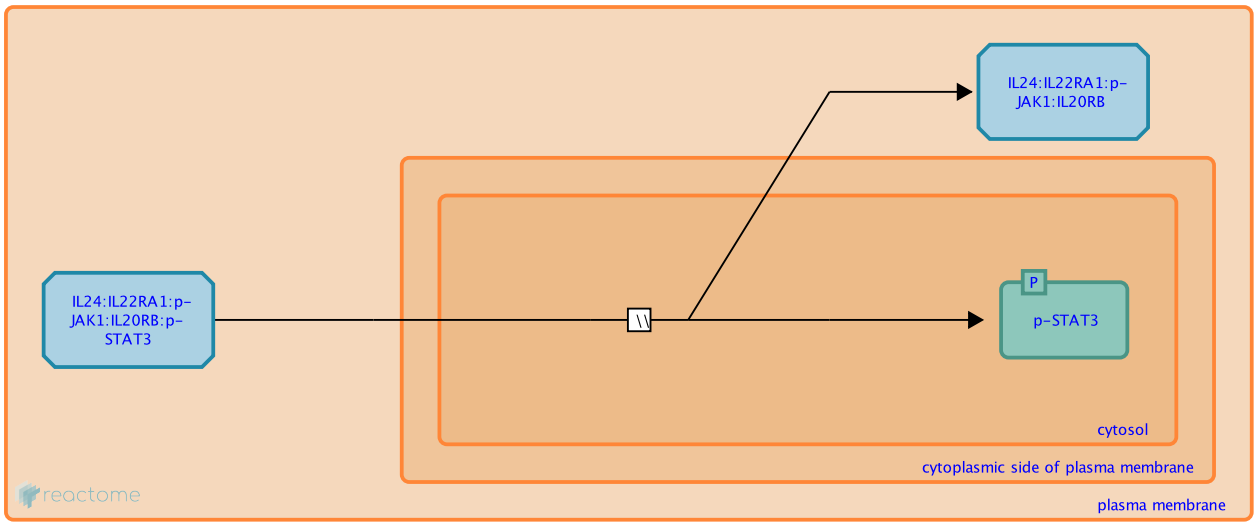
p-STAT3 dissociates from IL24:IL22RA1:p-JAK1:IL20RB:p-STAT3

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987161

Type: omitted

Compartments: cytosol, extracellular region, plasma membrane



Phosphorylated Signal transducer and activator of transcription 3 (STAT3) dissociates from Interleukin-24 (IL24) activated receptor complex. This activated receptor complex is formed by IL24 ligand, Interleukin-22 receptor subunit alpha-1 (IL22RA1), phosphorylated Tyrosine-protein kinase JAK1 (JAK) and Interleukin-20 receptor subunit beta (IL20RB) (Parrish-Novak et al. 2002).

This is a black box event since there is no direct evidence of this dissociation but there is evidence dissociation occurs before translocation in other interleukin signaling cascades.

Preceded by: IL24:IL22RA1:p-JAK1:IL20RB:STAT3 phosphorylates STAT3

Followed by: p-STAT3 dimerizes

Literature references

Parrish-Novak, J., Xu, W., Brender, T., Yao, L., Jones, C., West, J. et al. (2002). Interleukins 19, 20, and 24 signal through two distinct receptor complexes. Differences in receptor-ligand interactions mediate unique biological functions. *J Biol Chem, 277*, 47517-23.

Wang, M., Tan, Z., Zhang, R., Kotenko, SV., Liang, P. (2002). Interleukin 24 (MDA-7/MOB-5) signals through two heterodimeric receptors, IL-22R1/IL-20R2 and IL-20R1/IL-20R2. *J. Biol. Chem., 277*, 7341-7.

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

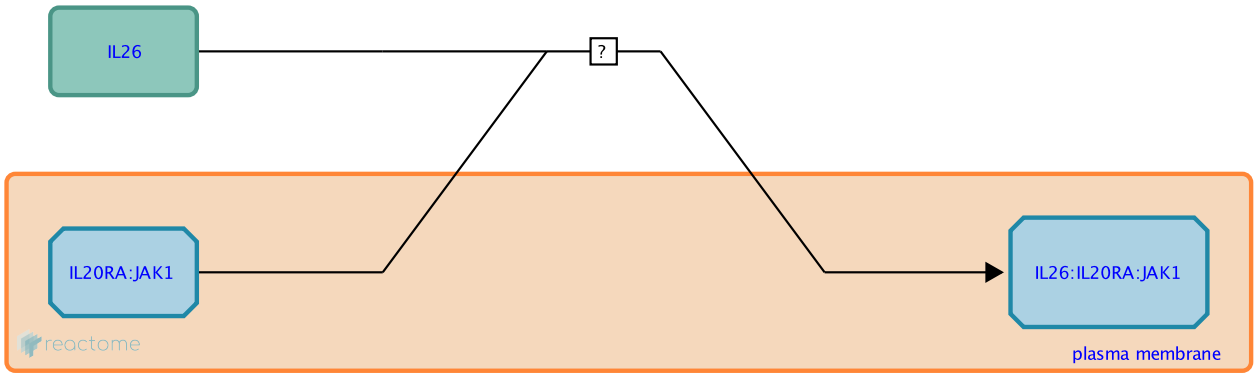
IL26 binds IL20RA:JAK1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8986446

Type: uncertain

Compartments: extracellular region, plasma membrane, cytosol



Interleukin 26 is believed to bind to its receptor complex which is formed by Interleukin 20 receptor subunit alpha and JAK1 (Yoon et al. 2006, Yoon et al. 2010, Sheikh et al. 2004). This is a black box event because constitutive pre association of JAK1 with IL20RA is inferred from the observation that IL20RA belongs to the cytokine receptor type II family, which has a common domain necessary for binding of JAK1 and release signaling (Ferrao et al. 2016, Hor et al. 2004).

Preceded by: JAK1 binds IL20RA

Followed by: IL26:IL20RA:JAK1 binds IL10RB:TYK2

Literature references

Sheikh, F., Baurin, VV., Lewis-Antes, A., Shah, NK., Smirnov, SV., Anantha, S. et al. (2004). Cutting edge: IL-26 signals through a novel receptor complex composed of IL-20 receptor 1 and IL-10 receptor 2. *J. Immunol., 172*, 2006-10. ↗

Hör, S., Pirzer, H., Dumoutier, L., Bauer, F., Wittmann, S., Sticht, H. et al. (2004). The T-cell lymphokine interleukin-26 targets epithelial cells through the interleukin-20 receptor 1 and interleukin-10 receptor 2 chains. *J. Biol. Chem., 279*, 33343-51. ↗

Yoon, SI., Jones, BC., Logsdon, NJ., Harris, BD., Deshpande, A., Radaeva, S. et al. (2010). Structure and mechanism of receptor sharing by the IL-10R2 common chain. *Structure, 18*, 638-48. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

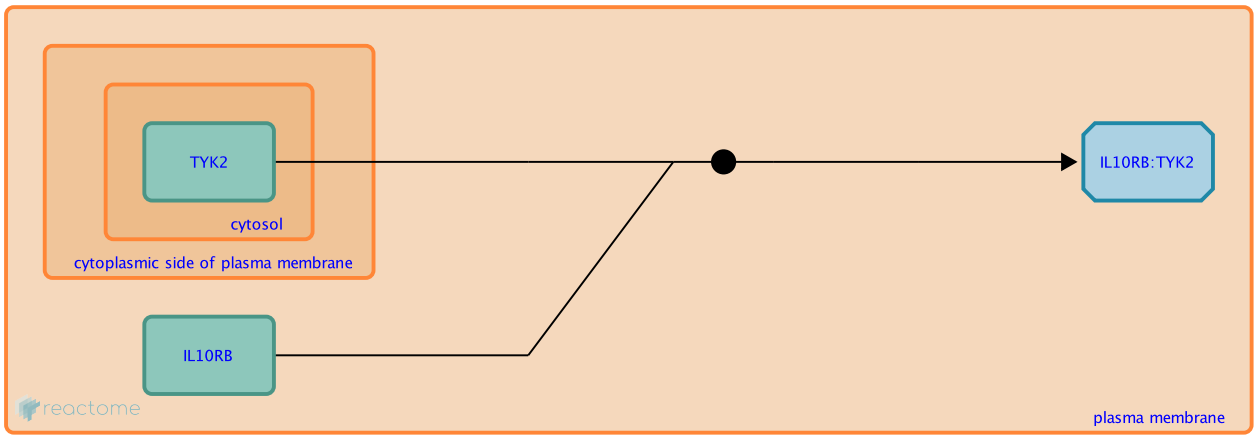
IL10RB binds TYK2 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987223

Type: binding

Compartments: plasma membrane, cytosol



Interleukin-10 receptor subunit beta (IL10RB, IL10R2) binds non-receptor tyrosine-protein kinase TYK2 (TYK2). Interleukin-10 receptor subunit alpha (IL10RA, IL10R1) and IL10RB extracellular domains bind Interleukin-10 (IL10), their intracellular domains are constitutively associated with Tyrosine-protein kinase JAK1 (JAK1) and TYK2 kinases, respectively (Finbloom & Winestock 1995, Ho et al. 1995).

The function of the IL10RB Intracellular domain is to provide a docking site for TYK2, which provides a generic activation signal that can be used to activate signaling pathways associated with the four different Receptor 1 chains, Interleukin-20 receptor subunit alpha (IL20RA), Interleukin-22 receptor subunit alpha-1 (IL22RA1), Interferon lambda receptor 1 (IFNLR1) and Interleukin-10 receptor subunit alpha (IL10RA).

Followed by: IFNL2,IFNL3 bind IL10RB:TYK2 and IFNLR1:JAK1, IL26:IL20RA:JAK1 binds IL10RB:TYK2, IL22:IL22RA1:JAK1 binds IL10RB:TYK2, IFNL1 binds IL10RB:TYK2 and IFNLR1:JAK1

Literature references

Walter, MR. (2014). The molecular basis of IL-10 function: from receptor structure to the onset of signaling. *Curr. Top. Microbiol. Immunol., 380*, 191-212. ↗

Sheikh, F., Baurin, VV., Lewis-Antes, A., Shah, NK., Smirnov, SV., Anantha, S. et al. (2004). Cutting edge: IL-26 signals through a novel receptor complex composed of IL-20 receptor 1 and IL-10 receptor 2. *J. Immunol., 172*, 2006-10. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

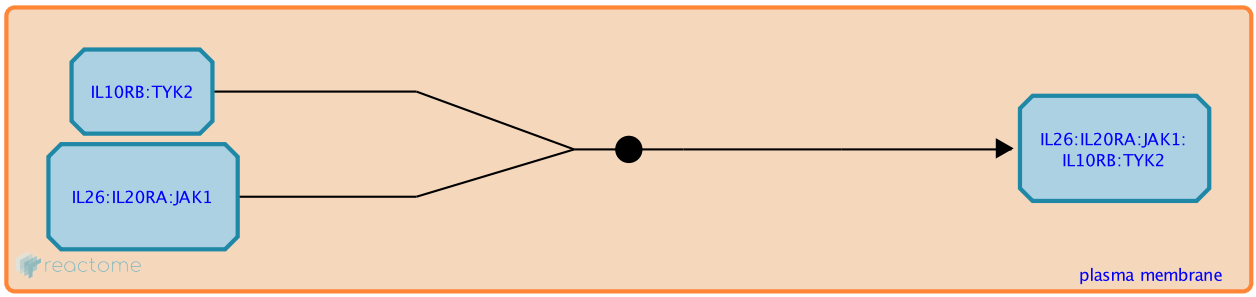
IL26:IL20RA:JAK1 binds IL10RB:TYK2

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8986480

Type: binding

Compartments: plasma membrane, extracellular region, cytosol



The interaction of Interleukin-26 (IL26) with Interleukin-20 receptor subunit alpha (IL20RA) induces conformational changes that allow it to bind Interleukin-10 receptor subunit beta (IL10RB) (Yoon et al. 2006, 2010), which is pre associated with Non-receptor tyrosine-protein kinase TYK2 (TYK2) (another citation).

