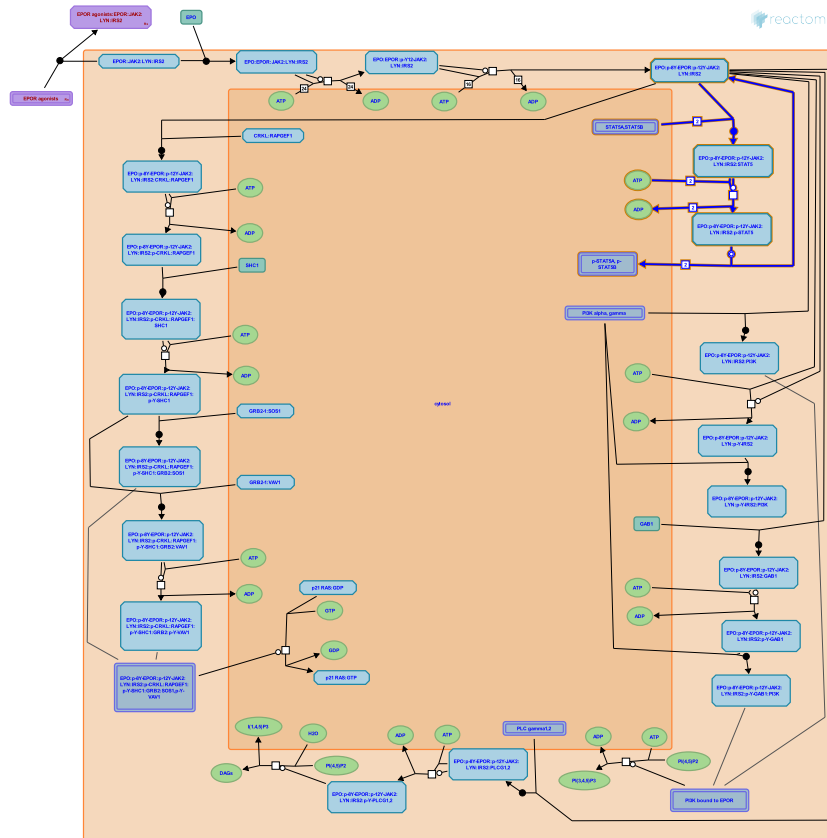


# Erythropoietin activates STAT5



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/Textbook/).

29/04/2024

## 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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## Literature references

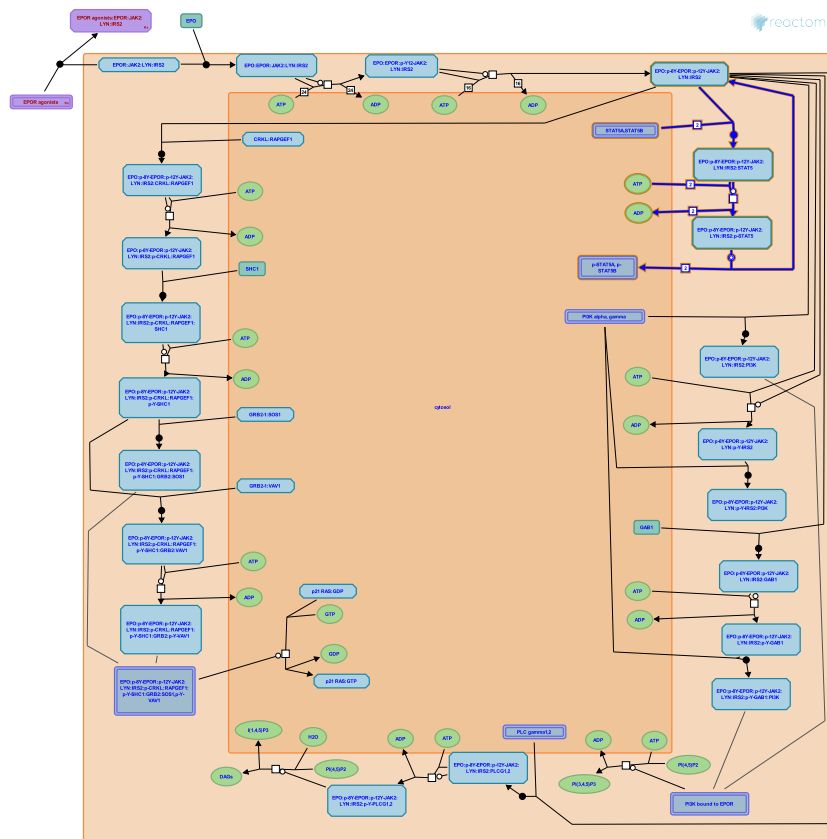
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Reactome database release: 88

