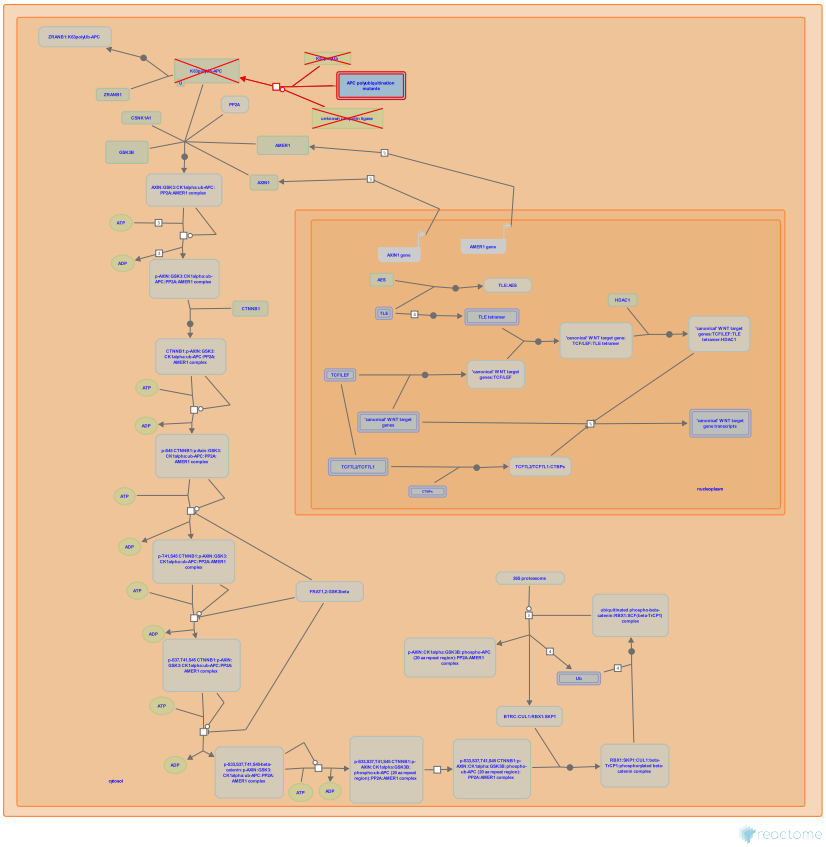
APC truncation mutants are not K63 polyubiquitinated



Matthews, L., Rothfels, K., Salahshor, S., Woodgett, J.

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

15/05/2024

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. ↗

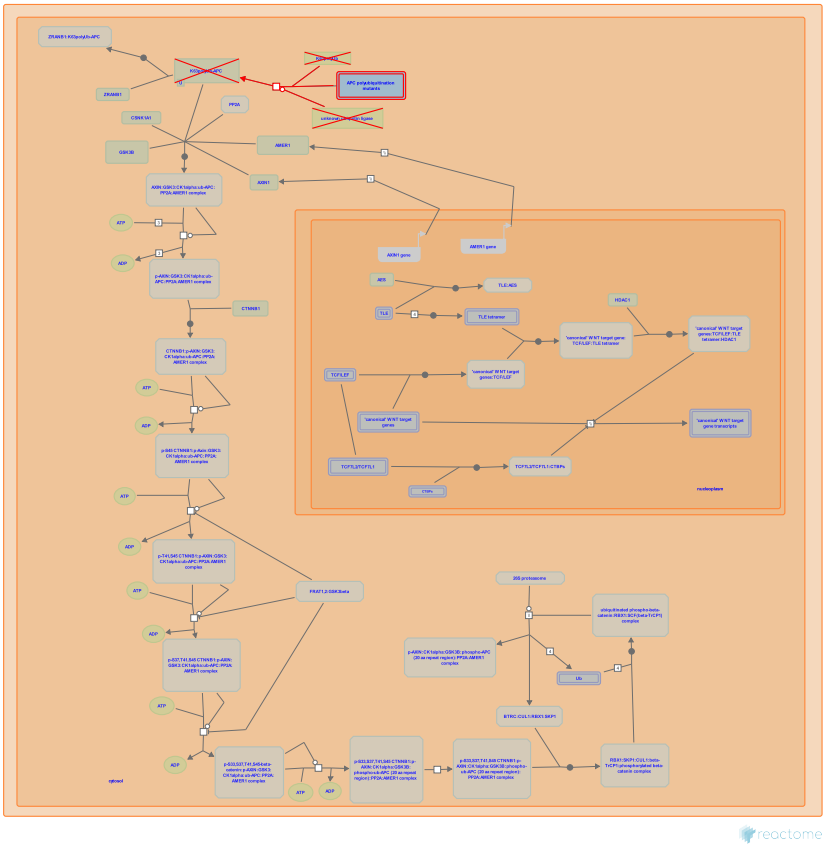
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

APC truncation mutants are not K63 polyubiquitinated ↗

Stable identifier: R-HSA-5467333

Diseases: cancer



APC has been shown to be reversibly modified with K63-linked polyubiquitin chains. This modification is required for the assembly of the destruction complex and subsequent degradation of beta-catenin in the absence of WNT ligand. K63-polyubiquitination of APC is lacking in a number of colorectal cancer cell lines expressing truncated forms of APC, and these lines have aberrantly high beta-catenin levels and WNT pathway activation (Tran and Polakis, 2012).

