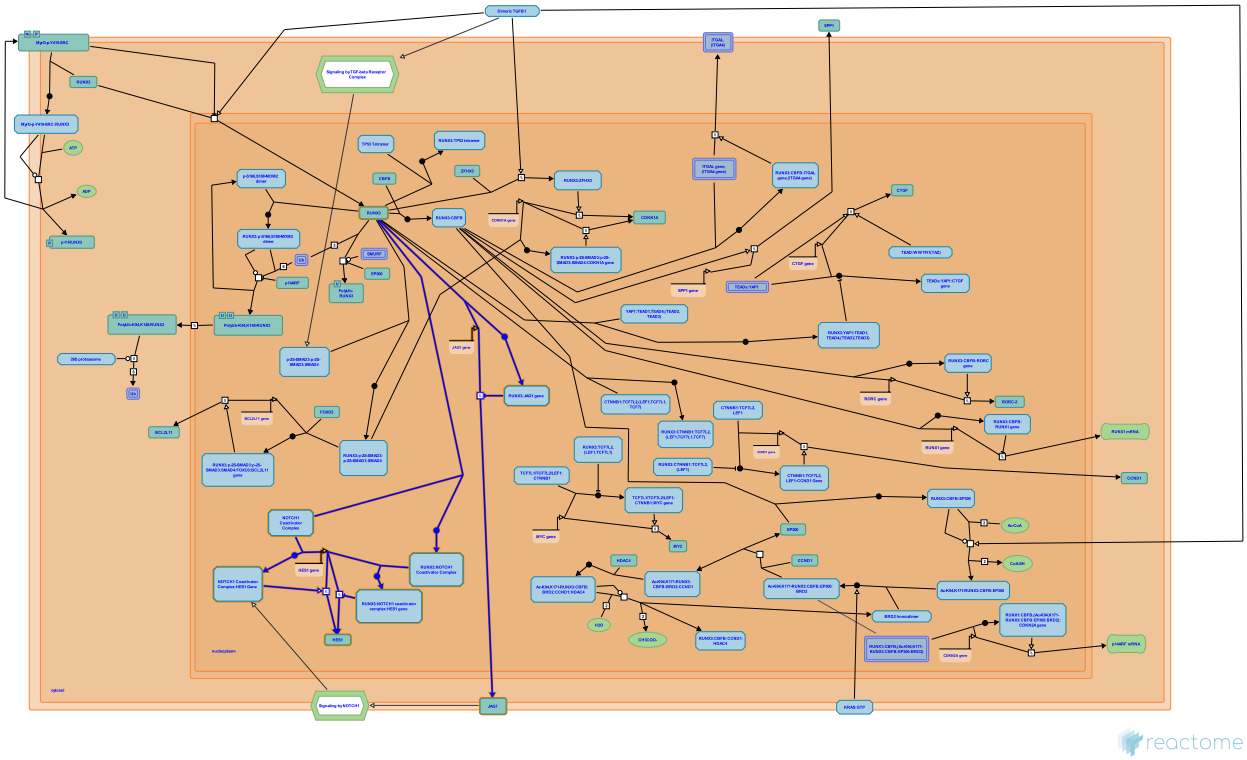
RUNX3 regulates NOTCH signaling



Chuang, LS., D'Eustachio, P., Egan, SE., Haw, R., Ito, Y., Orlic-Milacic, M.

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

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.

