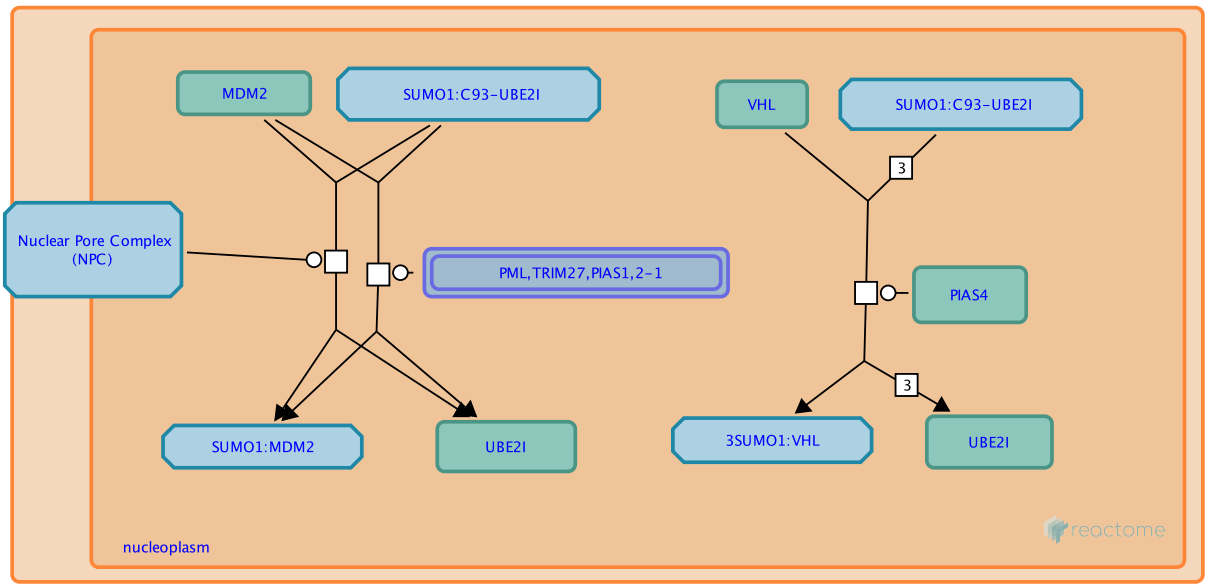
SUMOylation of ubiquitinylation proteins



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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

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. ↗

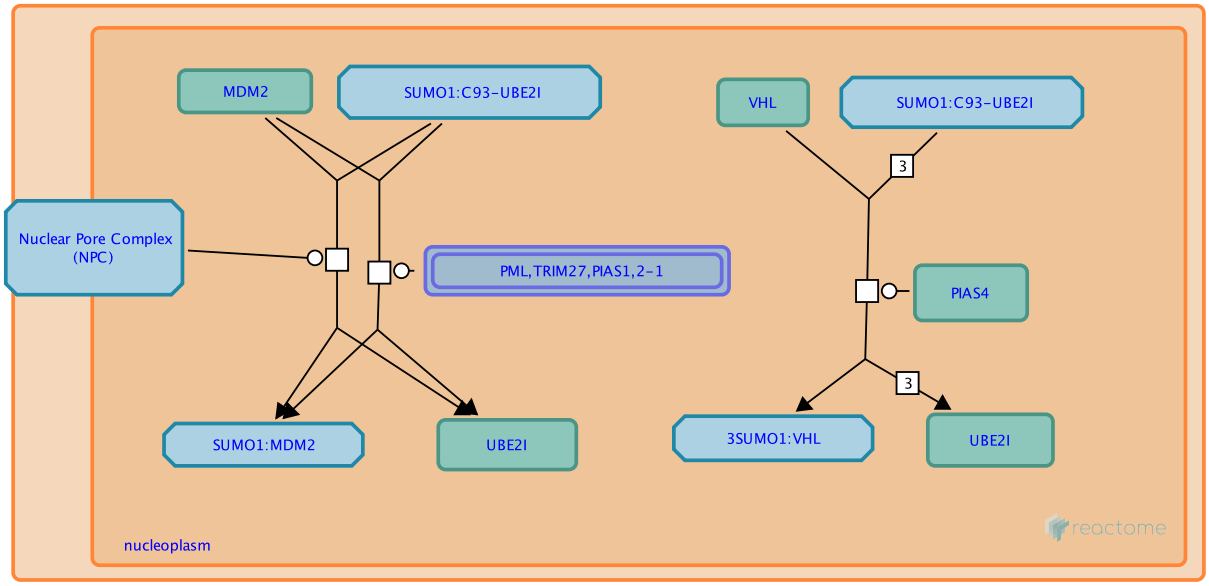
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