Preceded by: IL26 binds IL20RA:JAK1, IL10RB binds TYK2

Followed by: IL26:IL20RA:JAK1:IL10RB:TYK2 phosphorylates JAK1, TYK2

Literature references

Yoon, SI., Logsdon, NJ., Sheikh, F., Donnelly, RP., Walter, MR. (2006). Conformational changes mediate interleukin-10 receptor 2 (IL-10R2) binding to IL-10 and assembly of the signaling complex. *J. Biol. Chem., 281*, 35088-96.

Yoon, SI., Jones, BC., Logsdon, NJ., Harris, BD., Deshpande, A., Radaeva, S. et al. (2010). Structure and mechanism of receptor sharing by the IL-10R2 common chain. *Structure, 18*, 638-48.

Sheikh, F., Baurin, VV., Lewis-Antes, A., Shah, NK., Smirnov, SV., Anantha, S. et al. (2004). Cutting edge: IL-26 signals through a novel receptor complex composed of IL-20 receptor 1 and IL-10 receptor 2. *J. Immunol., 172*, 2006-10.

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

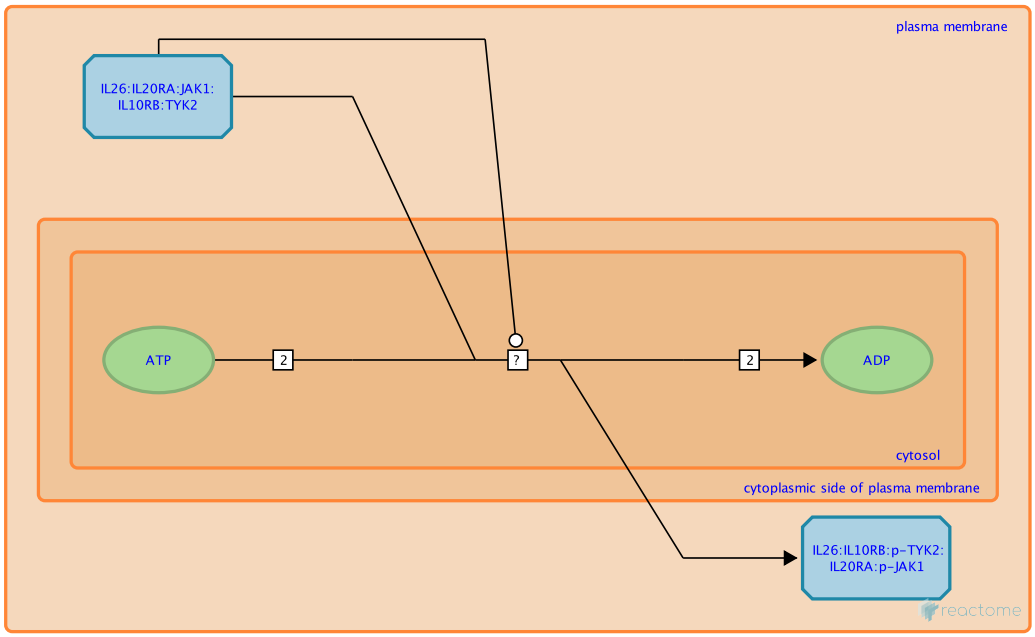
IL26:IL20RA:JAK1:IL10RB:TYK2 phosphorylates JAK1, TYK2 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8986994

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine-protein kinase JAK1 (JAK1) and Non-receptor tyrosine-protein kinase TYK2 (TYK2) are believed to be phosphorylated after Interleukin-26 (IL26) ligand/receptor interaction. The Interleukin-10 receptor subunit beta (IL10RB) component of the IL26 receptor is also a component of the IL10 receptor, where it associates with TYK2 (Finbloom & Winestock 1995). The Interleukin-20 receptor subunit alpha (IL20RA) component of the IL26 receptor, like the Interleukin-10 receptor subunit alpha (IL10RA) subunit of the IL10 receptor, is a type II cytokine receptor, suggested by homology with IL10RA to be capable of binding JAK1 (Ferrao et al. 2016). Structural models of the IL10 receptor suggest that the space between the two receptor subunits is occupied by JAK1 and TYK2 (Yoon et al. 2006, 2010). Taken together, these observations suggest that IL26 receptor signaling involves JAK1 and TYK2 activation.

Preceded by: IL26:IL20RA:JAK1 binds IL10RB:TYK2

Followed by: IL26:IL10RB:p-TYK2:IL20RA:p-JAK1 binds STAT1, STAT3

Literature references

Yoon, SI., Jones, BC., Logsdon, NJ., Harris, BD., Deshpande, A., Radaeva, S. et al. (2010). Structure and mechanism of receptor sharing by the IL-10R2 common chain. *Structure, 18*, 638-48. ↗

Yoon, SI., Logsdon, NJ., Sheikh, F., Donnelly, RP., Walter, MR. (2006). Conformational changes mediate interleukin-10 receptor 2 (IL-10R2) binding to IL-10 and assembly of the signaling complex. *J. Biol. Chem., 281*, 35088-96. ↗

Sheikh, F., Baurin, VV., Lewis-Antes, A., Shah, NK., Smirnov, SV., Anantha, S. et al. (2004). Cutting edge: IL-26 signals through a novel receptor complex composed of IL-20 receptor 1 and IL-10 receptor 2. *J. Immunol., 172*, 2006-10. ↗

Finbloom, DS., Winestock, KD. (1995). IL-10 induces the tyrosine phosphorylation of tyk2 and Jak1 and the differential assembly of STAT1 alpha and STAT3 complexes in human T cells and monocytes. *J. Immunol., 155*, 1079-90. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

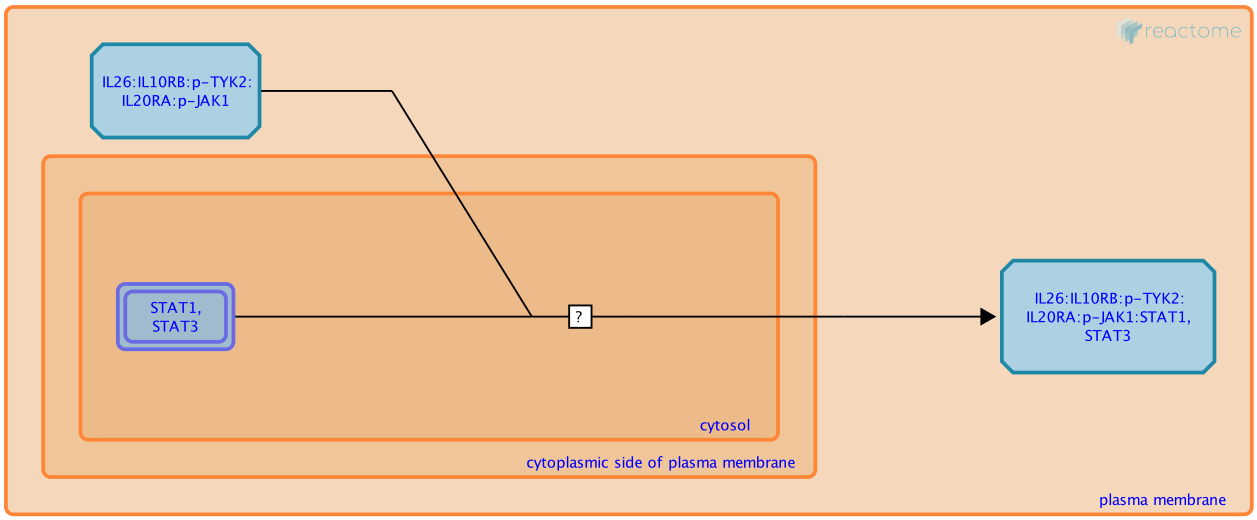
IL26:IL10RB:p-TYK2:IL20RA:p-JAK1 binds STAT1, STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987080

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Signal transducer and activator of transcription 1 alpha/beta (STAT1) or Signal transducer and activator of transcription 3 (STAT3) are believed to bind the Interleukin-26 (IL26) receptor complex (You et al. 2013), which consists of IL26, Interleukin-10 receptor subunit beta (IL10RB), phosphorylated Non-receptor tyrosine-protein kinase TYK2 (TYK2), Interleukin-20 receptor subunit alpha (IL20RA) and phosphorylated Tyrosine-protein kinase JAK1 (JAK1) (Sheikh et al. 2004).

This is a black box event since there is no direct evidence that STAT1 or STAT3 bind to the receptor complex before being phosphorylated but this can be inferred from the signaling mechanism of other related interleukin receptors such as IL10 (Weber-Nordt et al. 1996, Braum et al. 2013). JAK1 association can also be inferred from the presence of a JAK1 binding domain in IL20RA that has been demonstrated to be a JAK1 binding site in several related interleukin receptors including IL22RA1 and IL10RA (Ferrao et al. 2016).

Preceded by: IL26:IL20RA:JAK1:IL10RB:TYK2 phosphorylates JAK1, TYK2

Followed by: IL26:IL10RB:p-TYK2:IL20RA:p-JAK1:STAT1,STAT3 phosphorylates STAT1,STAT3

Literature references

Sheikh, F., Baurin, VV., Lewis-Antes, A., Shah, NK., Smirnov, SV., Anantha, S. et al. (2004). Cutting edge: IL-26 signals through a novel receptor complex composed of IL-20 receptor 1 and IL-10 receptor 2. *J. Immunol., 172*, 2006-10. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

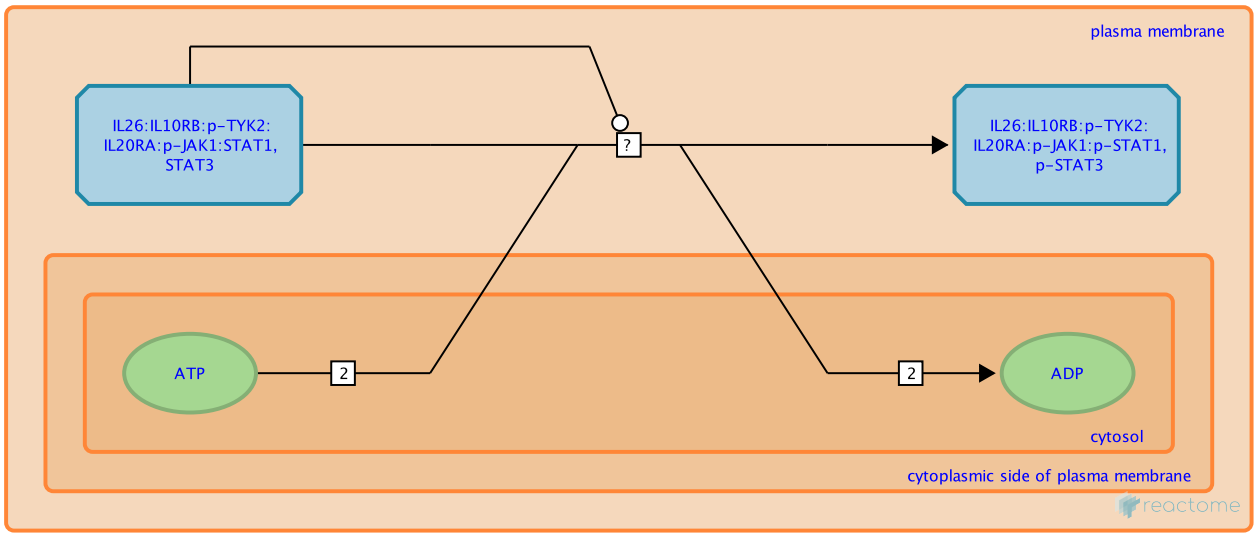
IL26:IL10RB:p-TYK2:IL20RA:p-JAK1:STAT1,STAT3 phosphorylates STAT1,STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987255

Type: uncertain

Compartments: plasma membrane, cytosol, extracellular region



Signal transducer and activator of transcription 1 alpha/beta (STAT1) or Signal transducer and activator of transcription 3 (STAT3) are believed to be phosphorylated by the Interleukin 26 (IL26) receptor complex,which consists of IL26, Interleukin-10 receptor subunit beta (IL10RB), phosphorylated Non-receptor tyrosine-protein kinase TYK2 (TYK2), Interleukin-20 receptor subunit alpha (IL20RA), phosphorylated Tyrosine-protein kinase JAK1 (JAK1) (Sheikh et al. 2004), STAT1 and STAT3.

