CDK8 phosphorylates xNICD1

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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. ↗

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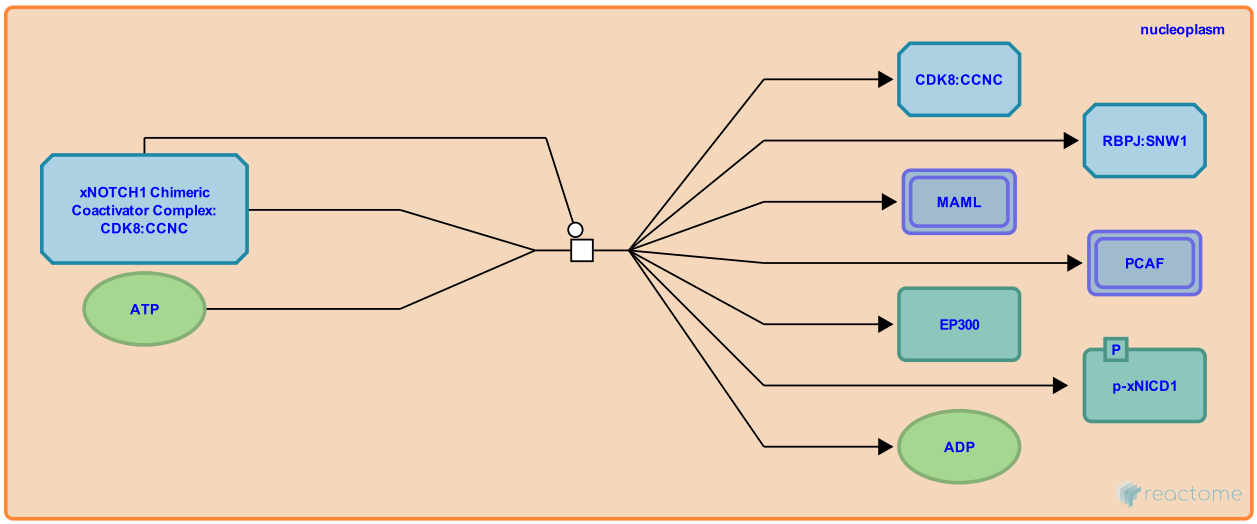
Stable identifier: R-NUL-2065178

Type: transition

Compartments: nucleoplasm



TAD and PEST domains of NOTCH intracellular domain contain multiple conserved cyclin-dependent kinase phosphorylation sites. In vitro, recombinant human CDK8 in complex with recombinant human cyclin C (CDK8:CCNC) readily phosphorylates recombinant Xenopus NICD1 (xNICD1). This phosphorylation also occurs when these recombinant proteins are expressed in HeLa cells, and was directly shown to involve conserved serine residues in the PEST domain. Phosphorylation by CDK8 targets xNICD1 for ubiquitination and subsequent degradation, thereby coordinating NICD1 transcriptional activity with NICD1 turnover.

Literature references

Fryer, CJ., White, JB., Jones, KA. (2004). Mastermind recruits CycC:CDK8 to phosphorylate the Notch ICD and coordinate activation with turnover. *Mol Cell, 16*, 509-20. ↗

Editions

2011-11-14	Authored	Egan, SE., Orlic-Milacic, M.
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