

# p-NICD1 PEST domain mutants do not bind FBXW7

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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 reaction ([see Table of Contents](#))

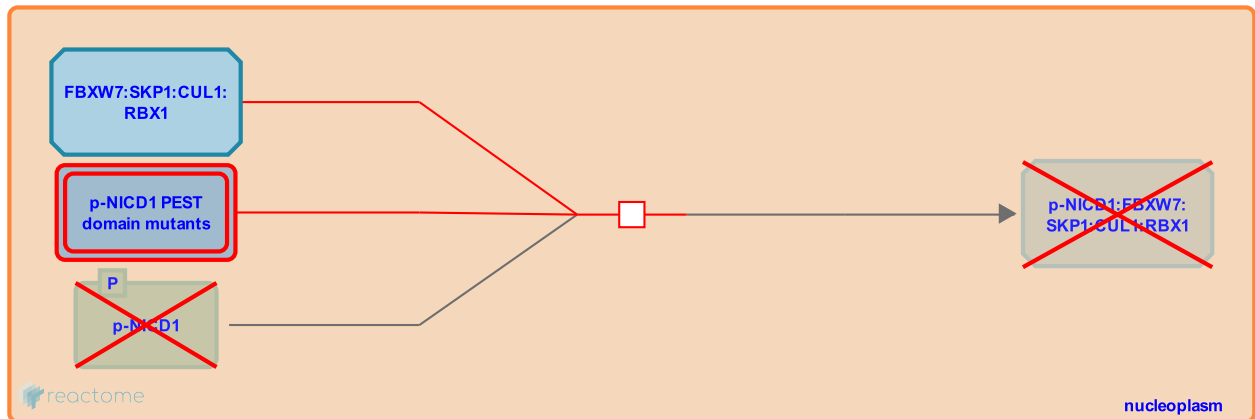
## p-NICD1 PEST domain mutants do not bind FBXW7 [↗](#)

**Stable identifier:** R-HSA-2220967

**Type:** transition

**Compartments:** nucleoplasm

**Diseases:** cancer, T-cell leukemia



As binding of WD40 repeats of FBXW7 requires conserved phosphodegron in the PEST domain of NICD1, especially phosphorylation of threonine residue T2511 and serine residue S2513, FBXW7 cannot bind NICD1 PEST domain mutants which lack the conserved phosphodegron due to truncation of the PEST domain, or are not phosphorylated on conserved threonine and serine residues due to point mutations. Inability to bind FBXW7 and undergo FBXW7-mediated ubiquitination and degradation prolongs the half-life of NICD1 PEST domain mutants and results in persistent NOTCH1 signaling (O'Neil et al. 2007, Thompson et al. 2007).

### Literature references

Thompson, BJ., Buonamici, S., Sulis, ML., Palomero, T., Vilimas, T., Basso, G. et al. (2007). The SCFFBW7 ubiquitin ligase complex as a tumor suppressor in T cell leukemia. *J Exp Med*, 204, 1825-35. [↗](#)

O'Neil, J., Grim, J., Strack, P., Rao, S., Tibbitts, D., Winter, C. et al. (2007). FBW7 mutations in leukemic cells mediate NOTCH pathway activation and resistance to gamma-secretase inhibitors. *J Exp Med*, 204, 1813-24. [↗](#)

### Editions

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