This document contains 1 pathway and 3 reactions ([see Table of Contents](#))

# Erythropoietin activates STAT5 ↗

Stable identifier: R-HSA-9027283



STAT5 (STAT5A or STAT5B) directly binds the phosphorylated cytoplasmic domain of EPOR, where it is phosphorylated by JAK2 and LYN (Oda et al. 1998, inferred from mouse homologs, reviewed in Kuhrt and Wojchowski 2015). Phosphorylated STAT5 then dissociates from EPOR, dimerizes, and transits to the nucleus where it activates gene expression.

## Literature references

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Oda, A., Koike, T., Druker, BJ., Sawada, K., Ozaki, K., Koizumi, K. et al. (1998). Erythropoietin induces tyrosine phosphorylation of Jak2, STAT5A, and STAT5B in primary cultured human erythroid precursors. *Blood*, 92, 443-51. ↗

## Editions

2017-10-29	Authored, Edited	May, B.
2018-08-14	Reviewed	McGraw, KL.

## EPO:phospho-EPOR:phospho-JAK2:LYN:IRS2 binds STAT5 ↗

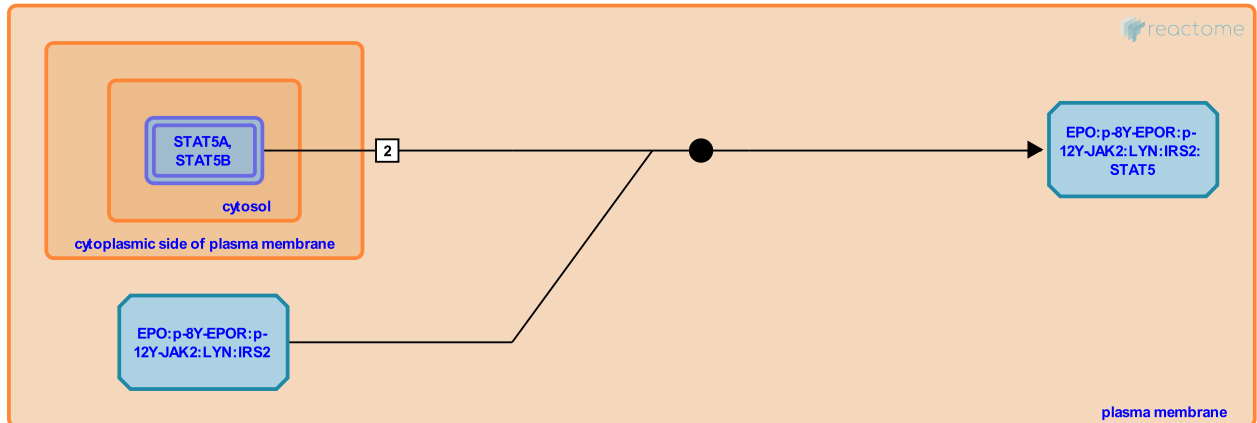
**Location:** [Erythropoietin activates STAT5](#)

**Stable identifier:** R-HSA-9012654

**Type:** binding

**Compartments:** plasma membrane

**Inferred from:** [phospho-Epor:phospho-Jak2:Lyn:Irs2 binds Stat5 \(Mus musculus\)](#)



STAT5 (STAT5A or STAT5B) binds the phosphorylated cytoplasmic domain of EPOR via phosphotyrosine-343 and phosphotyrosine-479 of EPOR (Chretien et al. 1996, McGraw et al. 2012, and inferred from mouse homologs). STAT5 may also bind the EPOR complex indirectly via CRKL (Ota et al. 1998).

