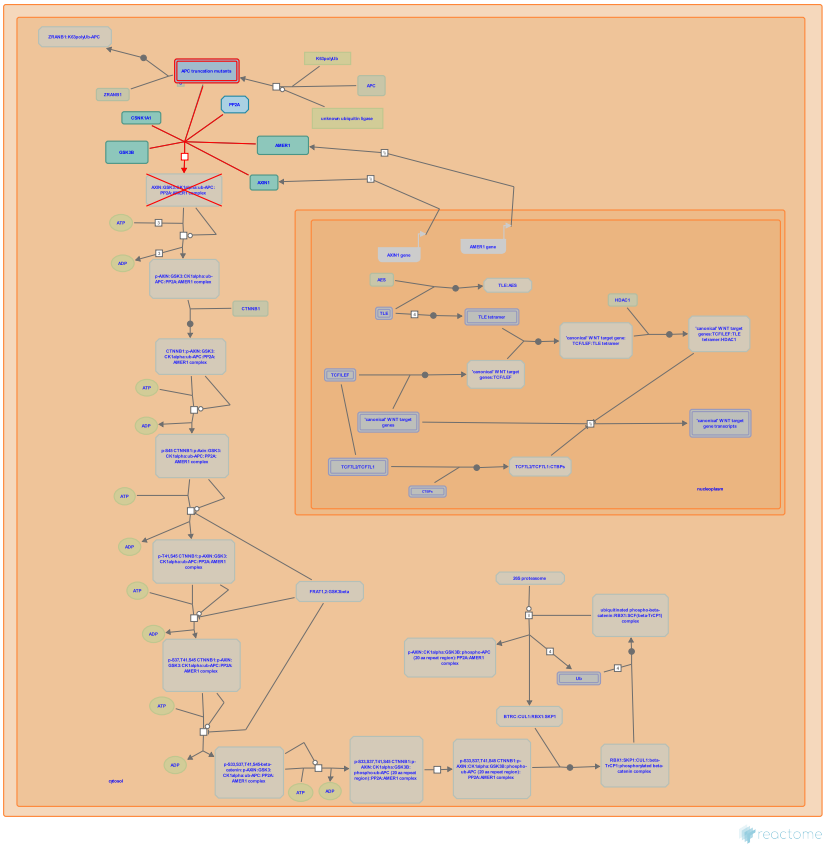
APC truncation mutants have impaired AXIN binding



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.

30/04/2024

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. ↗

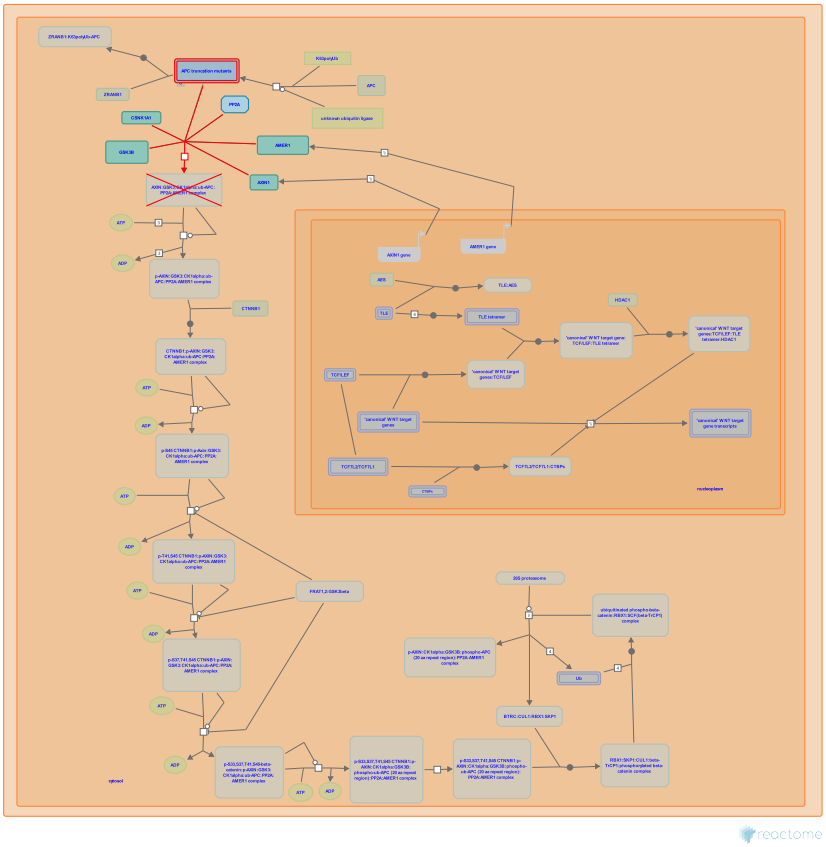
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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 have impaired AXIN binding ↗

Stable identifier: R-HSA-5467337

Diseases: cancer



Mutations in the APC tumor suppressor gene are common in colorectal and other cancers and cluster in the central mutation cluster region (MCR) of the gene (Miyoshi et al, 1992; Nagase and Nakamura, 1993; Dihlmann et al, 1999; reviewed in Bienz and Clevers, 2000). These mutations generally result in truncated proteins that destabilize the destruction complex and result in elevated WNT pathway activation (reviewed in Polakis, 2000).