28/04/2024

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

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. ↗

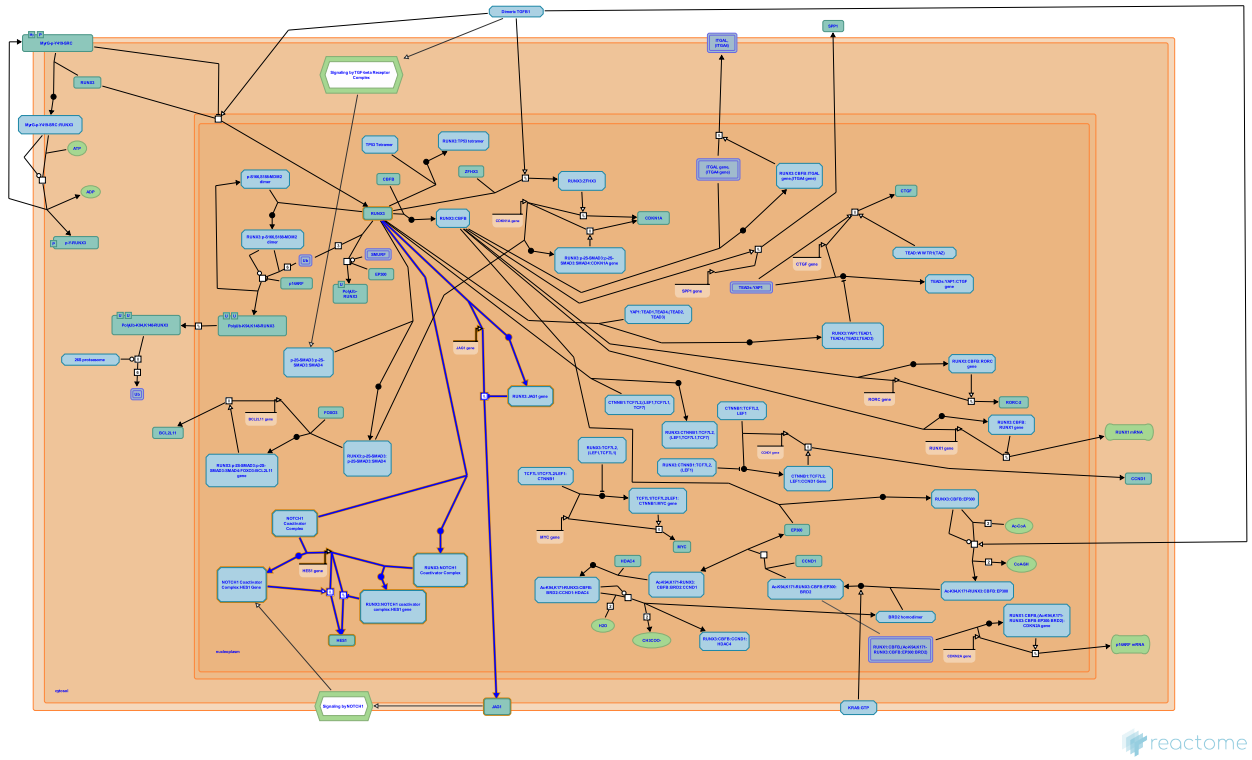
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

RUNX3 regulates NOTCH signaling ↗

Stable identifier: R-HSA-8941856



RUNX3 negatively regulates NOTCH signaling, which contributes to the tumor suppressor role of RUNX3 in hepatocellular carcinoma. RUNX3 binds the promoter of the JAG1 gene, encoding NOTCH ligand JAG1 and inhibits its transcription (Nishina et al. 2011). In addition, RUNX3 also binds to the NOTCH1 coactivator complex at the promoter of HES1, a NOTCH target gene, and inhibits HES1 transcription (Gao et al. 2010).

Literature references

Nakanishi, Y., Matsubara, M., Iwamuro, M., Yagi, T., Tanaka, S., Yamamoto, K. et al. (2011). Restored expression of the tumor suppressor gene RUNX3 reduces cancer stem cells in hepatocellular carcinoma by suppressing Jagged1-Notch signaling. *Oncol. Rep., 26,* 523-31. ↗

Gao, J., Chen, Y., Du, R., Zhao, YQ., Xu, HL., Fan, DM. et al. (2010). RUNX3 directly interacts with intracellular domain of Notch1 and suppresses Notch signaling in hepatocellular carcinoma cells. *Exp. Cell Res., 316,* 149-57. ↗

Editions

2016-12-13	Authored	Orlic-Milacic, M.
2017-01-31	Reviewed	Ito, Y., Chuang, LS.
2017-01-31	Edited	Orlic-Milacic, M.