**Followed by:** [JAK2 and LYN phosphorylate STAT5 in EPO:phospho-EPOR:phospho-JAK2:LYN:IRS2](#)

### Literature references

Shimamura, S., Suzu, S., Kimura, F., Nagata, N., Ota, J., Wakimoto, N. et al. (1998). Association of CrkL with STAT5 in hematopoietic cells stimulated by granulocyte-macrophage colony-stimulating factor or erythropoietin. *Biochem. Biophys. Res. Commun.*, 252, 779-86. ↗

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Clark, JA., Johnson, JO., McGraw, KL., Sokol, L., Fuhler, GM., Caceres, GC. et al. (2012). Erythropoietin receptor signaling is membrane raft dependent. *PLoS ONE*, 7, e34477. ↗

### Editions

2017-06-17	Authored, Edited	May, B.
2018-08-14	Reviewed	McGraw, KL.

## JAK2 and LYN phosphorylate STAT5 in EPO:phospho-EPOR:phospho-JAK2:LYN:IRS2



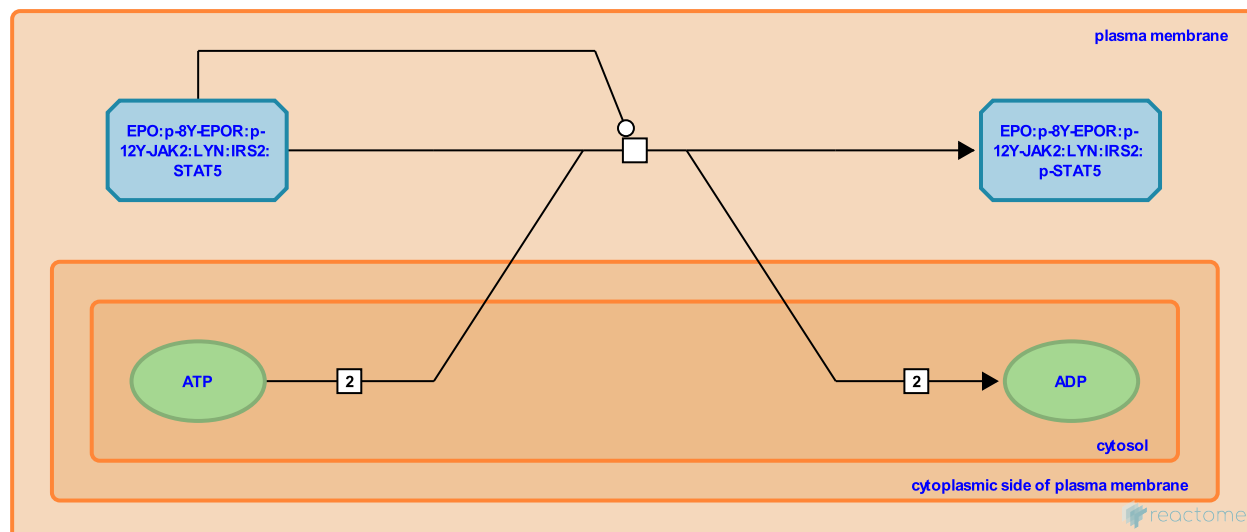
**Location:** Erythropoietin activates STAT5

**Stable identifier:** R-HSA-9012650

**Type:** transition

**Compartments:** plasma membrane

**Inferred from:** EPO:p-8Y-Epor:p-12Y-Jak2:Lyn:Irs2 phosphorylates Stat5 (Mus musculus)



After STAT5 binds the EPO:EPOR complex, phosphorylated JAK2 and LYN phosphorylate STAT5 (STAT5A or STAT5B) (Gouilleux et al. 1995, Pallard et al. 1995, Hoefsloot et al. 1997, Miura et al. 1998, Oda et al. 1998, Okajima et al. 1998, Erickson-Miller et al. 2000, and inferred from mouse homologs). STAT5A (MGH-STAT5) is phosphorylated on tyrosine-694 (Gouilleux et al. 1995, Arcasoy et al. 1999). Activation of STAT5 appears to be impaired in myelodysplastic syndrome (Hoefsloot et al. 1997). IGF-I enhances STAT5 phosphorylation in response to EPO (Okajima et al. 1998).