Literature references

Nagase, H., Nakamura, Y. (1993). Mutations of the APC (adenomatous polyposis coli) gene. *Hum. Mutat., 2*, 425-34. ↗

Polakis, P. (2000). Wnt signaling and cancer. *Genes Dev., 14*, 1837-51. ↗

Gebert, J., Herfarth, C., Siermann, A., von Knebel Doeberitz, M., Dihlmann, S. (1999). Dominant negative effect of the APC1309 mutation: a possible explanation for genotype-phenotype correlations in familial adenomatous polyposis. *Cancer Res., 59*, 1857-60. ↗

Clevers, HC., Bienz, M. (2000). Linking colorectal cancer to Wnt signaling. *Cell, 103*, 311-20. ↗

Mori, T., Ando, H., Nagase, H., Ichii, S., Horii, A., Nakamura, Y. et al. (1992). Somatic mutations of the APC gene in colorectal tumors: mutation cluster region in the APC gene. *Hum. Mol. Genet., 1*, 229-33. ↗

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 have impaired AXIN binding ↗

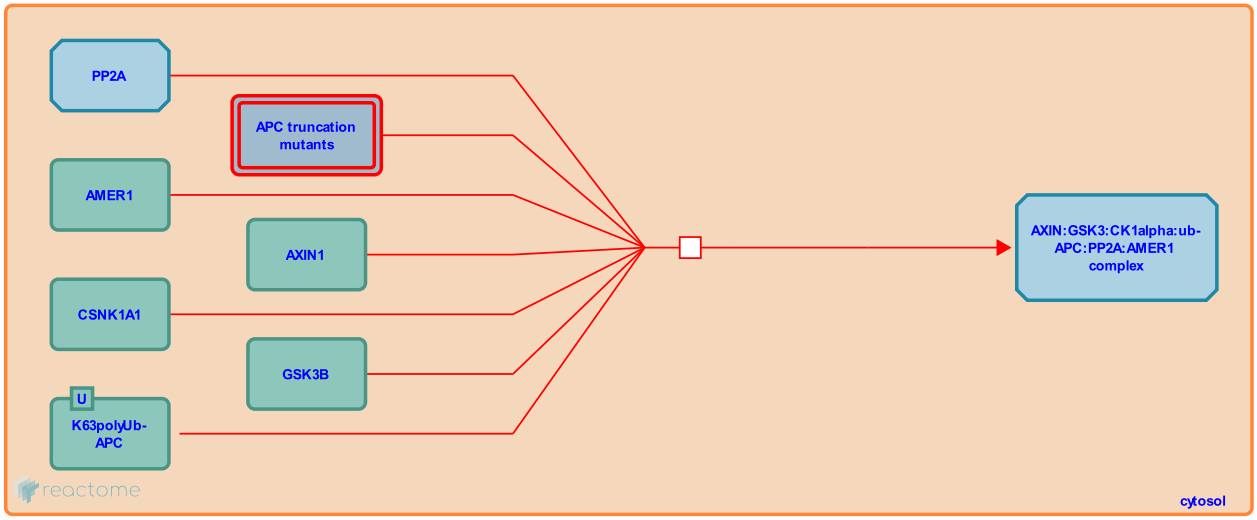
Location: APC truncation mutants have impaired AXIN binding

Stable identifier: R-HSA-4791278

Type: transition

Compartments: cytosol

Diseases: colorectal cancer, cancer



The tumor suppressor APC is a central component of the destruction complex that makes direct, functionally important contacts with a number of other destruction complex members, including AXIN, beta-catenin and GSK3 (Behrens et al, 1998; Kishida et al, 1998; Hart et al, 1998; Rubinfeld et al, 1993; Su et al, 1993; Rubinfeld et al, 1996). These protein-protein interactions are critical to APC's role in promoting the proteasome-mediated degradation of beta-catenin, and are abrogated by APC truncations that are common in the vast majority of colorectal cancers (reviewed in Saito-Diaz et al, 2013; Polakis, 2000; Polakis, 2012). Cancer cells with expressing truncated forms of APC have high levels of free beta-catenin and aberrant WNT target gene expression (Morin et al, 1997; Shih et al, 2000; Roh et al, 2001).

Literature references

Yu, J., Kinzler, KW., Shih, IM., Vogelstein, B., He, TC. (2000). The beta-catenin binding domain of adenomatous polyposis coli is sufficient for tumor suppression. *Cancer Res., 60*, 1671-6. ↗

Grosschedl, R., Wedlich, D., Bruhn, L., Kühl, M., Birchmeier, W., von Kries, JP. et al. (1996). Functional interaction of beta-catenin with the transcription factor LEF-1. *Nature, 382*, 638-42. ↗

Roh, H., Drebin, JA., Green, DW., Pippin, JA., Boswell, CB. (2001). Suppression of beta-catenin inhibits the neoplastic growth of APC-mutant colon cancer cells. *Cancer Res., 61*, 6563-8. ↗

Barker, N., Clevers, HC., Morin, PJ., Kinzler, KW., Vogelstein, B., Korinek, V. et al. (1997). Activation of beta-catenin-Tcf signaling in colon cancer by mutations in beta-catenin or APC. *Science, 275*, 1787-90. ↗

Polakis, P. (2012). Wnt signaling in cancer. *Cold Spring Harb Perspect Biol, 4*. ↗

Editions

2013-10-07	Authored	Rothfels, K.
2014-04-03	Edited	Matthews, L.
2014-05-12	Reviewed	Salahshor, S.
2014-05-22	Reviewed	Woodgett, J.

Table of Contents

Introduction 1

APC truncation mutants have impaired AXIN binding 2

APC truncation mutants have impaired AXIN binding 3

Table of Contents 4