APC is K63-polyubiquitinated

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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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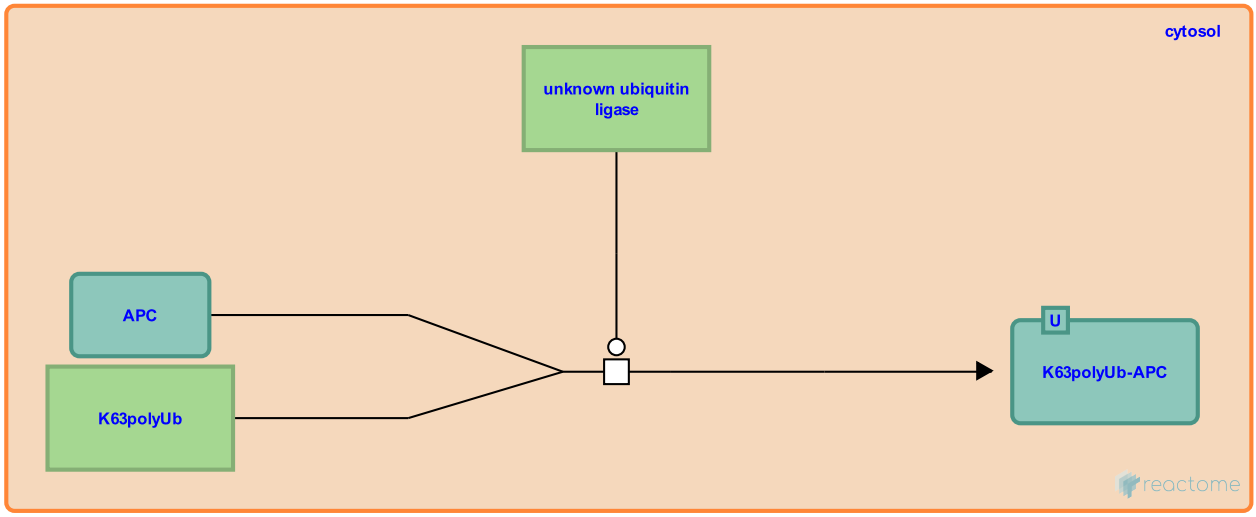
Stable identifier: R-HSA-5246693

Type: transition

Compartments: cytosol



In unstimulated cells, APC is K63 polyubiquitinated in a manner that depends on its association with AXIN. Although the precise timing of APC polyubiquitination is unclear, it is disrupted by abrogation of GSK3 kinase activity and in the presence of phosphodegron mutants of beta-catenin, suggesting that the formation of a functional destruction complex is required. Destruction complex formation is also dependent upon AXIN levels, which may be regulated at least in part by the balance of its ubiquitination and sumoylation (Kim et al, 2008).

Upon WNT3A stimulation, APC K63 polyubiquitination is lost coincident with disruption of the APC-AXIN interaction (Tran and Polakis, 2012). Interestingly, another study has shown that DVL is K63 polyubiquitinated upon WNT signaling (Tauriello et al, 2010), suggesting a possible model in which WNT signaling promotes a change in AXIN-K63 polyubiquitin binding partner to destabilize the destruction complex and promote pathway activation. Alternately, APC K63 polyubiquitination may protect beta-catenin from PP2A-mediated dephosphorylation and thus favour its degradation (Su et al, 2008).

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Editions

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