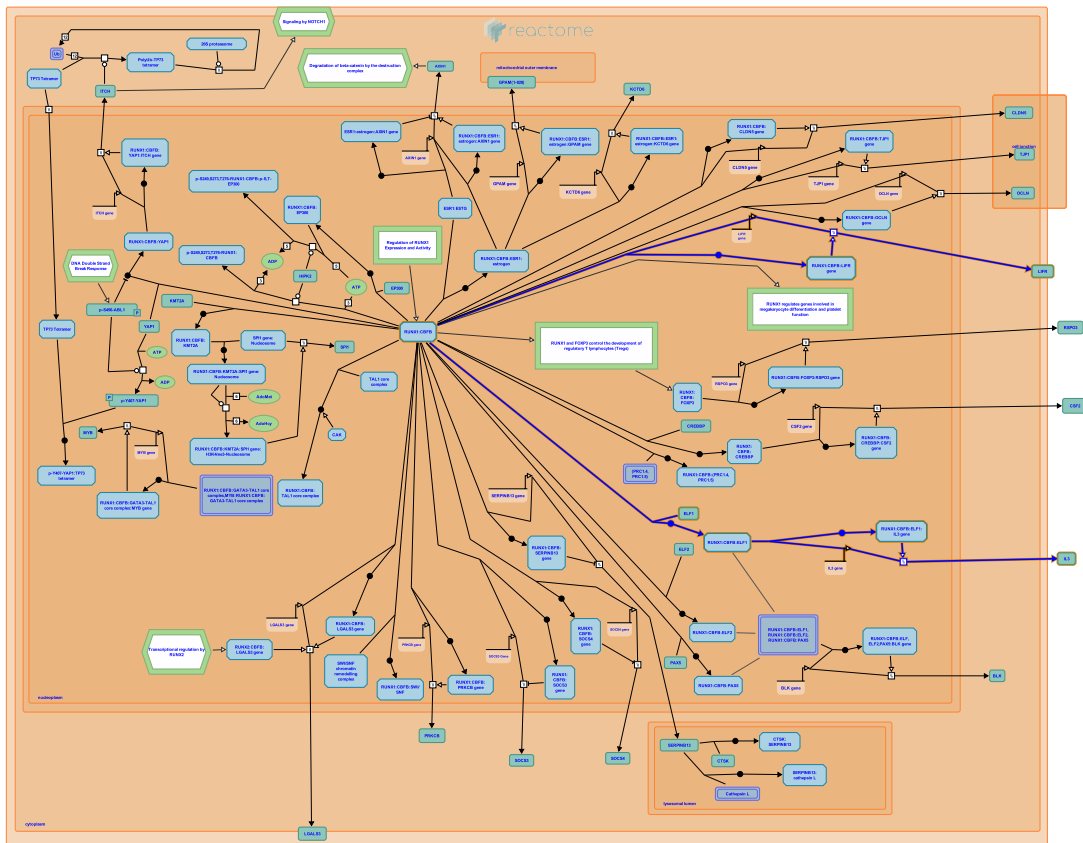


RUNX1 regulates transcription of genes involved in interleukin signaling



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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