This is a black box event since there is no direct evidence that STAT1 or STAT3 bind the receptor complex before being phosphorylated, but this can be inferred from the signaling mechanism of other related interleukin receptors such as IL10 (Weber-Nordt et al. 1996, Braum et al. 2013).

Preceded by: IL26:IL10RB:p-TYK2:IL20RA:p-JAK1 binds STAT1, STAT3

Followed by: p-STAT1 and p-STAT3 dissociates from IL26:IL10RB:p-TYK2:IL20RA:p-JAK1

Literature references

Sheikh, F., Baurin, VV., Lewis-Antes, A., Shah, NK., Smirnov, SV., Anantha, S. et al. (2004). Cutting edge: IL-26 signals through a novel receptor complex composed of IL-20 receptor 1 and IL-10 receptor 2. *J. Immunol., 172*, 2006-10. ↗

Editions

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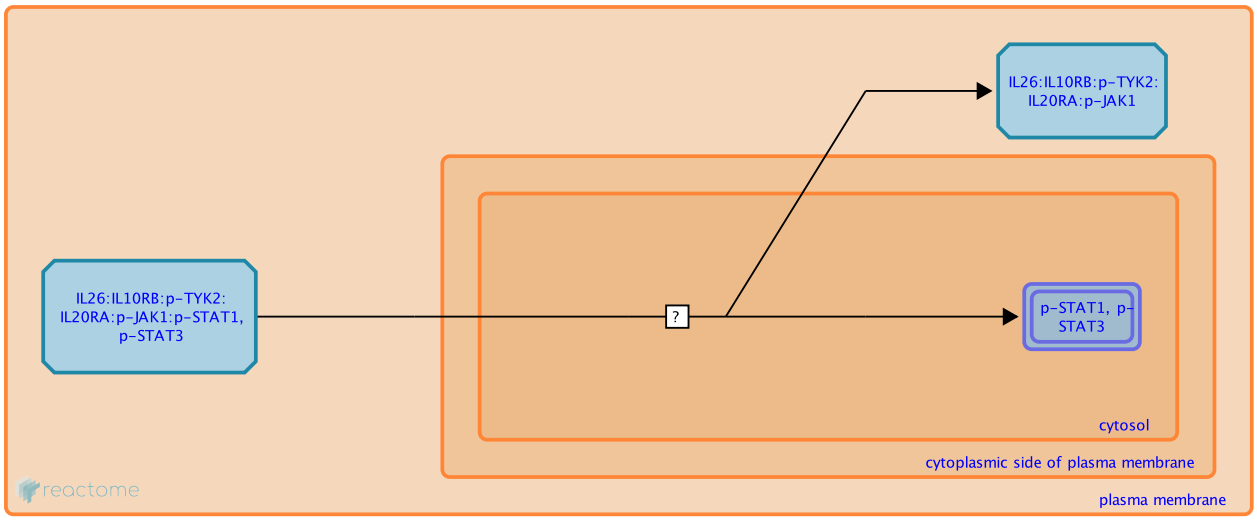
p-STAT1 and p-STAT3 dissociates from IL26:IL10RB:p-TYK2:IL20RA:p-JAK1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987230

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Phosphorylated Signal transducer and activator of transcription 3 (STAT3) and Signal transducer and activator of transcription 1 alpha/beta (STAT1) are believed to dissociate from the Interleukin-26 (IL26) receptor complex. This is a black-box event because dissociation is inferred from other interleukin signaling cascades, e.g. Interleukin-10 (Niemand et al. 2003, Braum et al. 2013, Xiong et al. 2014, Sheikh et al. 2006, You et al. 2013) where dissociation occurs before dimerization and translocation to the nucleus.

Preceded by: IL26:IL10RB:p-TYK2:IL20RA:p-JAK1:STAT1,STAT3 phosphorylates STAT1,STAT3

Followed by: p-STAT1 dimerizes, p-STAT3 dimerizes

Literature references

You, W., Tang, Q., Zhang, C., Wu, J., Gu, C., Wu, Z. et al. (2013). IL-26 promotes the proliferation and survival of human gastric cancer cells by regulating the balance of STAT1 and STAT3 activation. *PLoS ONE, 8*, e63588. ↗

Editions

2017-03-16	Authored	Duenas, C.
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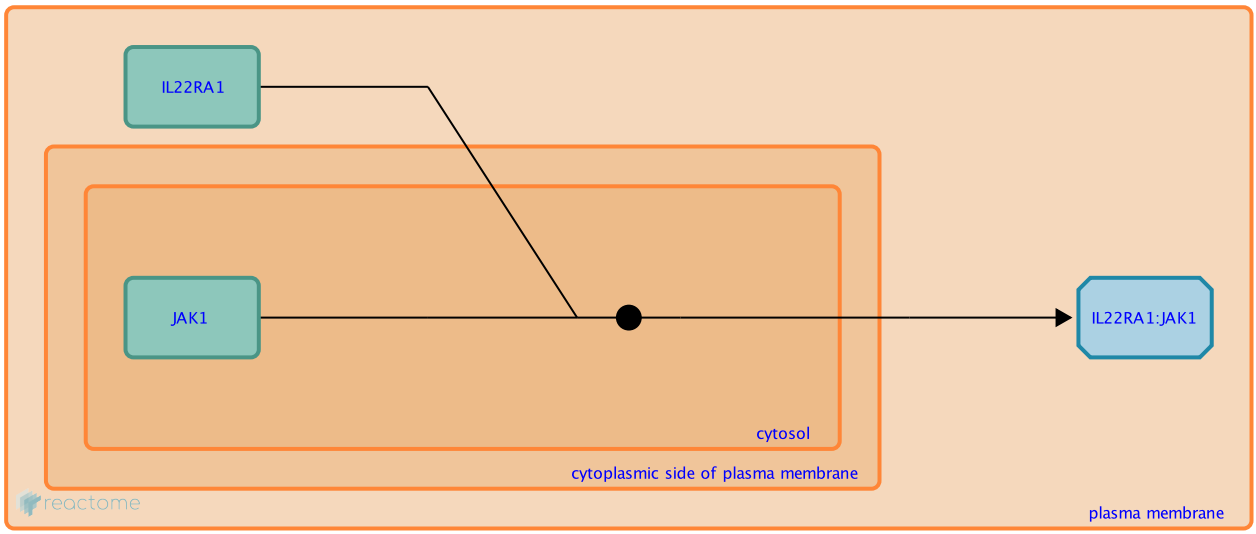
IL22RA1 binds JAK1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987043

Type: binding

Compartments: cytosol, plasma membrane



Tyrosine protein kinase JAK1 (JAK1) binds to Interleukin-22 receptor subunit alpha 1 (IL22RA1). IL22RA1 was identified as one of several interleukin receptors able to bind JAK1 in coimmunoprecipitation experiments (Ferrao et al. 2016).

Followed by: IL22 binds IL22RA1:JAK1 receptor complex

Literature references

Ferrao, R., Wallweber, HJ., Ho, H., Tam, C., Franke, Y., Quinn, J. et al. (2016). The Structural Basis for Class II Cytokine Receptor Recognition by JAK1. *Structure, 24*, 897-905. ↗

Editions

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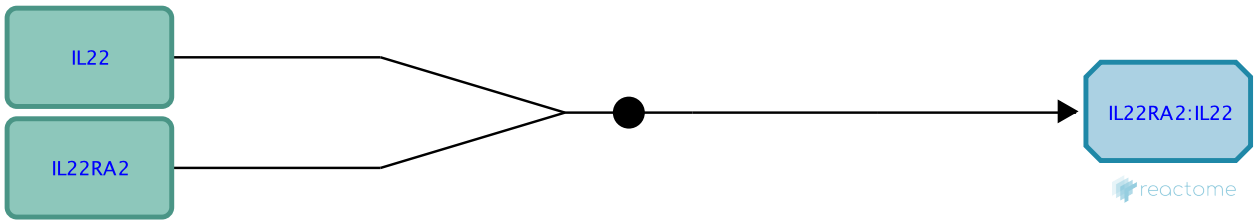
IL22RA2 binds IL22 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-448741

Type: binding

Compartments: extracellular region, plasma membrane



Interleukin-22 receptor subunit alpha-2 (IL22RA2), also known as Interleukin-22 binding protein (IL22BP), is a soluble receptor that binds Interleukin-22 (IL22) within the extracellular region, preventing IL22 from binding to the functional membrane-associated IL22 receptor (Xu et al. 2001, De Moura et al. 2009, Dumoutier et al. 2001, Kotenko et al. 2001). This may play a regulatory role in inflammation.

Followed by: IL22 binds IL22RA1:JAK1 receptor complex

Literature references

Dumoutier, L., Lejeune, D., Colau, D., Renauld, JC. (2001). Cloning and characterization of IL-22 binding protein, a natural antagonist of IL-10-related T cell-derived inducible factor/IL-22. *J Immunol, 166*, 7090-5. ↗

Kotenko, SV., Izotova, LS., Mirochnitchenko, OV., Esterova, E., Dickensheets, H., Donnelly, RP. et al. (2001). Identification, cloning, and characterization of a novel soluble receptor that binds IL-22 and neutralizes its activity. *J Immunol, 166*, 7096-103. ↗

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2014-06-04	Authored	Jupe, S.
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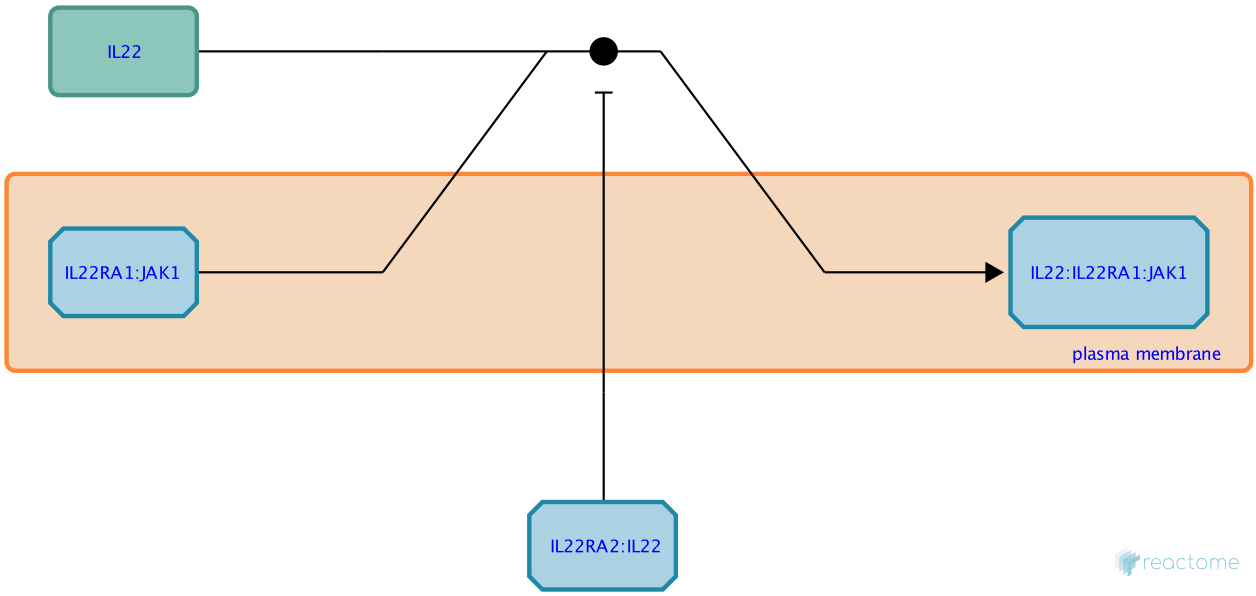
IL22 binds IL22RA1:JAK1 receptor complex ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-448480

Type: binding

Compartments: extracellular region, plasma membrane, cytosol



Temporal models suggest that the first event in IL22 receptor formation is binding of Interleukin-22 (IL22) to IL22RA1), which pre associates with JAK1 (Li et al. 2004, Jones et al. 2008, Xie et al. 2000, Xu et al. 2001).

