XIAP monoubiquinates TLE

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06/05/2024

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

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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. ↗

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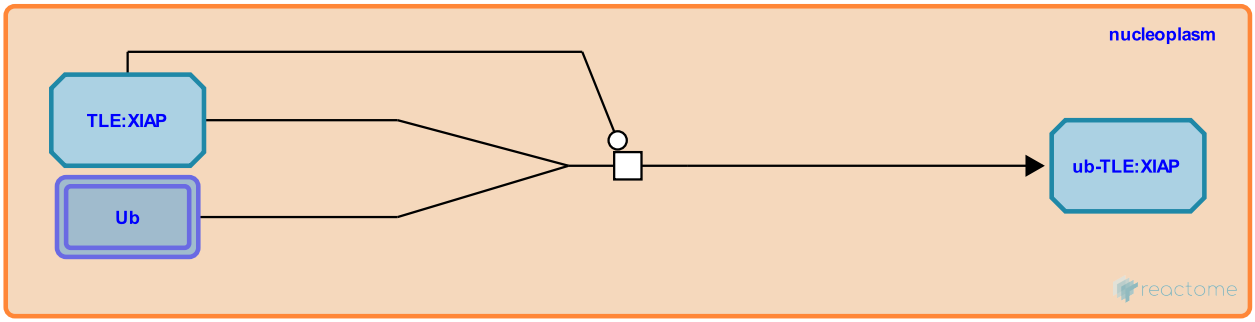
Stable identifier: R-HSA-3322429

Type: transition

Compartments: nucleoplasm



XIAP has been shown to ubiquitinate all human isoforms of TLE in vitro, likely in the conserved Q domain. Ubiquitination does not appear to affect the stability, localization or tetramerization of TLE; rather ubiquitination affects the interaction with TCF/LEF. Ubiquitinated TLE3 is not able to bind TCF7L2 (TCF4) in vitro and addition of XIAP to TLE3-TCF7L2 complexes promotes the dissociation of TLE from TCF7L2. Although XIAP ubiquitinates TLE in a constitutive manner, XIAP only co-immunoprecipitates with TCF7L2 upon activation of the WNT signalling pathway. These data support a model where XIAP regulates the interaction between TLE and TCF/LEF by limiting the pool of free nuclear TLE that is available for binding, and by potentially disrupting existing repression complexes at WNT-responsive promoters. By disrupting the interaction between TLE and TCF/LEF, XIAP may facilitate the recruitment of beta-catenin and the establishment of an activation complex at WNT-responsive promoters (Hanson et al, 2012)

Literature references

Beauchamp, RD., Freeman, TJ., Wallace, HA., Hanson, AJ., Lee, E., Lee, LA. (2012). XIAP monoubiquitylates Groucho/TLE to promote canonical Wnt signaling. *Mol. Cell, 45*, 619-28.

Editions

2013-05-30	Authored	Rothfels, K.
2013-10-03	Edited	Gillespie, ME.
2014-01-22	Reviewed	Rajakulendran, N.
2014-02-15	Reviewed	van Amerongen, R.
2014-04-22	Reviewed	Kikuchi, A.