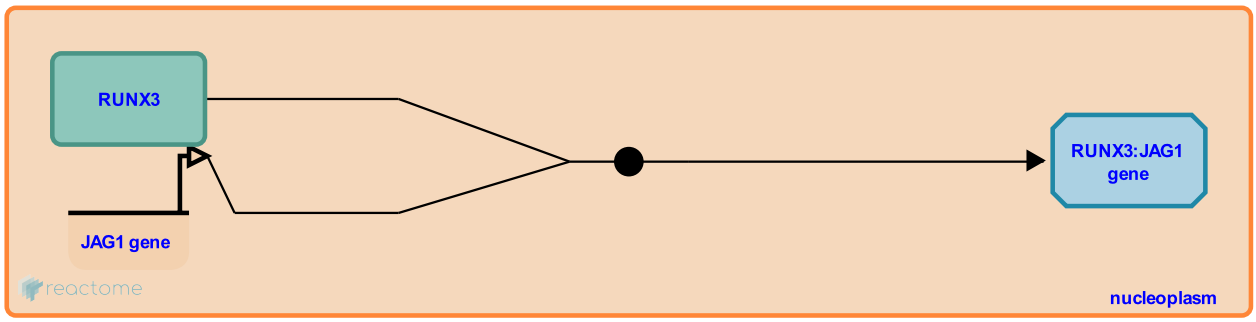
RUNX3 binds the JAG1 gene promoter ↗

Location: RUNX3 regulates NOTCH signaling

Stable identifier: R-HSA-8878193

Type: binding

Compartments: nucleoplasm



RUNX3 binds the promoter of the JAG1 gene, which encodes a ligand for NOTCH receptors (Nishina et al. 2011).

Followed by: JAG1 gene expression is inhibited by RUNX3

Literature references

Nakanishi, Y., Matsubara, M., Iwamuro, M., Yagi, T., Tanaka, S., Yamamoto, K. et al. (2011). Restored expression of the tumor suppressor gene RUNX3 reduces cancer stem cells in hepatocellular carcinoma by suppressing Jagged1-Notch signaling. *Oncol. Rep., 26*, 523-31. ↗

Editions

2016-12-13	Authored	Orlic-Milacic, M.
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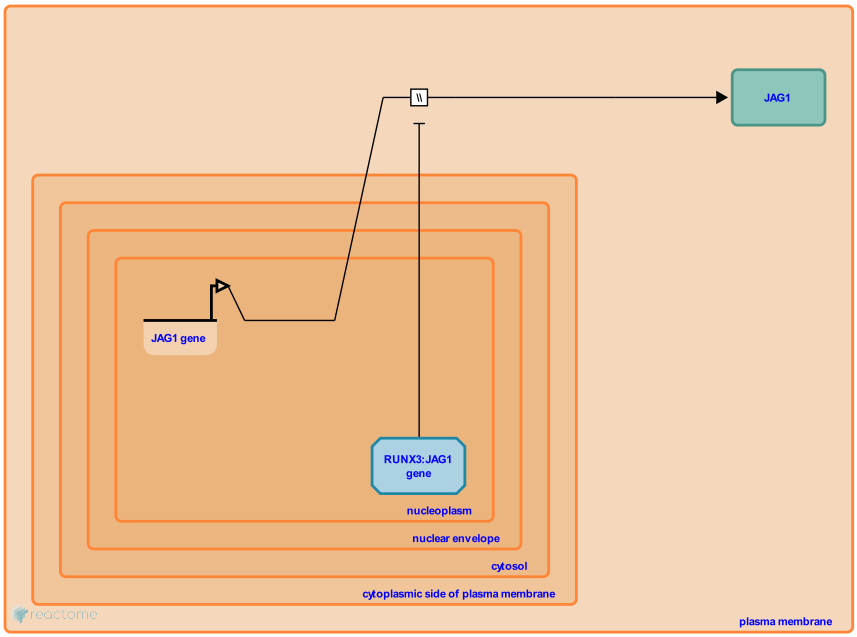
JAG1 gene expression is inhibited by RUNX3 ↗

Location: RUNX3 regulates NOTCH signaling

Stable identifier: R-HSA-8878212

Type: omitted

Compartments: plasma membrane, nucleoplasm



Binding of RUNX3 to the JAG1 gene promoter inhibits transcription of JAG1, which correlates with reduced amount of cleaved JAG1 receptor, NOTCH1. There is an inverse correlation between the expression levels of RUNX3 and JAG1 in hepatocellular carcinoma (HCC) cell lines and tumor samples. HCC cell lines with higher RUNX3 levels have reduced tumorigenic capacity (Nishina et al. 2011).