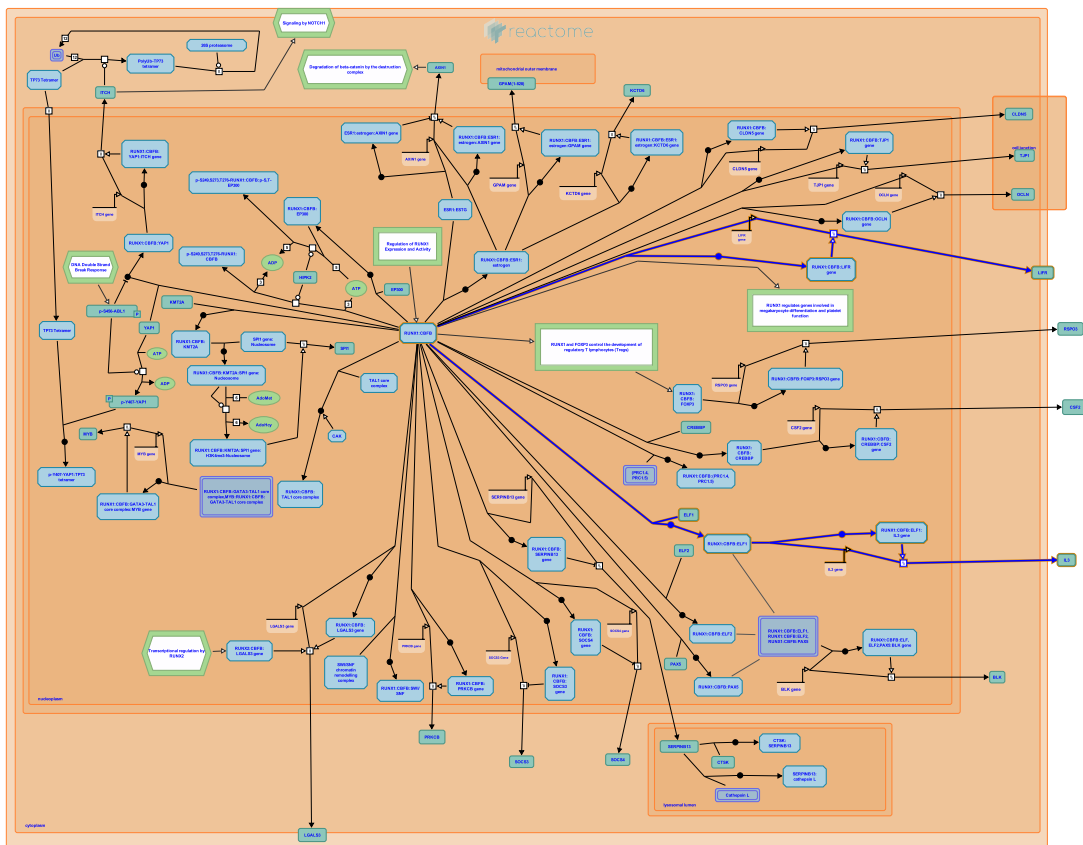
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Reactome database release: 70

This document contains 1 pathway and 5 reactions ([see Table of Contents](#))

RUNX1 regulates transcription of genes involved in interleukin signaling ↗

Stable identifier: R-HSA-8939247



The RUNX1:CBFB complex regulates transcription of at least a couple of genes involved in interleukin signaling. The LIFR gene, a direct transcriptional target of the RUNX1:CBFB complex (Qadi et al. 2016), encodes the receptor for the leukemia inhibitory factor (LIF), a member of the interleukin-6 family. LIFR is implicated in hematopoiesis, embryo implantation, placental formation and nervous system development (Nicola et al. 2015). In association with its co-activator ELF1, the RUNX1:CBFB complex stimulates transcription of the IL3 gene, encoding interleukin-3 (Mao et al. 1999).

Literature references

Nicola, NA., Babon, JJ. (2015). Leukemia inhibitory factor (LIF). *Cytokine Growth Factor Rev.*, 26, 533-44. ↗

Qadi, AA., Taberlay, PC., Phillips, JL., Young, A., West, AC., Brettingham-Moore, KH. et al. (2016). The Leukemia Inhibitory Factor Receptor Gene Is a Direct Target of RUNX1. *J. Cell. Biochem.*, 117, 49-58. ↗

Mao, S., Frank, RC., Zhang, J., Miyazaki, Y., Nimer, SD. (1999). Functional and physical interactions between AML1 proteins and an ETS protein, MEF: implications for the pathogenesis of t(8;21)-positive leukemias. *Mol. Cell. Biol.*, 19, 3635-44. ↗

Editions

2016-09-14	Authored	Orlic-Milacic, M.
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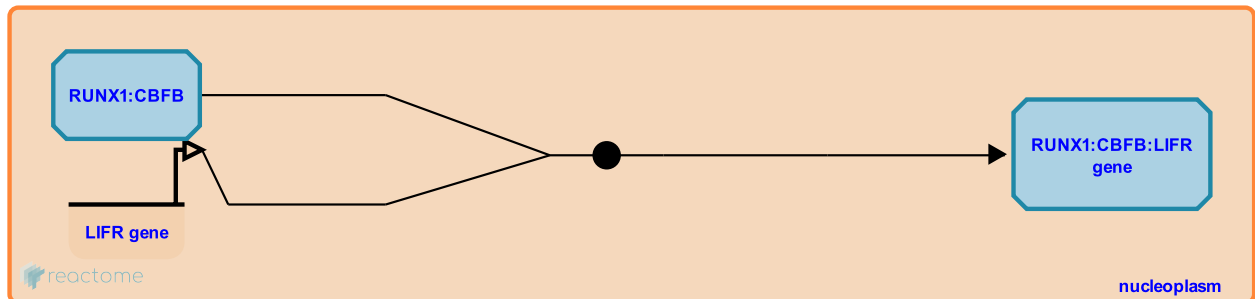
RUNX1:CBFB binds the LIFR gene promoter ↗