The Interleukin-22 receptor consists of IL22RA1 and Interleukin-10 receptor subunit beta (IL10RB), which is also a component of the receptors for Interleukin-10 (IL10), Interleukin-22 (IL22), Interleukin-26 (IL26), Interleukin-28 (IL28), and Interferon lambda-1 (IFNL1).

Preceded by: IL22RA1 binds JAK1, IL22RA2 binds IL22

Followed by: IL22:IL22RA1:JAK1 binds IL10RB:TYK2

Literature references

Xie, MH., Aggarwal, S., Ho, WH., Foster, J., Zhang, Z., Stinson, J. et al. (2000). Interleukin (IL)-22, a novel human cytokine that signals through the interferon receptor-related proteins CRF2-4 and IL-22R. *J Biol Chem, 275*, 31335-9. ↗

Xu, W., Presnell, SR., Parrish-Novak, J., Kindsvogel, W., Jaspers, S., Chen, Z. et al. (2001). A soluble class II cytokine receptor, IL-22RA2, is a naturally occurring IL-22 antagonist. *Proc Natl Acad Sci U S A, 98*, 9511-6. ↗

Li, J., Tomkinson, KN., Tan, XY., Wu, P., Yan, G., Spaulding, V. et al. (2004). Temporal associations between interleukin 22 and the extracellular domains of IL-22R and IL-10R2. *Int. Immunopharmacol., 4*, 693-708. ↗

Jones, BC., Logsdon, NJ., Walter, MR. (2008). Structure of IL-22 bound to its high-affinity IL-22R1 chain. *Structure, 16*, 1333-44. ↗

Editions

2014-06-04	Authored	Jupe, S.
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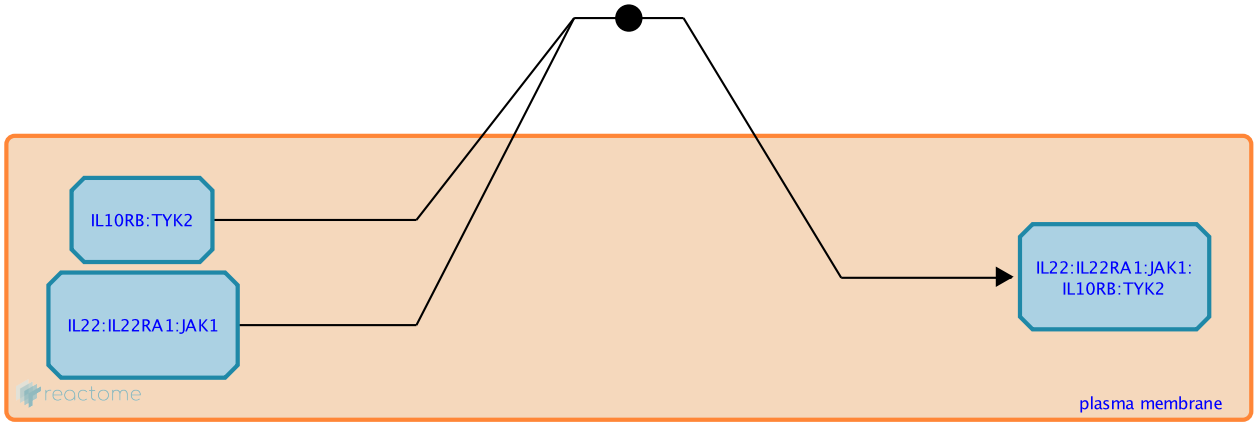
IL22:IL22RA1:JAK1 binds IL10RB:TYK2 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8854645

Type: binding

Compartments: extracellular region, plasma membrane, cytosol



Temporal models suggest that binding of Interleukin‐22 (IL22) to Interleukin‐22 receptor subunit alpha 1 (IL22RA1) creates a surface that is bound by the extracellular region of Interleukin‐10 receptor beta chain (IL10RB) (Li et al. 2004, Bleicher et al. 2008).

Preceded by: IL22 binds IL22RA1:JAK1 receptor complex, IL10RB binds TYK2

Followed by: IL22:IL22RA1:JAK1:IL10RB:TYK2 phosphorylates JAK1,TYK2

Literature references

Li, J., Tomkinson, KN., Tan, XY., Wu, P., Yan, G., Spaulding, V. et al. (2004). Temporal associations between interleukin 22 and the extracellular domains of IL-22R and IL-10R2. *Int. Immunopharmacol., 4*, 693-708. ↗

Editions

2014-06-04	Authored	Jupe, S.
2016-01-28	Edited	Jupe, S.
2016-01-28	Reviewed	Meldal, BH.

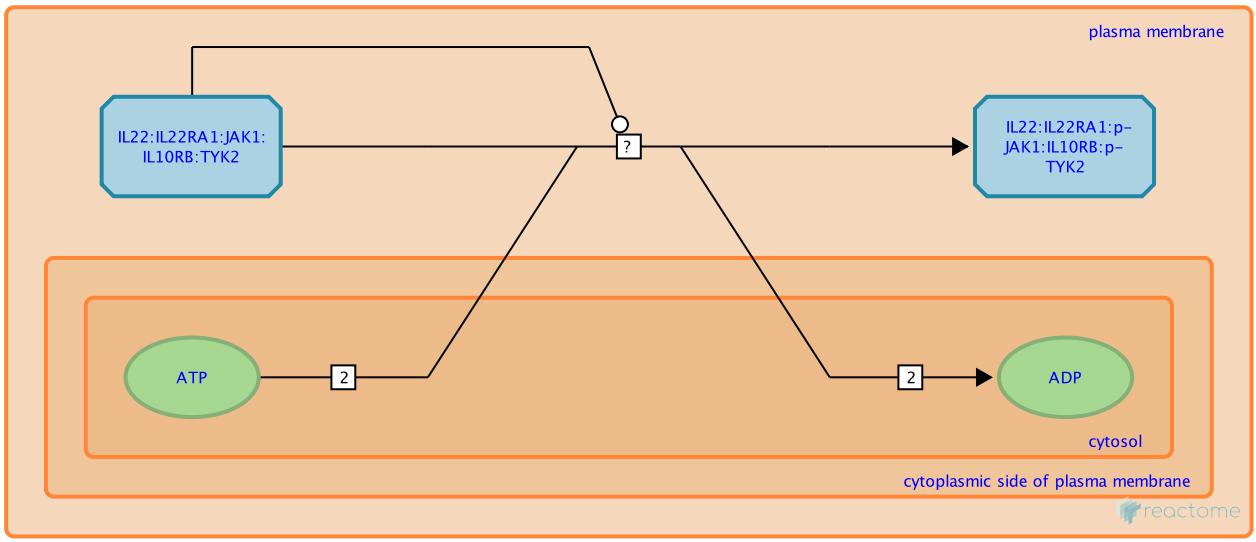
IL22:IL22RA1:JAK1:IL10RB:TYK2 phosphorylates JAK1,TYK2 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987042

Type: uncertain

Compartments: plasma membrane, cytosol, extracellular region



Inferred from rat, mouse, human :Tyrosine protein kinase JAK1 (JAK1) and Non-receptor tyrosine-protein kinase TYK2 (TYK2) are believed to be phosphorylated after Interleukin-22 interacts with its receptor. The receptor is a complex formed by Interleukin-22 receptor subunit alpha-1 (IL22RA1), JAK1, Interleukin-10 receptor subunit beta (IL10RB) and TYK2 (Lejeune et al. 2002, Sabat et al. 2014).

This is a black-box event because the JAK1/TYK2 coordinates phosphorylated after IL22 stimulus are unknown.

Preceded by: IL22:IL22RA1:JAK1 binds IL10RB:TYK2

Followed by: IL22:IL22RA1:p-JAK1:IL10RB:p-TYK2 phosphorylates IL22RA

Literature references

Lejeune, D., Dumoutier, L., Constantinescu, S., Kruijer, W., Schuringa, JJ., Renauld, JC. (2002). Interleukin-22 (IL-22) activates the JAK/STAT, ERK, JNK, and p38 MAP kinase pathways in a rat hepatoma cell line. Pathways that are shared with and distinct from IL-10. *J. Biol. Chem., 277*, 33676-82. ↗

Editions

2017-03-16	Authored	Duenas, C.
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2017-11-15	Reviewed	Datta, SK.

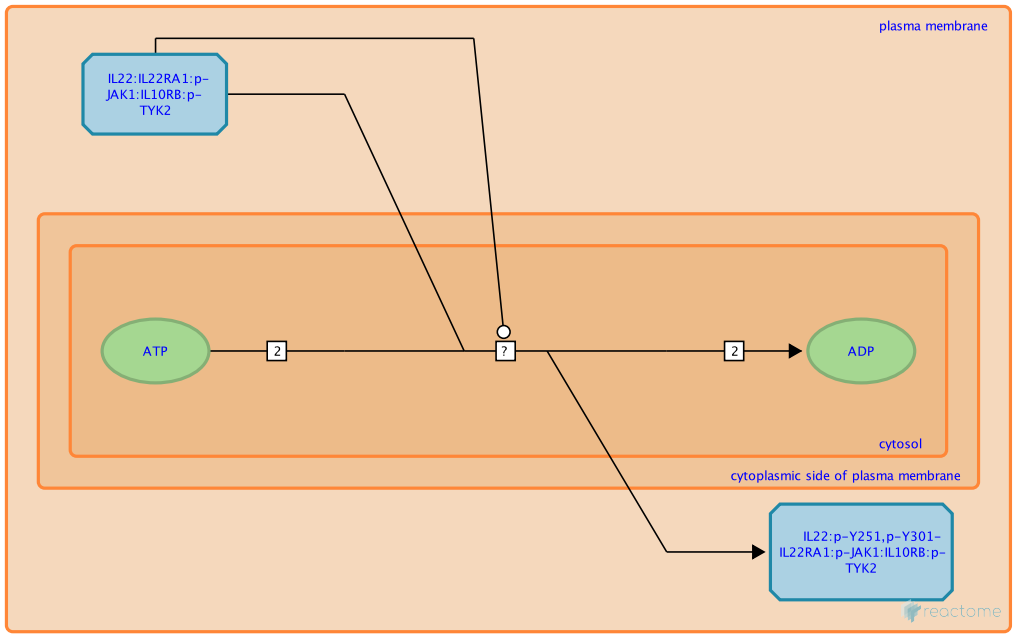
IL22:IL22RA1:p-JAK1:IL10RB:p-TYK2 phosphorylates IL22RA ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8986995

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Interleukin-22 receptor subunit alpha-1 (IL22RA1) is phosphorylated within the receptor complex, which consists of Interleukin-22 (IL22), IL22RA1 associated with phosphorylated Tyrosine protein kinase JAK1 (JAK1) and Interleukin-10 receptor subunit beta (IL10RB) associated with phosphorylated non-receptor tyrosine-protein kinase TYK2 (TYK2). IL22 stimulated IL22RA1 tyrosine phosphorylation and recruitment of Tyrosine protein phosphatase non receptor type 11 (PTPN11, SHP2). PTPN11 binding was abolished by mutation of Tyrosines-251 and 301 (Meng et al. 2010).

