

Truncated AMER1 mutants destabilize the destruction complex

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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.

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. [↗](#)

Reactome database release: 75

This document contains 1 reaction ([see Table of Contents](#))

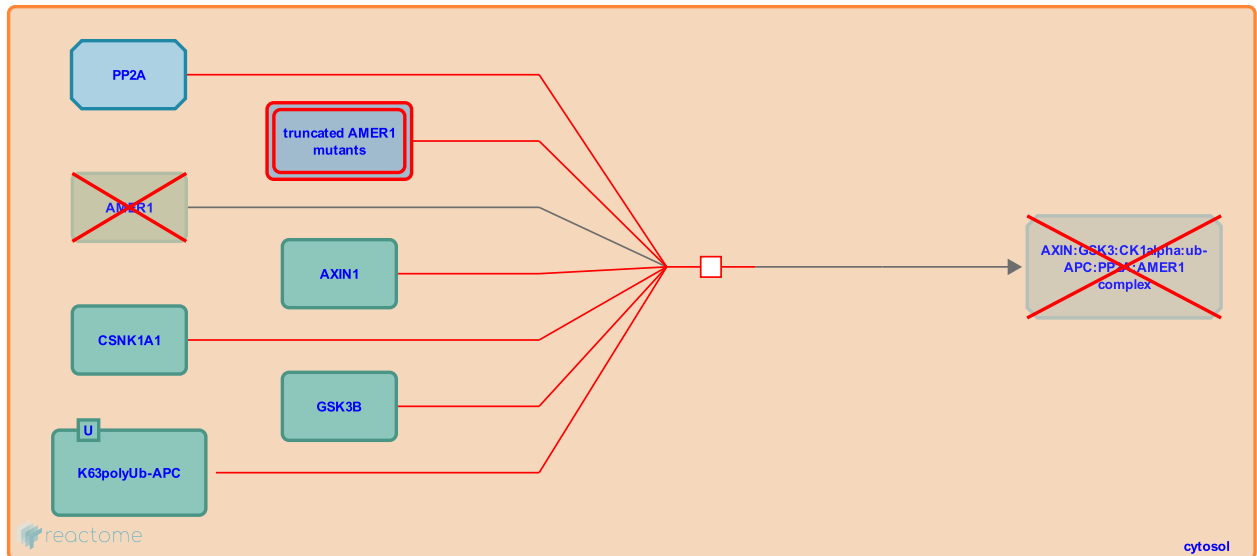
Truncated AMER1 mutants destabilize the destruction complex [↗](#)

Stable identifier: R-HSA-4839746

Type: transition

Compartments: cytosol

Diseases: kidney cancer, nephroblastoma, cancer



AMER1/WTX is a known component of the destruction complex and interacts directly with beta-catenin through the C-terminal half (Major et al, 2007). siRNA depletion of AMER1 in mammalian cells stabilizes cellular beta-catenin levels and increases the expression of a beta-catenin-dependent reporter gene, suggesting that AMER1 is a tumor suppressor gene (Major et al, 2007; reviewed in Huff, 2011). Consistent with this, nonsense and missense mutations that truncate AMER1 and result in loss of the beta-catenin binding region have been identified in Wilms tumor, a pediatric kidney cancer (Ruteshouser et al, 2008; Wegert et al, 2009).

Literature references

- Major, MB., Camp, ND., Berndt, JD., Yi, X., Goldenberg, SJ., Hubbert, C. et al. (2007). Wilms tumor suppressor WTX negatively regulates WNT/beta-catenin signaling. *Science*, 316, 1043-6. [↗](#)
- Ruteshouser, EC., Robinson, SM., Huff, V. (2008). Wilms tumor genetics: mutations in WT1, WTX, and CTNNB1 account for only about one-third of tumors. *Genes Chromosomes Cancer*, 47, 461-70. [↗](#)
- Huff, V. (2011). Wilms' tumours: about tumour suppressor genes, an oncogene and a chameleon gene. *Nat. Rev. Cancer*, 11, 111-21. [↗](#)
- Wegert, J., Wittmann, S., Leuschner, I., Geissinger, E., Graf, N., Gessler, M. (2009). WTX inactivation is a frequent, but late event in Wilms tumors without apparent clinical impact. *Genes Chromosomes Cancer*, 48, 1102-11. [↗](#)

Editions

2013-10-30	Authored	Rothfels, K.
2014-04-03	Edited	Matthews, L.
2014-05-12	Reviewed	Salahshor, S.
2014-05-22	Reviewed	Woodgett, J.