Location: [RUNX1 regulates transcription of genes involved in interleukin signaling](#)

Stable identifier: R-HSA-8934688

Type: binding

Compartments: nucleoplasm



The RUNX1:CBFB complex binds both the general and the placental promoter of the LIFR gene (Qadi et al. 2016).

Followed by: [LIFR gene expression](#)

Literature references

Qadi, AA., Taberlay, PC., Phillips, JL., Young, A., West, AC., Brettingham-Moore, KH. et al. (2016). The Leukemia Inhibitory Factor Receptor Gene Is a Direct Target of RUNX1. *J. Cell. Biochem.*, 117, 49-58. ↗

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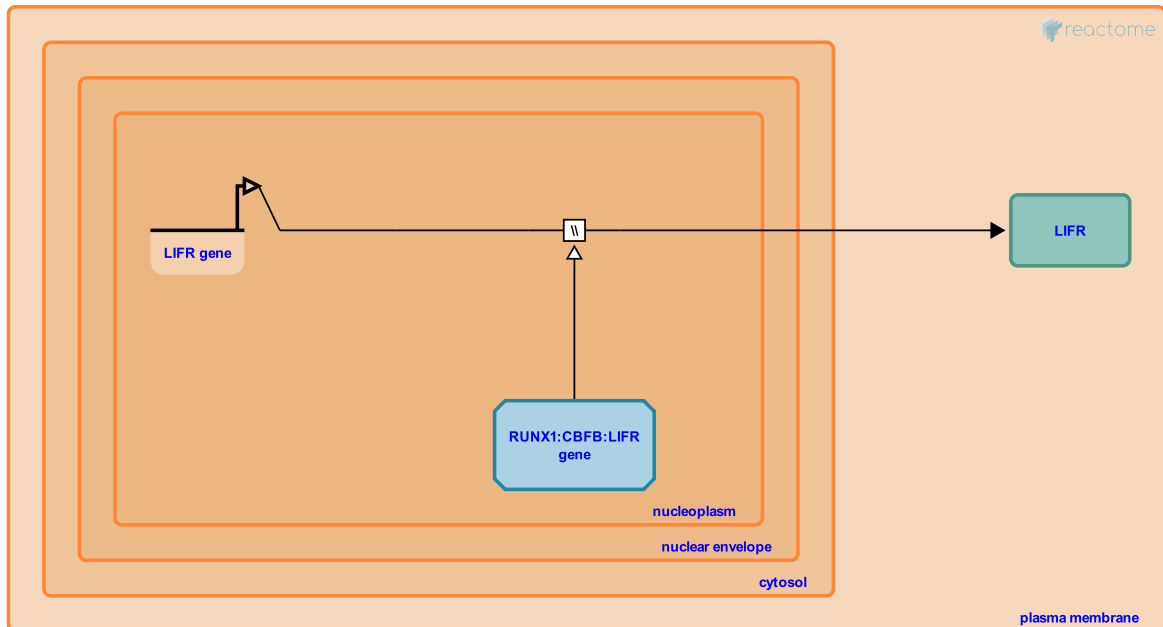
LIFR gene expression ↗

Location: [RUNX1 regulates transcription of genes involved in interleukin signaling](#)

Stable identifier: R-HSA-8934690

Type: omitted

Compartments: nucleoplasm, plasma membrane



Binding of the RUNX1:CBFB complex to the promoter of the LIFR gene stimulates LIFR transcription. In contrast, the oncogenic fusion protein RUNX1-ETO, the product of t(8;21) translocation in acute myeloid leukemia (AML), represses transcription of the LIFR gene (Qadi et al. 2016). LIFR encodes the receptor for the leukemia inhibitory factor (LIF), a member of the interleukin-6 (IL6) cytokine family. Signaling by LIFR is implicated in hematopoiesis, embryo implantation, placental formation and nervous system development (Nicola and Babon 2015).