This is a black-box event because it is not clear which kinase is responsible for IL22RA1 phosphorylation.

Preceded by: IL22:IL22RA1:JAK1:IL10RB:TYK2 phosphorylates JAK1,TYK2

Followed by: IL22:p□Y251,p□Y301□IL22RA1:p□JAK1:PTPN11:IL10RB:p□TYK2 binds PTPN11

Literature references

Meng, S., Gui, Q., Xu, Q., Lu, K., Jiao, X., Fan, J. et al. (2010). Association of Shp2 with phosphorylated IL-22R1 is required for interleukin-22-induced MAP kinase activation. *J Mol Cell Biol, 2,* 223-30. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

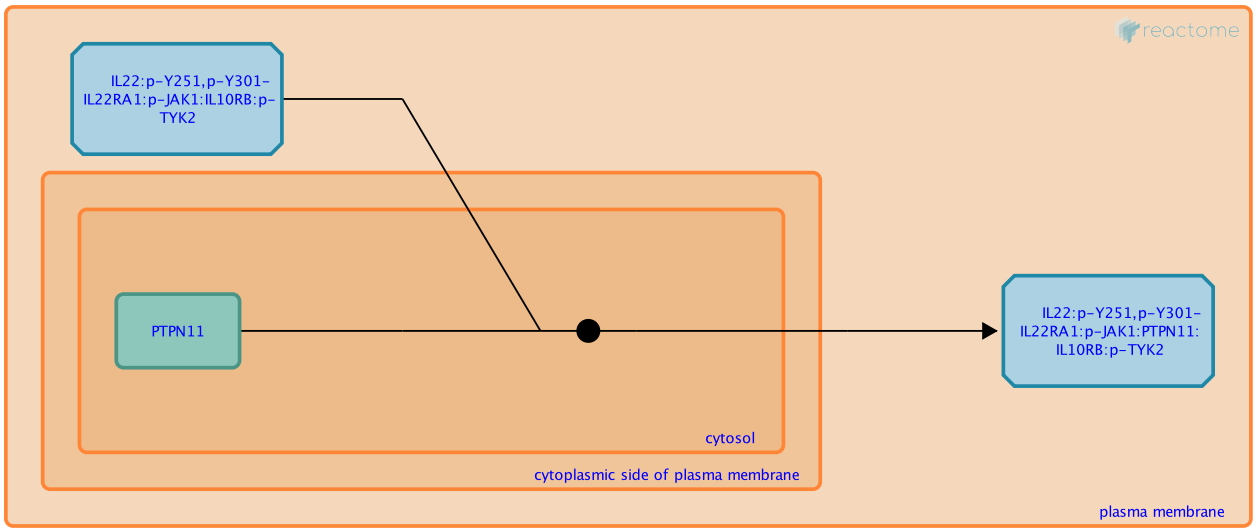
IL22:p□Y251,p□Y301□IL22RA1:p□JAK1:PTPN11:IL10RB:p□TYK2 binds PTPN11 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987132

Type: binding

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine-protein phosphatase non-receptor type 11 (PTPN11, SHP2) binds the Interleukin-22 (IL22) receptor complex. Tyrosines 251 and 301 of IL22RA1 are required for PTPN11 binding (Meng et al. 2010).

Preceded by: IL22:IL22RA1:p-JAK1:IL10RB:p-TYK2 phosphorylates IL22RA

Followed by: IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:PTPN11:IL10RB:p-TYK2 binds STAT3

Literature references

Meng, S., Gui, Q., Xu, Q., Lu, K., Jiao, X., Fan, J. et al. (2010). Association of Shp2 with phosphorylated IL-22R1 is required for interleukin-22-induced MAP kinase activation. *J Mol Cell Biol, 2*, 223-30. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

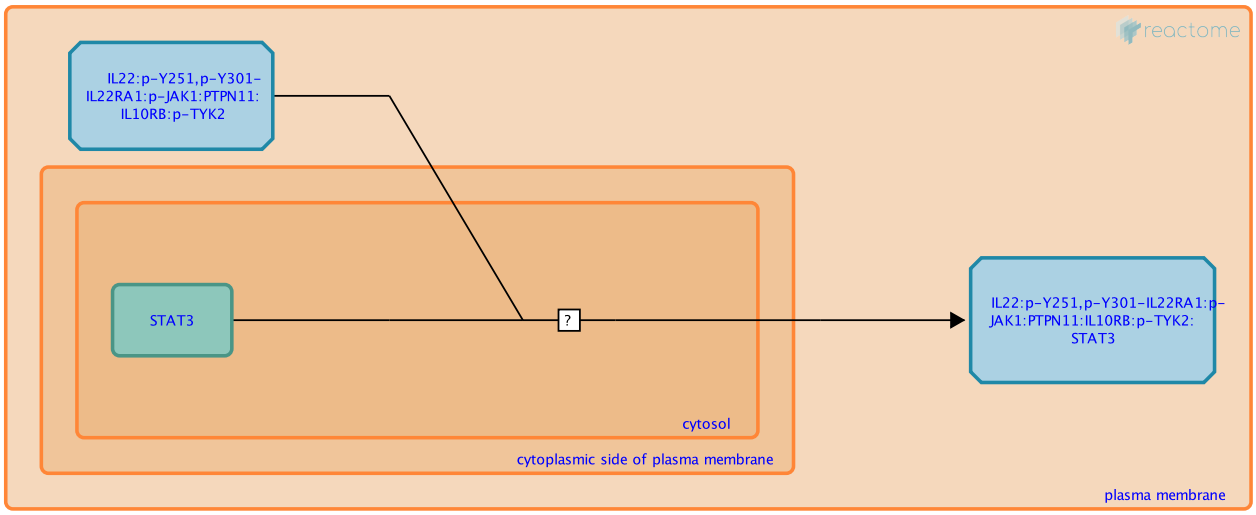
IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:PTPN11:IL10RB:p-TYK2 binds STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987014

Type: uncertain

Compartments: cytosol, plasma membrane, extracellular region



Signal transducer and activator of transcription 3 (STAT3) is believed to bind the Interleukin-22 (IL22) receptor complex, which consists of IL22, phosphorylated Interleukin-22 receptor subunit alpha-1 (IL22RA1), phosphorylated Tyrosine-protein kinase JAK1 (JAK1), Interleukin-10 receptor subunit beta (IL10RB), phosphorylated Non-receptor tyrosine-protein kinase TYK2 (TYK2) and Tyrosine-protein phosphatase non-receptor type 11 (PTPN11 or SHP2) (Meng et al. 2010, Sestito et al. 2011). STAT3 has been reported to pre-associate with IL22RA in the absence of phosphorylated receptor tyrosines (Dumoutier et al. 2009).

This is a black box event because STAT3 binding is represented here as a post-receptor phosphorylation event, inferred from the consensus on interleukin receptor JAK-STAT signaling (Li et al. 2008, Santos et al. 2011).

Preceded by: IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:PTPN11:IL10RB:p-TYK2 binds PTPN11

Followed by: IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:IL10RB:p-TYK2:STAT3 phosphorylates STAT3

Literature references

Sestito, R., Madonna, S., Scarponi, C., Cianfarani, F., Failla, CM., Cavani, A. et al. (2011). STAT3-dependent effects of IL-22 in human keratinocytes are counterregulated by sirtuin 1 through a direct inhibition of STAT3 acetylation. *FASEB J., 25*, 916-27. ↗

Editions

2017-03-16	Authored	Duenas, C.
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2017-11-15	Reviewed	Datta, SK.

IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:IL10RB:p-TYK2:STAT3 phosphorylates STAT3

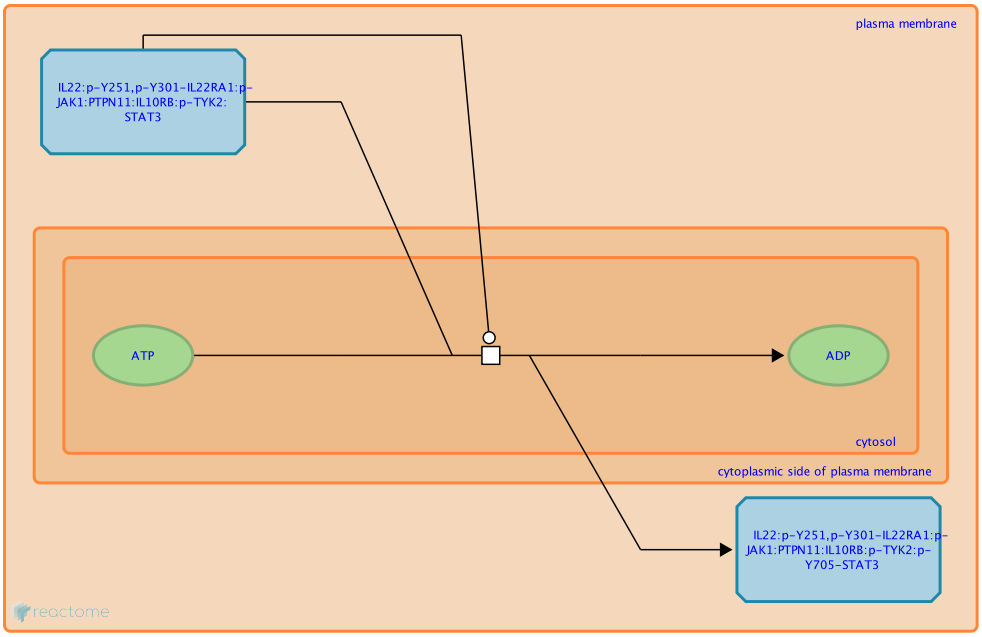
↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987070

Type: transition

Compartments: cytosol, extracellular region, plasma membrane



Signal transducer and activator of transcription 3 (STAT3) is phosphorylated by the Interleukin-22 (IL22) receptor complex (Lejeune et al. 2002, Dumoutier et al. 2009, Lindemanns et al. 2015), which consists of IL22, phosphorylated Interleukin-22 receptor subunit alpha-1 (IL22RA1), phosphorylated Tyrosine-protein kinase JAK1 (JAK1), Interleukin-10 receptor subunit beta (IL10RB), phosphorylated Non-receptor tyrosine-protein kinase TYK2 (TYK2) and STAT3 (Meng et al. 2010, Sestito et al. 2011).

Preceded by: IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:PTPN11:IL10RB:p-TYK2 binds STAT3

Followed by: p-Y705-STAT3 dissociates from IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:IL10RB:p-TYK2:p-Y705-STAT3

Literature references

Sestito, R., Madonna, S., Scarponi, C., Cianfarani, F., Failla, CM., Cavani, A. et al. (2011). STAT3-dependent effects of IL-22 in human keratinocytes are counterregulated by sirtuin 1 through a direct inhibition of STAT3 acetylation. *FASEB J., 25*, 916-27. ↗

Editions

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2017-11-15	Reviewed	Datta, SK.