Literature references

Polakis, P., Tran, H. (2012). Reversible modification of adenomatous polyposis coli (APC) with K63-linked polyubiquitin regulates the assembly and activity of the ?-catenin destruction complex. *J. Biol. Chem., 287*, 28552-63. ↗

Editions

2014-01-17	Authored	Rothfels, K.
2014-04-03	Edited	Matthews, L.
2014-05-12	Reviewed	Salahshor, S.
2014-05-22	Reviewed	Woodgett, J.

APC truncation mutants are not K63 polyubiquitinated ↗

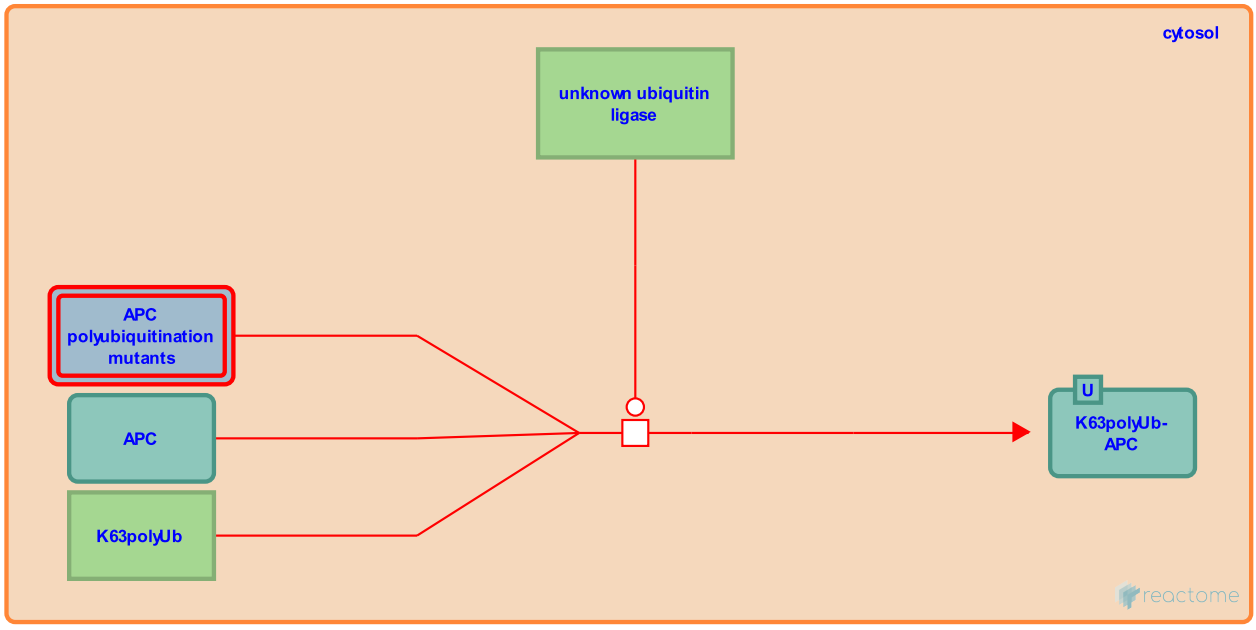
Location: APC truncation mutants are not K63 polyubiquitinated

Stable identifier: R-HSA-5246696

Type: transition

Compartments: cytosol

Diseases: colorectal cancer



APC is K63 polyubiquitinated in the absence of WNT signal and this modification correlates with AXIN binding. Depletion of AXIN or beta-catenin by RNAi abrogates APC polyubiquitination, as does inhibition of GSK3 kinase activity, suggesting that polyubiquitination depends on the assembly of a functional destruction complex. WNT3A pathway activation promotes a loss of APC-AXIN interaction concurrent with loss of APC polyubiquitination (Tran and Polakis, 2012).
Polyubiquitination of APC is lost in a number of human cancer cell lines that express truncated forms of APC and which show hyperactivation of the WNT signaling pathway (Tran and Polakis, 2012). The loss of APC polyubiquitination in these lines may reflect the fact that the APC mutants are compromised in their ability to interact with AXIN due to truncation/loss of the AXIN-binding SAMP repeats (Spink et al, 2000); alternately, the truncations may remove as-yet unidentified polyubiquitination sites. APC polyubiquitination is also lost in cancer lines carrying mutations in AXIN that disrupt interaction with GSK3 as well as in cell lines with phosphodegron mutations of beta-catenin (Tran and Polakis, 2012).

Literature references

Polakis, P., Tran, H. (2012). Reversible modification of adenomatous polyposis coli (APC) with K63-linked polyubiquitin regulates the assembly and activity of the ?-catenin destruction complex. *J. Biol. Chem., 287,* 28552-63. ↗

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