Preceded by: [RUNX1:CBFB binds the LIFR gene promoter](#)

Literature references

Qadi, AA., Taberlay, PC., Phillips, JL., Young, A., West, AC., Brettingham-Moore, KH. et al. (2016). The Leukemia Inhibitory Factor Receptor Gene Is a Direct Target of RUNX1. *J. Cell. Biochem.*, 117, 49-58. ↗

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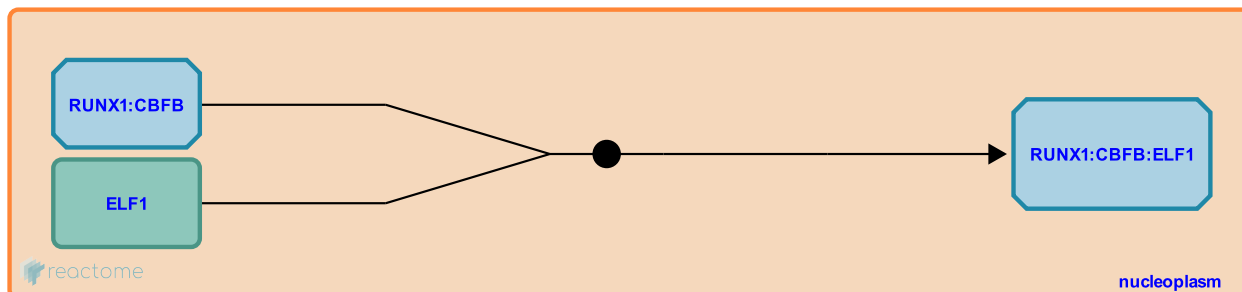
RUNX1 binds ELF1 ↗

Location: [RUNX1 regulates transcription of genes involved in interleukin signaling](#)

Stable identifier: R-HSA-8938913

Type: binding

Compartments: nucleoplasm



The RUNX1:CBFB complex binds to ELF1 (MEF), a member of the ETS family of transcription factors (Mao et al. 1999, Cho et al. 2004). The interaction involves the ETS-interacting subdomain (EID) in the C-terminal portion of the RUNX1 Runt domain and a region of ELF1 that is N-terminal to its ETS domain. ELF1 does not directly interact with CBFB (Mao et al. 1999).

Followed by: [RUNX1 and ELF1 bind the IL3 gene promoter](#)

Literature references

Mao, S., Frank, RC., Zhang, J., Miyazaki, Y., Nimer, SD. (1999). Functional and physical interactions between AML1 proteins and an ETS protein, MEF: implications for the pathogenesis of t(8;21)-positive leukemias. *Mol. Cell. Biol.*, 19, 3635-44. ↗

Cho, JY., Akbarali, Y., Zerbini, LF., Gu, X., Boltax, J., Wang, Y. et al. (2004). Isoforms of the Ets transcription factor NERF/ELF-2 physically interact with AML1 and mediate opposing effects on AML1-mediated transcription of the B cell-specific blk gene. *J. Biol. Chem.*, 279, 19512-22. ↗

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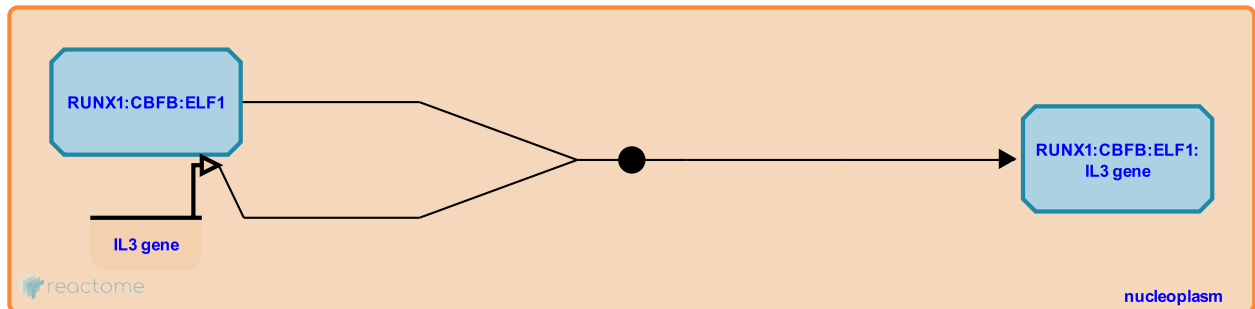
RUNX1 and ELF1 bind the IL3 gene promoter ↗