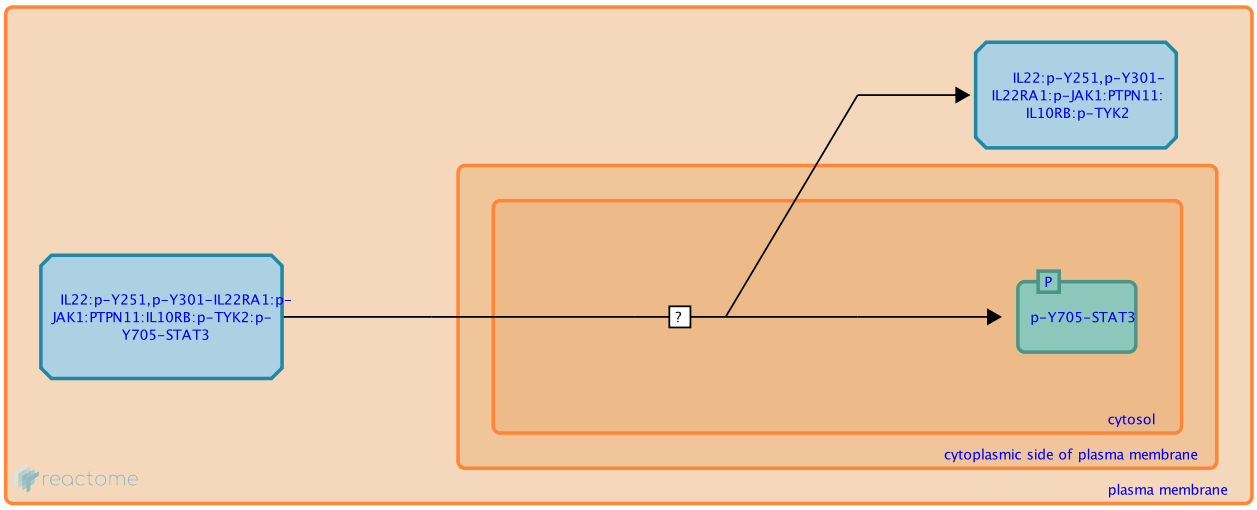
p-Y705-STAT3 dissociates from IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:IL10RB:p-TYK2:p-Y705-STAT3 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987236

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Phosphorylated Signal transducer and activator of transcription 3 (STAT3) dissociates from the Interleukin-22 (IL22) receptor complex, which consists of IL22, phosphorylated Interleukin-22 receptor subunit alpha 1 (IL22RA1), phosphorylated Tyrosine-protein kinase JAK1 (JAK1), Interleukin-10 receptor subunit beta (IL10RB), phosphorylated Non-receptor tyrosine protein-kinase TYK2 (TYK2) and Tyrosine protein phosphatase non receptor type 11 (PTPN11 or SHP2) and STAT3. This is a black-box event because dissociation is inferred from other interleukin signaling cascades e.g. Interleukin-10 (Niemand et al. 2003, Braum et al. 2013, Xiong et al. 2014, Sheikh et al. 2006, You et al. 2013) where dissociation occurs before STAT dimerization and translocation to the nucleus.

Preceded by: IL22:p-Y251,p-Y301-IL22RA1:p-JAK1:IL10RB:p-TYK2:STAT3 phosphorylates STAT3

Followed by: p-Y705-STAT3 dimerizes

Literature references

Liu, L., McBride, KM., Reich, NC. (2005). STAT3 nuclear import is independent of tyrosine phosphorylation and mediated by importin-alpha3. *Proc. Natl. Acad. Sci. U.S.A., 102*, 8150-5. ↗

Akira, S., Nishio, Y., Inoue, M., Wang, XJ., Wei, S., Matsusaka, T. et al. (1994). Molecular cloning of APRF, a novel IFN-stimulated gene factor 3 p91-related transcription factor involved in the gp130-mediated signaling pathway. *Cell, 77*, 63-71. ↗

Editions

2017-03-16	Authored	Duenas, C.
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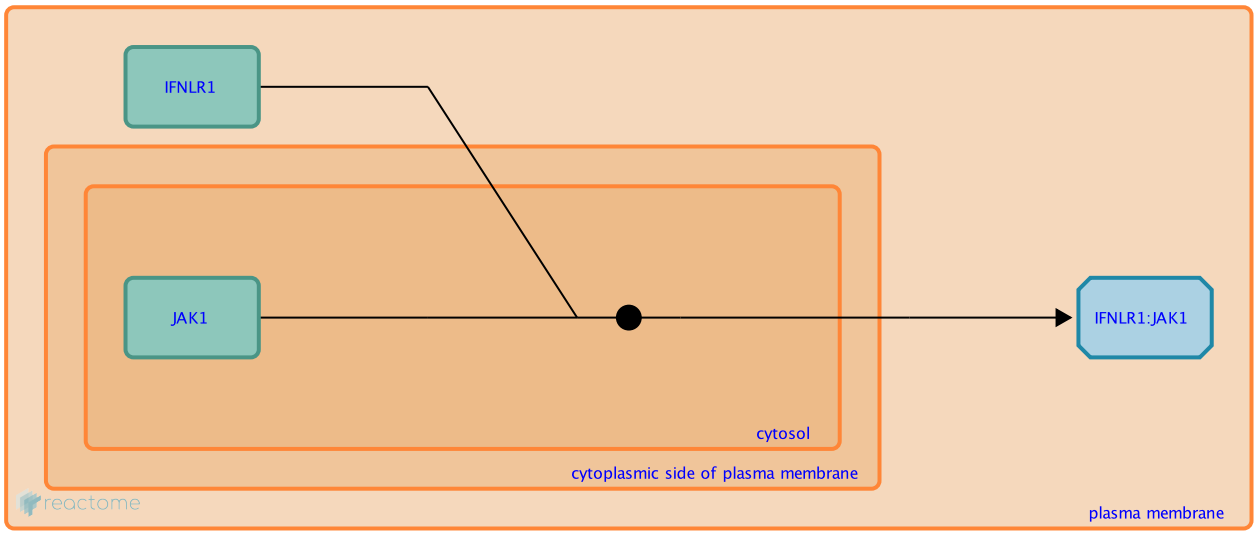
JAK1 binds IFNLR1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987120

Type: binding

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine protein kinase JAK1 (JAK1) binds Interferon lambda receptor 1 (IFNLR1).

The Box1 of IFNLR1 binds to the F2 subdomain of the JAK1 FERM, in a cleft formed by helices F2 alpha2, F2 alpha3, and F2 alpha4 (Ferrao et al. 2017).

Followed by: IFNL2,IFNL3 bind IL10RB:TYK2 and IFNLR1:JAK1, IFNL1 binds IL10RB:TYK2 and IFNLR1:JAK1

Literature references

Ferrao, R., Lupardus, PJ. (2017). The Janus Kinase (JAK) FERM and SH2 Domains: Bringing Specificity to JAK-Receptor Interactions. *Front Endocrinol (Lausanne), 8*, 71. ↗

Editions

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2017-11-15	Reviewed	Datta, SK.

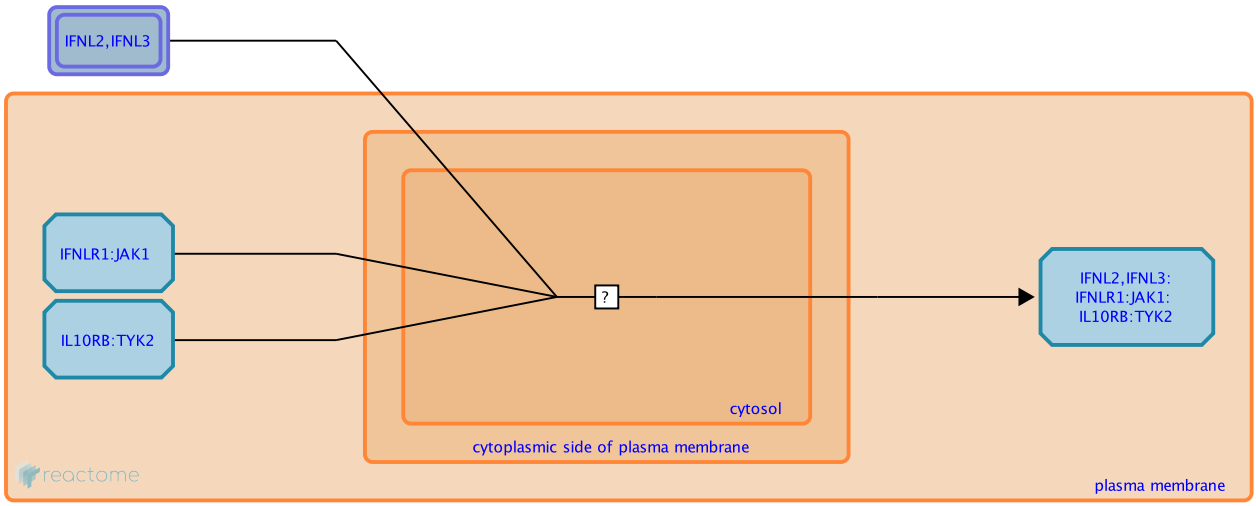
IFNL2,IFNL3 bind IL10RB:TYK2 and IFNLR1:JAK1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987105

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Interferon lambda-1 (IFNL1) binds Interleukin-10 receptor subunit beta (IL10RB), which is associated with Non-receptor tyrosine-protein kinase TYK2 (TYK2), and Interferon lambda receptor-1 (IFNLR1), which is associated with Tyrosine-protein kinase JAK1 (JAK1). Interferon lambda-2 (IFNL2, IL28A), Interleukin-28B (IL28B, Interferon lambda-3) and Interferon lambda-1 (IFNL1, Interleukin-29) are related cytokines, collectively known as the type III interferons. They are distantly related to the type I interferons (IFNs) and are members of the class II cytokine family, which includes type I, II, and III interferons and the Interleukin-10 family (IL10, Interleukin-19 (IL19), Interleukin-20 (IL20), Interleukin-22 (IL22), Interleukin-24 (IL24), and Interleukin-26 (IL26)). They are encoded by genes that form a cluster on 19q13. Expression of all three IFNLs can be induced by viral infection. They share a heterodimeric class II cytokine receptor that consists of IFNLR1 and interleukin-10 receptor beta (IL10RB) (Kotenko et al. 2003, Sheppard et al. 2003). IL10RB is also part of the receptor complexes for IL10, IL22, IL24 and IL26. IFNL1, IFNL2 and IFNL3, like type I IFNs, can signal through ISRE regulatory sites and are likely to provide antiviral activity by the induction of at least a subset of IFN-stimulated genes (Dumoutier et al. 2004, Gad et al 2004, Sheppard et al. 2003).