**Preceded by:** EPO:phospho-EPOR:phospho-JAK2:LYN:IRS2 binds STAT5

**Followed by:** p-STAT5 dissociates from EPO:phospho-EPOR:phospho-JAK2:LYN:IRS2

### Literature references

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## Editions

2017-06-17	Authored, Edited	May, B.
2018-08-14	Reviewed	McGraw, KL.

## p-STAT5 dissociates from EPO:phospho-EPOR:phospho-JAK2:LYN:IRS2 [↗](#)

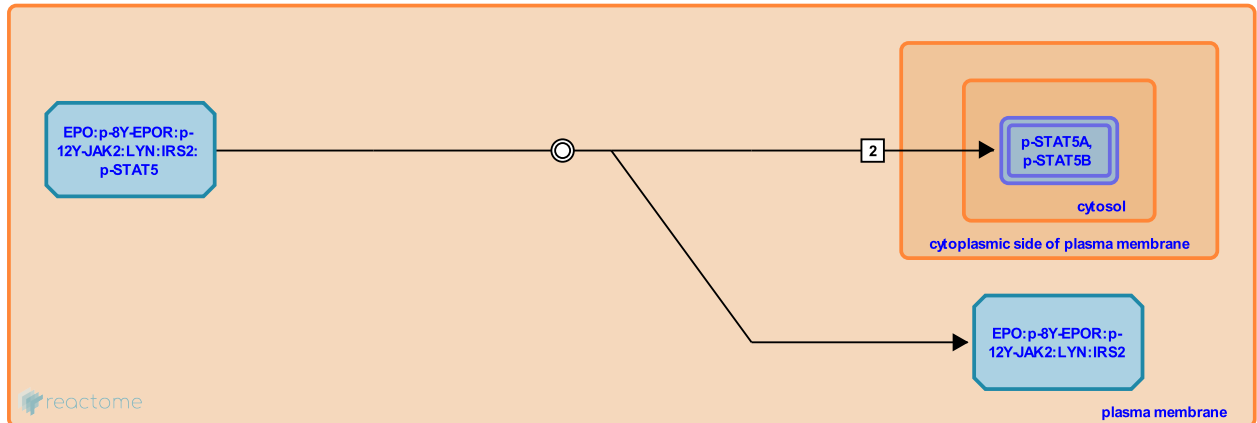
**Location:** Erythropoietin activates STAT5

**Stable identifier:** R-HSA-9012651

**Type:** dissociation

**Compartments:** plasma membrane

**Inferred from:** p-Stat5 dissociates from Epo:p-8Y-Epor:p-12Y-Jak2:Lyn:Irs2 (Mus musculus)



After being phosphorylated, phospho-STAT5 (STAT5A or STAT5B) dissociates from the EPO:EPOR complex, dimerizes, and transits to the nucleus where it activates transcription of target genes (Oda et al. 1998, and inferred from mouse homologs).

**Preceded by:** JAK2 and LYN phosphorylate STAT5 in EPO:phospho-EPOR:phospho-JAK2:LYN:IRS2

### Literature references

Oda, A., Koike, T., Druker, B.J., Sawada, K., Ozaki, K., Koizumi, K. et al. (1998). Erythropoietin induces tyrosine phosphorylation of Jak2, STAT5A, and STAT5B in primary cultured human erythroid precursors. *Blood*, 92, 443-51. [↗](#)

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2017-06-17	Authored, Edited	May, B.
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