Preceded by: RUNX3 binds the JAG1 gene promoter

Literature references

Nakanishi, Y., Matsubara, M., Iwamuro, M., Yagi, T., Tanaka, S., Yamamoto, K. et al. (2011). Restored expression of the tumor suppressor gene RUNX3 reduces cancer stem cells in hepatocellular carcinoma by suppressing Jagged1-Notch signaling. *Oncol. Rep., 26*, 523-31. ↗

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2016-12-13	Authored	Orlic-Milacic, M.
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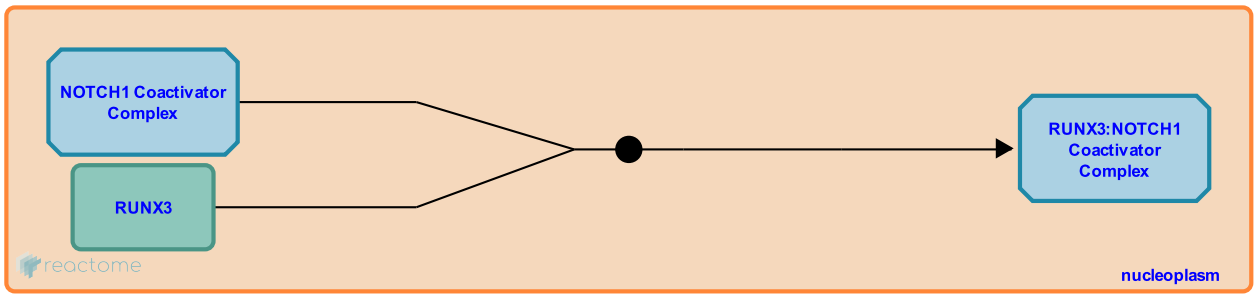
RUNX3 binds the NOTCH1 coactivator complex ↗

Location: RUNX3 regulates NOTCH signaling

Stable identifier: R-HSA-8878220

Type: binding

Compartments: nucleoplasm



RUNX3 binds the NOTCH1 coactivator complex by directly interacting with the NOTCH1 intracellular domain fragment (NICD1) (Gao et al. 2010).

Followed by: RUNX3:NOTCH1 coactivator complex binds the HES1 gene promoter

Literature references

Gao, J., Chen, Y., Du, R., Zhao, YQ., Xu, HL., Fan, DM. et al. (2010). RUNX3 directly interacts with intracellular domain of Notch1 and suppresses Notch signaling in hepatocellular carcinoma cells. *Exp. Cell Res., 316*, 149-57. ↗

Editions

2016-12-13	Authored	Orlic-Milacic, M.
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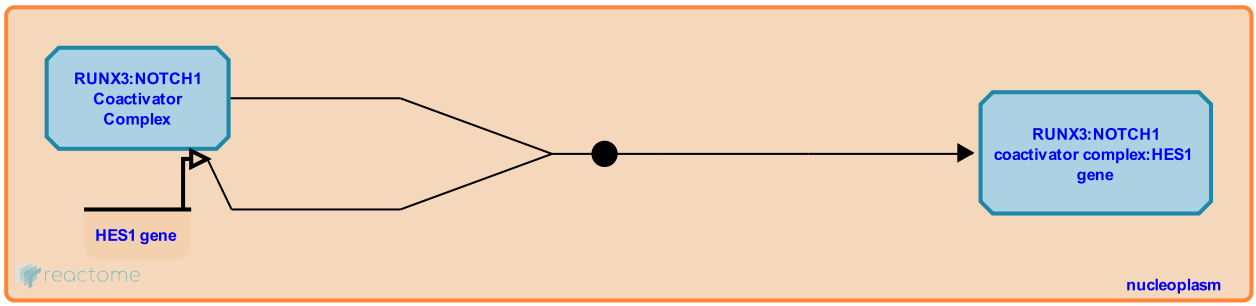
RUNX3:NOTCH1 coactivator complex binds the HES1 gene promoter ↗

Location: RUNX3 regulates NOTCH signaling

Stable identifier: R-HSA-8878237

Type: binding

Compartments: nucleoplasm



RUNX3, associated with the NOTCH1 coactivator complex, binds to the promoter of the HES1 gene (Gao et al. 2010).

