NOTCH precursor cleaved to form mature NOTCH

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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

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. ↗

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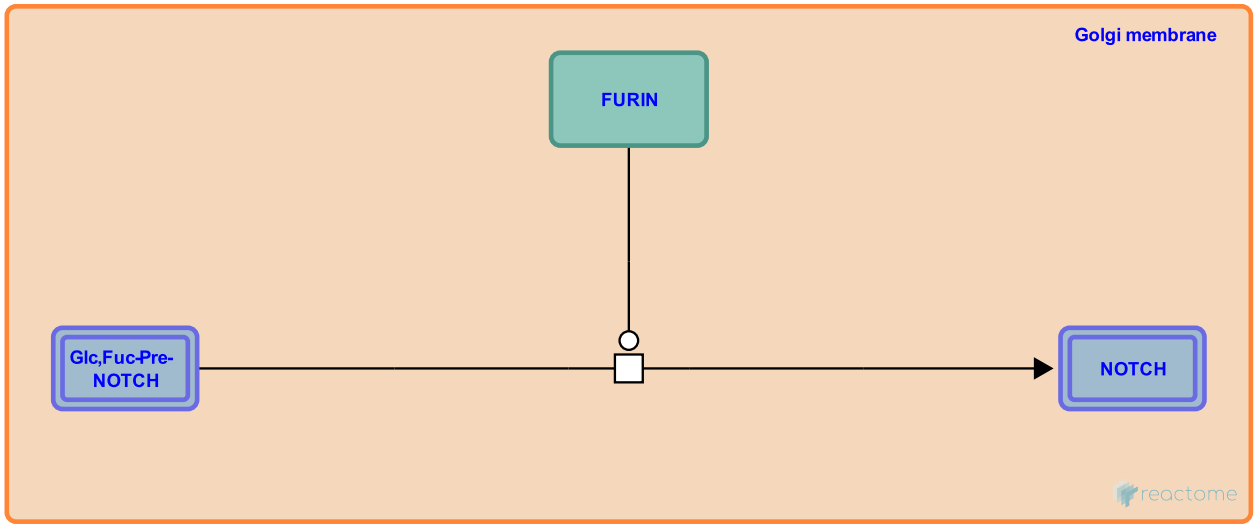
Stable identifier: R-HSA-1912369

Type: transition

Compartments: Golgi membrane



The NOTCH receptor is synthesized as a precursor polypeptide (approx. 300 kDa) associated with the endoplasmic reticulum membrane. The mature NOTCH receptor is produced by proteolytic cleavage to form a heterodimer. The enzyme responsible is a furin-like convertase which cleaves the full-length precursor into a transmembrane fragment (NTM) of approximate size 110 kDa and an extracellular fragment (NEC) of approximate size 180 kDa. The mature NOTCH receptor is reassembled as a heterodimer (Blaumueller et al. 1997, Logeat et al. 1998). Both disulfide bonds and calcium-mediated ionic interactions stabilize the heterodimer (Rand et al. 2000, Gordon et al. 2009). This process takes place in the trans-Golgi network . Mammalian NOTCH is predominantly presented as a heterodimer on the cell surface. Although FURIN-mediated cleavage is evolutionarily conserved, it may not be mandatory for Drosophila Notch function (Kidd et al. 2002).

Literature references

Seidah, NG., LeBail, O., Jarriault, S., Logeat, F. (1998). The Notch1 receptor is cleaved constitutively by a furin-like convertase. *Proc Natl Acad Sci U S A, 95*, 8108-12. ↗

L'Heureux, S., McArthur, DG., Blacklow, SC., Malecki, MJ., Mitchell, JL., Vardar-Ulu, D. et al. (2009). Effects of S1 cleavage on the structure, surface export, and signaling activity of human Notch1 and Notch2. *PLoS One, 4*, e6613. ↗

Kidd, S., Lieber, T. (2002). Furin cleavage is not a requirement for Drosophila Notch function. *Mech Dev, 115*, 41-51. ↗

Jan, YN., Chan, YM. (1998). Roles for proteolysis and trafficking in notch maturation and signal transduction. *Cell, 94* , 423-6. ↗

Blacklow, SC., Grimm, LM., Sklar, J., Artavanis-Tsakonas, S., Patriub, V., Rand, MD. (2000). Calcium depletion dissociates and activates heterodimeric notch receptors. *Mol Cell Biol, 20*, 1825-35. ↗

Editions

2004-12-15	Authored	Jassal, B.
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