JAK activation

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Introduction

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

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Literature references


Reactome database release: 83

This document contains 1 reaction (see Table of Contents)

https://reactome.org
The molecular mechanism of Jak activation upon cytokine stimulation is not understood in detail (Haan et al. 2008). Cytokine-induced receptor aggregation and the resulting close proximity of Jaks bound to the beta receptor subunit is believed to trigger trans-phosphorylation of Jak tyrosines in their kinase activation loop, conferring kinase activity. This active state is believed to be maintained by further autocatalytic tyrosine phosphorylations. For JAK1 the activation loop tyrosine residues are predicted by homology with models of JAK2 (Lindauer et al. 2001) to be Tyr-1034/1035. Mutation of Tyr-1034 abolishes JAK1 kinase activity (Liu et al. 1997). Evidence supporting JAK1 transphosphorylation includes JAK1 mutant cell lines, which cannot activate Tyk2 after stimulation with interferon alpha/beta (Velazquez et al. 1995) and the observation that IL-2 cannot activate JAK1 in the absence of JAK3 (Oakes et al. 1996). The receptor is not merely a docking site for JAKs as certain gp130 residues are required for JAK1 activation, but not essential for JAK1 binding (Haan et al. 2002).

**Literature references**


**Editions**

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