Preceded by: RUNX3 binds the NOTCH1 coactivator complex

Followed by: HES1 gene transcription is inhibited by RUNX3

Literature references

Gao, J., Chen, Y., Du, R., Zhao, YQ., Xu, HL., Fan, DM. et al. (2010). RUNX3 directly interacts with intracellular domain of Notch1 and suppresses Notch signaling in hepatocellular carcinoma cells. *Exp. Cell Res., 316*, 149-57. ↗

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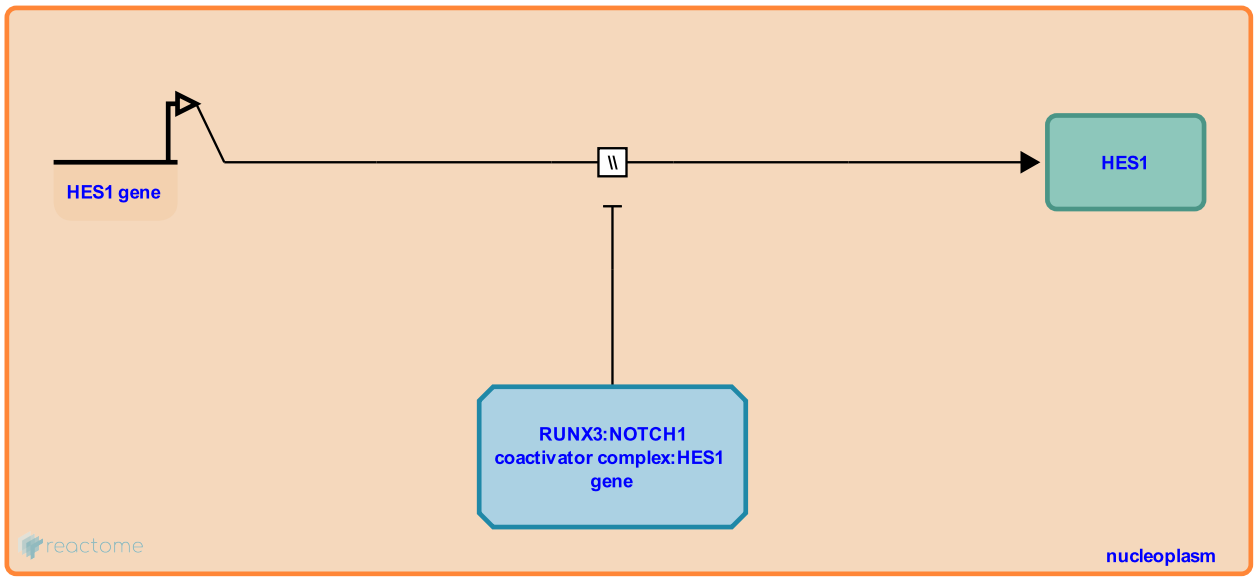
HES1 gene transcription is inhibited by RUNX3

Location: RUNX3 regulates NOTCH signaling

Stable identifier: R-HSA-8878243

Type: omitted

Compartments: nucleoplasm



Binding of RUNX3 to the NOTCH1 coactivator complex at the HES1 gene promoter results in repression of HES1 transcription downstream of NOTCH1 signaling (Gao et al. 2010).

Preceded by: RUNX3:NOTCH1 coactivator complex binds the HES1 gene promoter

Literature references

Gao, J., Chen, Y., Du, R., Zhao, YQ., Xu, HL., Fan, DM. et al. (2010). RUNX3 directly interacts with intracellular domain of Notch1 and suppresses Notch signaling in hepatocellular carcinoma cells. *Exp. Cell Res., 316,* 149-57.

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2016-12-13	Authored	Orlic-Milacic, M.
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NOTCH1 Coactivator Complex binds HES1 promoter ↗

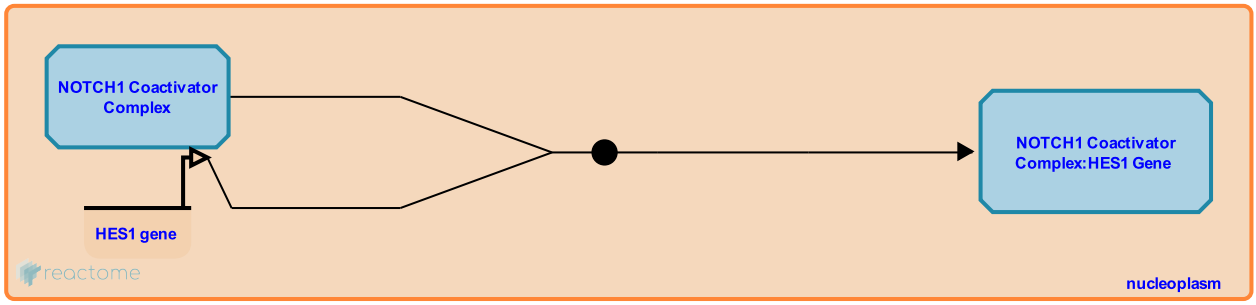
Location: RUNX3 regulates NOTCH signaling

Stable identifier: R-HSA-4396347

Type: binding

Compartments: nucleoplasm

Inferred from: mNICD1 Chimeric Enhancer Complex binds Hes1 promoter (Homo sapiens)



NOTCH1 coactivator complex binds the promoter of HES1 gene and directly stimulates HES1 transcription (Jarriault et al. 1995).