Preceded by: JAK1 binds IFNLR1, IL10RB binds TYK2

Literature references

Dumoutier, L., Tounsi, A., Michiels, T., Sommereyns, C., Kotenko, SV., Renauld, JC. (2004). Role of the interleukin (IL)-28 receptor tyrosine residues for antiviral and antiproliferative activity of IL-29/interferon-lambda 1: similarities with type I interferon signaling (Dumoutier et al.). *J. Biol. Chem., 279*, 32269-74. ↗

Gad, HH., Dellgren, C., Hamming, OJ., Vends, S., Paludan, SR., Hartmann, R. (2009). Interferon-lambda is functionally an interferon but structurally related to the interleukin-10 family. *J. Biol. Chem., 284*, 20869-75. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

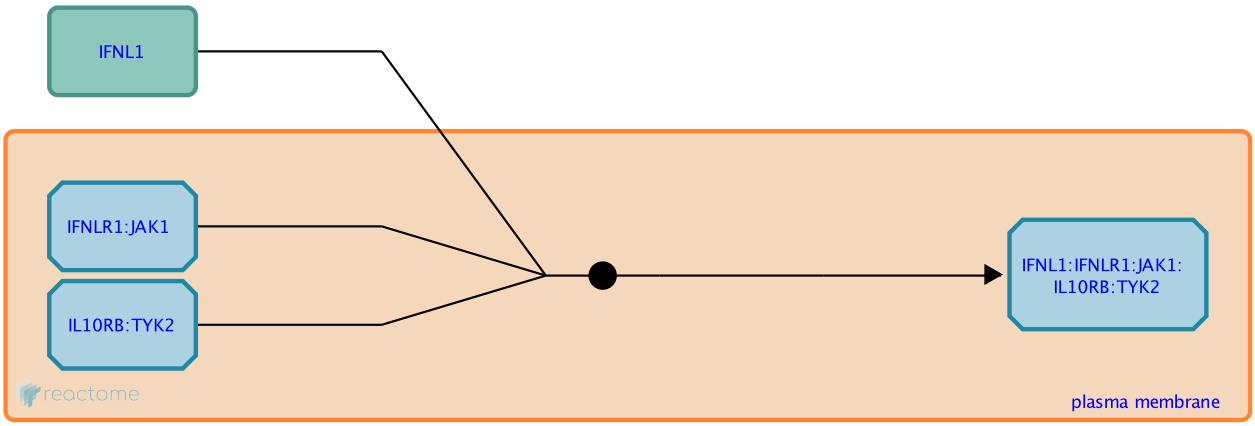
IFNL1 binds IL10RB:TYK2 and IFNLR1:JAK1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-448661

Type: binding

Compartments: plasma membrane, extracellular region, cytosol



Interferon lambda-1 (IFNL1) binds Interleukin-10 receptor subunit beta (IL10RB), which is associated with Non-receptor tyrosine-protein kinase TYK2 (TYK2), and Interferon lambda receptor-1 (IFNLR1), which is associated with Tyrosine-protein kinase JAK1 (JAK1). Interferon lambda-2 (IFNL2, IL28A), Interleukin-28B (IL28B, Interferon lambda-3) and Interferon lambda-1 (IFNL1, Interleukin-29) are related cytokines, collectively known as the type III interferons. They are distantly related to the type I interferons (IFNs) and are members of the class II cytokine family, which includes type I, II, and III interferons and the Interleukin-10 family (IL10, Interleukin-19 (IL19), Interleukin-20 (IL20), Interleukin-22 (IL22), Interleukin-24 (IL24), and Interleukin-26 (IL26)). They are encoded by genes that form a cluster on 19q13. Expression of all three IFNLs can be induced by viral infection. They share a heterodimeric class II cytokine receptor that consists of IFNLR1 and interleukin-10 receptor beta (IL10RB) (Kotenko et al. 2003, Sheppard et al. 2003). IL10RB is also part of the receptor complexes for IL10, IL22, IL24 and IL26. IFNL1, IFNL2 and IFNL3, like type I IFNs, can signal through ISRE regulatory sites and are likely to provide antiviral activity by the induction of at least a subset of IFN-stimulated genes (Dumoutier et al. 2004, Gad et al 2004, Sheppard et al. 2003).

Preceded by: JAK1 binds IFNLR1, IL10RB binds TYK2

Followed by: IFNL1:IFNLR1:JAK1:IL10RB:TYK2 phosphorylates JAK1,TYK2

Literature references

Sheppard, P., Kindsvogel, W., Xu, W., Henderson, K., Schlutsmeyer, S., Whitmore, TE. et al. (2003). IL-28, IL-29 and their class II cytokine receptor IL-28R. *Nat Immunol, 4*, 63-8. ↗

Vandenbroeck, K., Alvarez, J., Swaminathan, B., Alloza, I., Matesanz, F., Urcelay, E. et al. (2012). A cytokine gene screen uncovers SOCS1 as genetic risk factor for multiple sclerosis. *Genes Immun., 13*, 21-8. ↗

Prokunina-Olsson, L., Muchmore, B., Tang, W., Pfeiffer, RM., Park, H., Dickensheets, H. et al. (2013). A variant upstream of IFNL3 (IL28B) creating a new interferon gene IFNL4 is associated with impaired clearance of hepatitis C virus. *Nat. Genet., 45*, 164-71. ↗

Editions

2014-06-04	Authored	Jupe, S.
2016-01-28	Edited	Jupe, S.
2016-01-28	Reviewed	Meldal, BH.

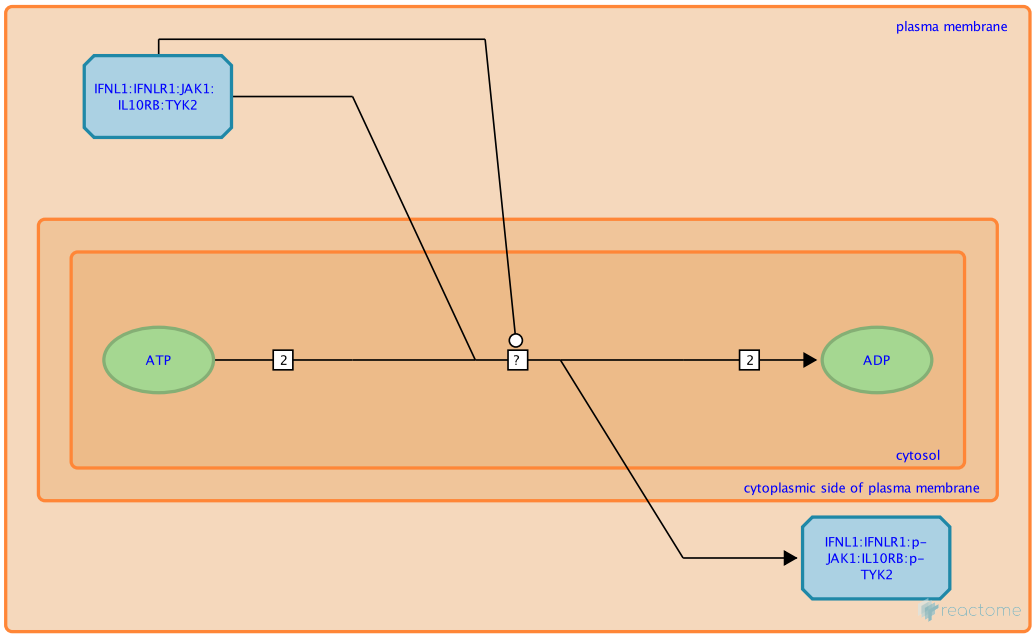
IFNL1:IFNLR1:JAK1:IL10RB:TYK2 phosphorylates JAK1,TYK2 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987202

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Tyrosine-protein kinase JAK1 (JAK1) and Non-receptor tyrosine-protein kinase TYK2 (TYK2) are phosphorylated after Interferon lambda-1 (IFNL1, IL29) interacts with its receptor complex, which consists of Interferon lambda receptor-1 (IFNLR1 (class II cytokine receptor)), JAK1, Interleukin-10 receptor beta (IL10RB) and TYK2 (Novak et al.2008, Dumoitier et al. 2004).This initiates a signaling cascade that involves Jak1 and Tyk2 dependent tyrosine phosphorylation of signal transducers and activators of transcription 1 (STAT1) and STAT2 proteins that interact with a third protein, the p48 DNA binding subunit, to form the IFN stimulated gene factor 3 complex (ISGF3).

This is a black box event since direct evidence for JAK1 and TYK2 binding after IFNL1 stimulation is lacking. However, this can be inferred from other cytokine signaling. In other cytokine ligand receptor cascades such as IFNalpha signaling, STAT activation occurs after phosphorylation by kinases associated with the receptor (Sheppard et al. 2003).

Preceded by: IFNL1 binds IL10RB:TYK2 and IFNLR1:JAK1

Followed by: IFNL1:IFNLR1:p-JAK1:IL10RB:p-TYK2 phosphorylates IFNLR1

Literature references

Novak, AJ., Grote, DM., Ziesmer, SC., Rajkumar, V., Doyle, SE., Ansell, SM. (2008). A role for IFN-lambda1 in multiple myeloma B cell growth. *Leukemia, 22*, 2240-6. ↗

Dumoutier, L., Tounsi, A., Michiels, T., Sommereyns, C., Kotenko, SV., Renauld, JC. (2004). Role of the interleukin (IL)-28 receptor tyrosine residues for antiviral and antiproliferative activity of IL-29/interferon-lambda 1: similarities with type I interferon signaling (Dumoutier et al.). *J. Biol. Chem., 279*, 32269-74. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

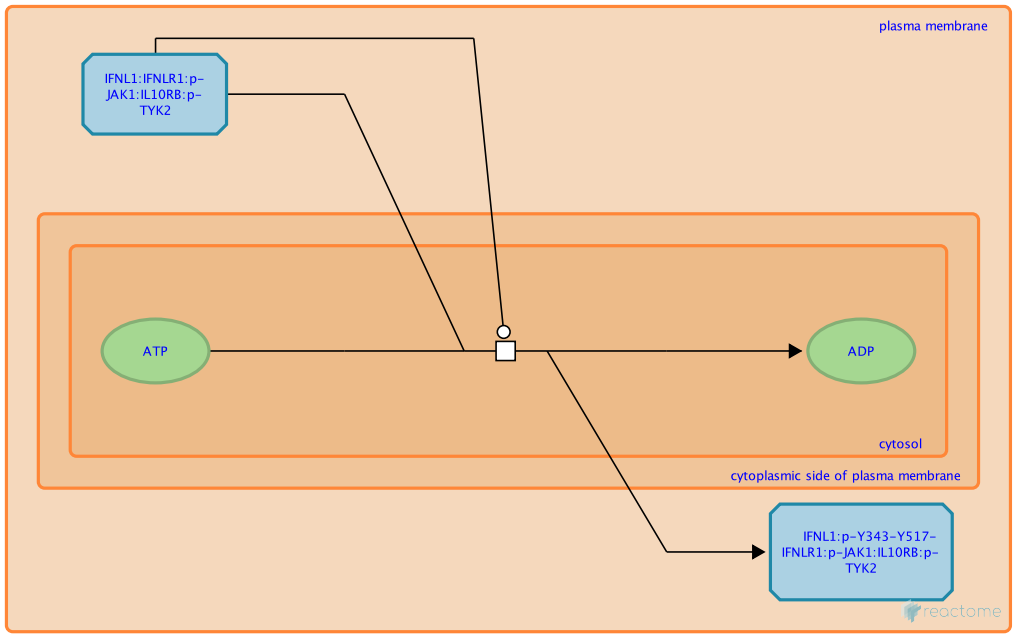
IFNL1:IFNLR1:p-JAK1:IL10RB:p-TYK2 phosphorylates IFNLR1 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987040

Type: transition

Compartments: cytosol, extracellular region, plasma membrane



Interferon lambda receptor 1 receptor (IFNLR1, IL28RA) is believed to be phosphorylated by the Interferon lambda-1 (IFNL1 or IL29) complex (Sheppard et al. 2003). This complex is formed by IFNL1, IFNLR1, which is associated with phosphorylated Tyrosine protein kinase JAK1 (JAK1) and Interleukin 10 receptor beta (IL10RB), which is associated with phosphorylated Non-receptor tyrosine-protein kinase TYK2 (TYK2). IFNL1 induced Signal transducer and activator of transcription 2 (STAT2) tyrosine phosphorylation but not that of other STATs is at least partly mediated by IFNLR1 tyrosines 343 and 517 (Dumoutier et al. 2004). This is a black box event because there is not enough evidence to associate specific tyrosines with the binding of STATs and because the phosphorylation of these tyrosines is inferred from the STAT signaling mechanisms of related receptors.