Location: [RUNX1 regulates transcription of genes involved in interleukin signaling](#)

Stable identifier: R-HSA-8938938

Type: binding

Compartments: nucleoplasm



RUNX1 (AML1) and ELF1 (MEF) bind to adjacent RUNX1- and ETS- response elements in the promoter of the IL3 gene, encoding interleukin-3. While RUNX1 and ELF1 can independently activate the IL3 gene transcription, formation of the complex between RUNX1 and ELF1 has a synergistic effect on IL3 expression (Mao et al. 1999).

Preceded by: [RUNX1 binds ELF1](#)

Followed by: [IL3 gene transcription is stimulated by RUNX1 and ELF1](#)

Literature references

Mao, S., Frank, RC., Zhang, J., Miyazaki, Y., Nimer, SD. (1999). Functional and physical interactions between AML1 proteins and an ETS protein, MEF: implications for the pathogenesis of t(8;21)-positive leukemias. *Mol. Cell. Biol.*, 19, 3635-44. ↗

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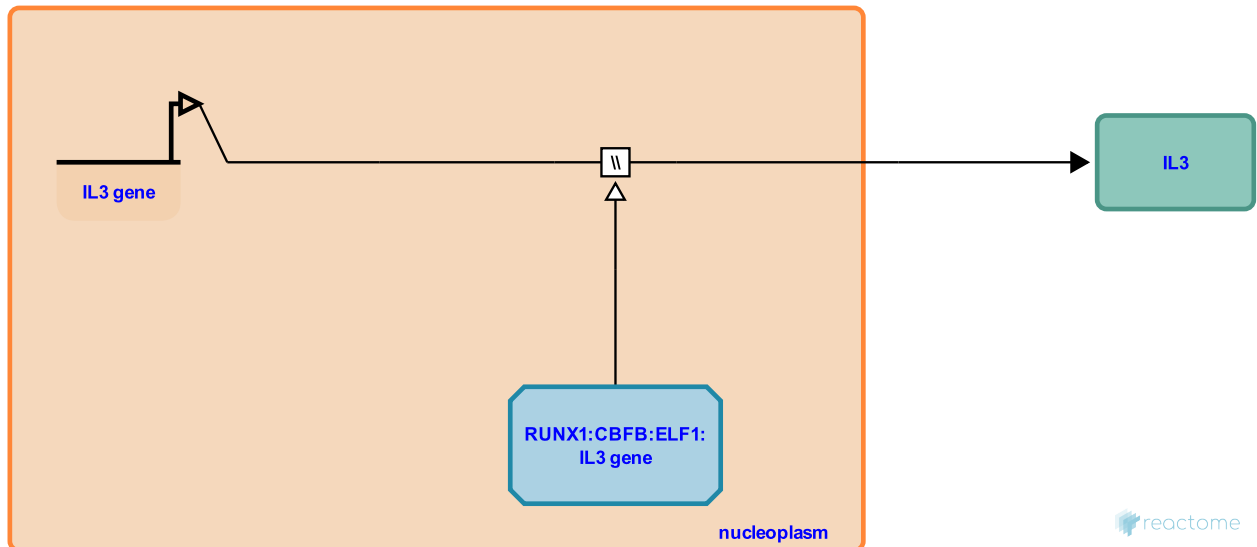
IL3 gene transcription is stimulated by RUNX1 and ELF1 ↗

Location: [RUNX1 regulates transcription of genes involved in interleukin signaling](#)

Stable identifier: R-HSA-8938981

Type: omitted

Compartments: nucleoplasm, extracellular region



Binding of the RUNX1:CBFB complex associated with ELF1, an ETS family member, to the promoter of the IL3 gene, encoding interleukin-3, stimulates IL3 transcription (Mao et al. 1999).

Preceded by: [RUNX1 and ELF1 bind the IL3 gene promoter](#)

Literature references

Mao, S., Frank, RC., Zhang, J., Miyazaki, Y., Nimer, SD. (1999). Functional and physical interactions between AML1 proteins and an ETS protein, MEF: implications for the pathogenesis of t(8;21)-positive leukemias. *Mol. Cell. Biol.*, 19, 3635-44. ↗

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