Followed by: NOTCH1 stimulates HES1 transcription

Literature references

Kopan, R., Schroeter, EH., Brou, C., Israel, A., Jarriault, S., Logeat, F. (1995). Signalling downstream of activated mammalian Notch. *Nature, 377*, 355-8. ↗

Editions

2011-11-14	Authored	Egan, SE., Orlic-Milacic, M.
2012-02-06	Reviewed	Haw, R.
2012-02-07	Edited	D'Eustachio, P.
2012-02-11	Edited	Orlic-Milacic, M.
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2017-01-31	Edited	Orlic-Milacic, M.

NOTCH1 stimulates HES1 transcription ↗

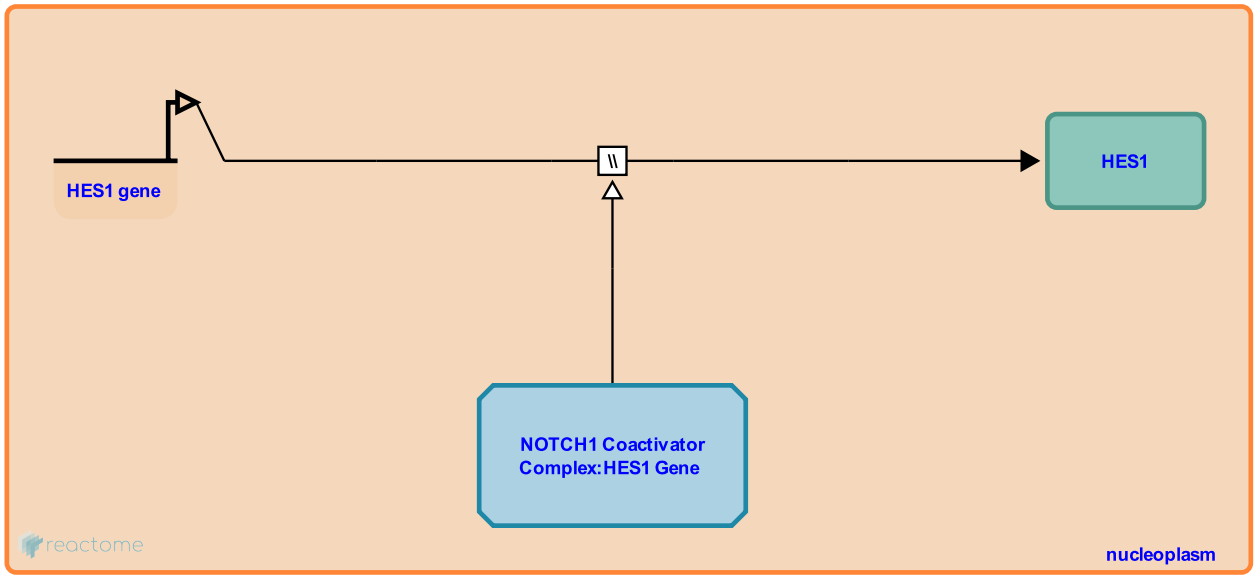
Location: RUNX3 regulates NOTCH signaling

Stable identifier: R-HSA-1980047

Type: omitted

Compartments: nucleoplasm

Inferred from: mNICD1 stimulates Hes1 transcription (Homo sapiens)



NOTCH1 coactivator complex binds the promoter of HES1 gene and directly stimulates HES1 transcription. HES1 belongs to the bHLH family of transcription factors (Jarriault et al. 1995).

Preceded by: NOTCH1 Coactivator Complex binds HES1 promoter

Literature references

Kopan, R., Schroeter, EH., Brou, C., Israel, A., Jarriault, S., Logeat, F. (1995). Signalling downstream of activated mammalian Notch. *Nature, 377*, 355-8. ↗

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2017-01-31	Reviewed	Ito, Y., Chuang, LS.
2017-01-31	Edited	Orlic-Milacic, M.

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