Preceded by: IFNL1:IFNLR1:JAK1:IL10RB:TYK2 phosphorylates JAK1,TYK2

Followed by: IFNL1:p-Y434,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2 binds STAT1, STAT2, STAT3, STAT4, STAT5

Literature references

Dumoutier, L., Tounsi, A., Michiels, T., Sommereyns, C., Kotenko, SV., Renauld, JC. (2004). Role of the interleukin (IL)-28 receptor tyrosine residues for antiviral and antiproliferative activity of IL-29/interferon-lambda 1: similarities with type I interferon signaling (Dumoutier et al.). *J. Biol. Chem., 279*, 32269-74. ↗

Sheppard, P., Kindsvogel, W., Xu, W., Henderson, K., Schlutsmeyer, S., Whitmore, TE. et al. (2003). IL-28, IL-29 and their class II cytokine receptor IL-28R. *Nat Immunol, 4*, 63-8. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

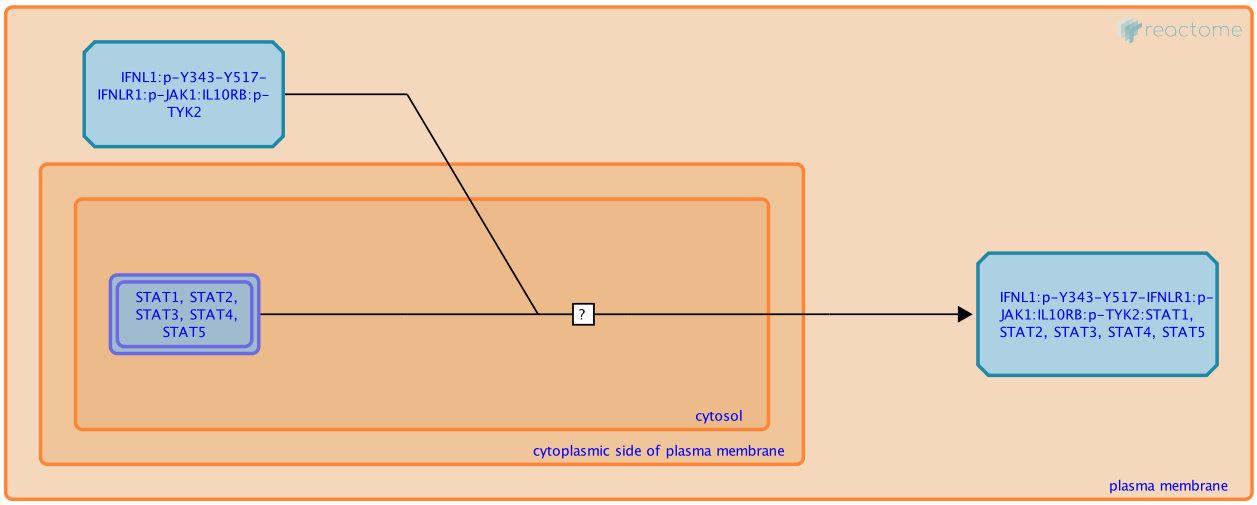
IFNL1:p-Y434,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2 binds STAT1, STAT2, STAT3, STAT4, STAT5 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987266

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



IFNL1 can induce phosphorylation of Signal transducer and activator of transcription 1 alpha/beta (STAT1), Signal transducer and activator of transcription 2 (STAT2) , Signal transducer and activator of transcription 3 (STAT3) , Signal transducer and activator of transcription 4 (STAT4) ,Signal transducer and activator of transcription 5 (STAT5) (Dumoutier et al. 2004, Novak et al. 2008), Signal transducer and activator of transcription 2 (STAT2)(Dickensheets et al. 2013), Signal transducer and activator of transcription 4 (STAT4) and Signal transducer and activator of transcription 5 (STAT5) (Dumoutier et al. 2004).

This is a black-box event because direct evidence for STAT4 and 5-binding and activation is lacking. STAT binding is inferred from subsequent phosphorylation in response to IFNL1 (Jordan et al. 2007).

Preceded by: IFNL1:IFNLR1:p-JAK1:IL10RB:p-TYK2 phosphorylates IFNLR1

Followed by: IFNL1:p-Y343,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2:STAT1 phosphorylates STAT1, STAT2, STAT3, STAT4 and STAT5

Literature references

Novak, AJ., Grote, DM., Ziesmer, SC., Rajkumar, V., Doyle, SE., Ansell, SM. (2008). A role for IFN-lambda1 in multiple myeloma B cell growth. *Leukemia, 22*, 2240-6. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

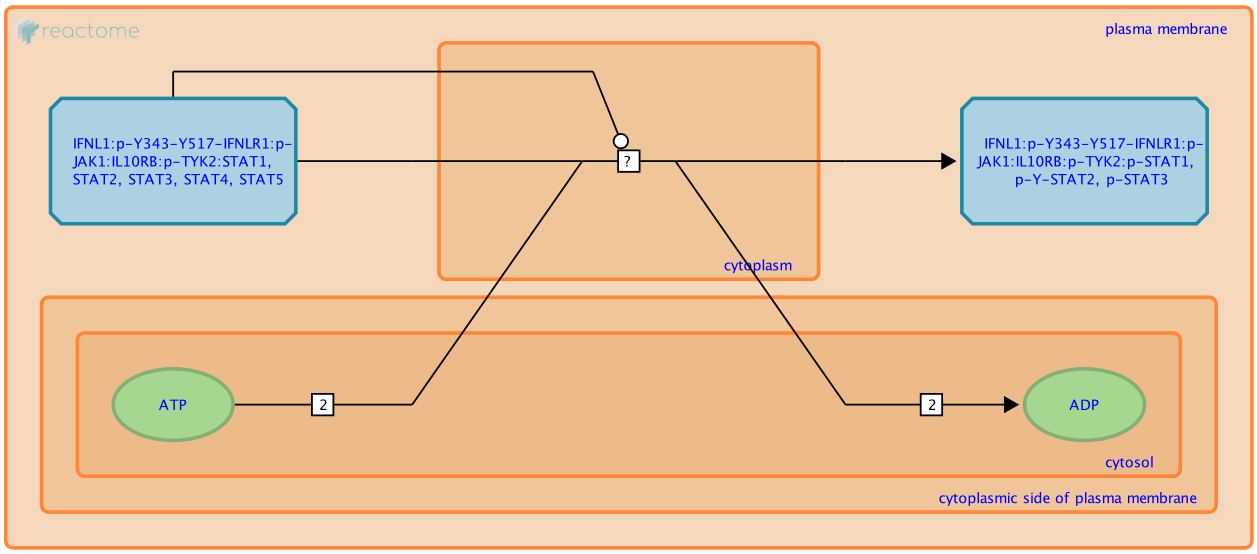
IFNL1:p-Y343,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2:STAT1 phosphorylates STAT1, STAT2, STAT3, STAT4 and STAT5 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8986985

Type: uncertain

Compartments: cytoplasm, extracellular region, plasma membrane



IFNL1 can induce phosphorylation of Signal transducer and activator of transcription 1 alpha/beta (STAT1), Signal transducer and activator of transcription 3 (STAT2), Signal transducer and activator of transcription 3 (STAT3), Signal transducer and activator of transcription 4 (STAT4) and Signal transducer and activator of transcription 5 (STAT5) (Dumoutier et al. 2004, Novak et al. 2008, Dickensheets et al. 2013) via stimulation of the Interferon lambda-1 (IFNL1) receptor complex. This complex consists of IFNL1, IFNLR1, which is associated with phosphorylated Tyrosine-protein kinase JAK1 (JAK1), Interleukin-10 receptor beta (IL10RB), which is associated with phosphorylated Non-receptor tyrosine-protein kinase TYK2 (TYK2) and STAT1.

This is a black-box event because direct evidence for STAT4 and 5 binding and activation is lacking (Jordan et al. 2007).

Preceded by: IFNL1:p-Y434,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2 binds STAT1, STAT2, STAT3, STAT4, STAT5

Followed by: p-STAT1, p-Y-STAT2, p-STAT3, p-STAT4, p-STAT5 dissociates from IFNL1:p-Y343,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2:p-STAT1,p-STAT2,p-STAT3,p-STAT4,p-STAT5

Literature references

Novak, AJ., Grote, DM., Ziesmer, SC., Rajkumar, V., Doyle, SE., Ansell, SM. (2008). A role for IFN-lambda1 in multiple myeloma B cell growth. *Leukemia, 22*, 2240-6. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

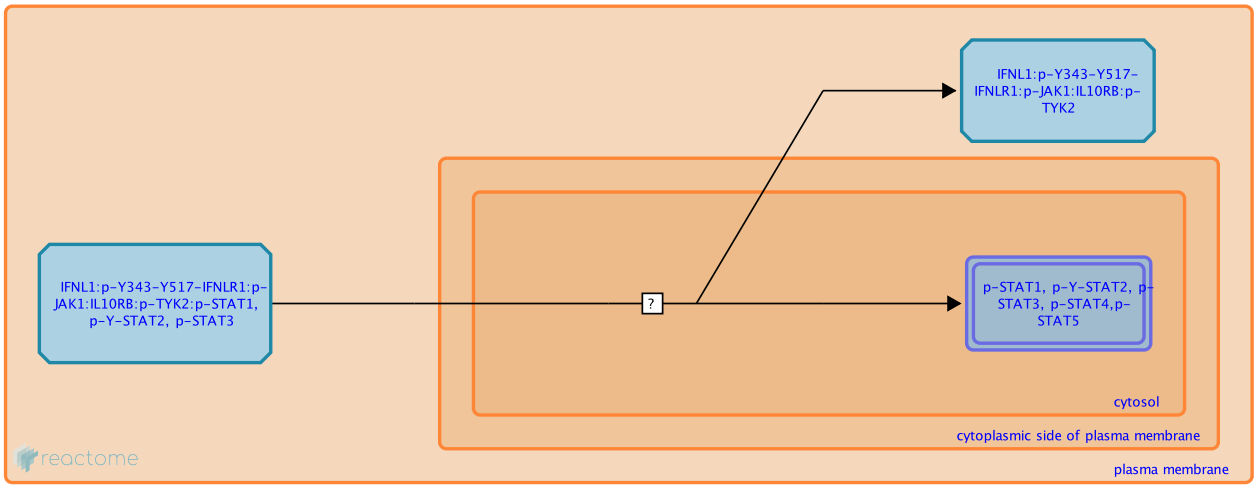
p-STAT1, p-Y-STAT2, p-STAT3, p-STAT4, p-STAT5 dissociates from IFNL1:p-Y343,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2:p-STAT1,p-STAT2,p-STAT3,p-STAT4,p-STAT5 ↗

Location: Interleukin-20 family signaling

Stable identifier: R-HSA-8987033

Type: uncertain

Compartments: cytosol, extracellular region, plasma membrane



Phosphorylated Signal transducer and activator of transcription 1 alpha/beta (STAT1), Phosphorylated Signal transducer and activator of transcription 2 (STAT2) , Phosphorylated Signal transducer and activator of transcription 3 (STAT3) , Phosphorylated Signal transducer and activator of transcription 4 (STAT4) and Phosphorylated Signal transducer and activator of transcription 5 (STAT5) are believed to dissociate from the receptor complex (Dumoutier et al. 2004, Novak et al. 2008). This is a black-box event because dissociation is inferred from other interleukin signaling cascades such as Interleukin-10 (Niemand et al. 2003, Braum et al. 2013, Xiong et al. 2014, Sheikh et al. 2006, You et al. 2013) where dissociation occurs before STAT dimerization and translocation to the nucleus.

Preceded by: IFNL1:p-Y343,Y517-IFNLR1:p-JAK1:IL10RB:p-TYK2:STAT1 phosphorylates STAT1, STAT2, STAT3, STAT4 and STAT5

Followed by: p-STAT1 dimerizes, p-STAT3 dimerizes

Literature references

Novak, AJ., Grote, DM., Ziesmer, SC., Rajkumar, V., Doyle, SE., Ansell, SM. (2008). A role for IFN-lambda1 in multiple myeloma B cell growth. *Leukemia, 22*, 2240-6. ↗

Editions

2017-03-16	Authored	Duenas, C.
2017-11-07	Edited	Jupe, S.
2017-11-15	Reviewed	Datta, SK.

Table of Contents