SUMOylation of ubiquitinylation proteins ↗

Stable identifier: R-HSA-3232142

Compartments: nucleoplasm



Several ubiquitin E3 ligases are regulated by SUMOylation (reviewed in Wilson and Heaton 2008). SUMOylation appears to be necessary for nuclear import of MDM2, the E3 ligase that ubiquitinylates TP53 (p53). SUMOylation of VHL abolishes its ubiquitin ligase activity. HERC2, RNF168, and BRCA1 are ubiquitin ligases that are SUMOylated during DNA damage response and repair.

Literature references

Wilson, VG., Heaton, PR. (2008). Ubiquitin proteolytic system: focus on SUMO. *Expert Rev Proteomics, 5*, 121-35. ↗

Editions

2013-03-23	Authored, Edited	May, B.
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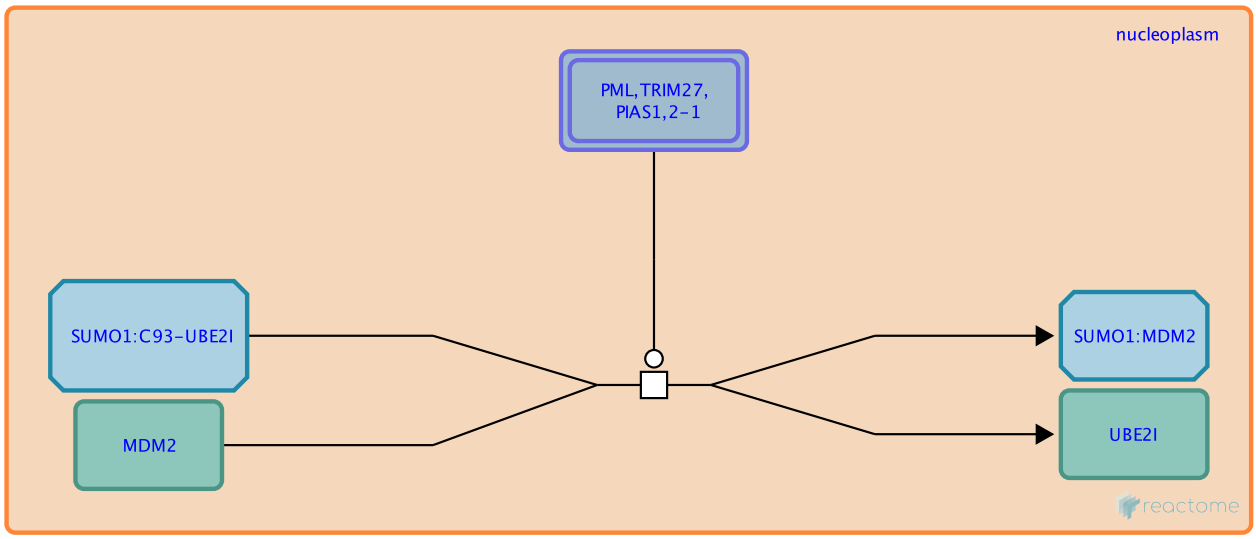
PML, TRIM27, PIAS1,2-1 SUMOylate MDM2 with SUMO1 ↗

Location: SUMOylation of ubiquitinylation proteins

Stable identifier: R-HSA-3000434

Type: transition

Compartments: nucleoplasm



PML TRIM27, PIAS1, and PIAS2-1 can each SUMOylate MDM2 with SUMO1 at lysine-182 (Miyauchi et al. 2002, Chu and Yang 2011). An unSUMOylatable mutant of MDM2 accumulates in the cytosol so SUMOylation may be part of the process of nuclear import of MDM2 (Miyauchi et al. 2002).

Literature references

Chu, Y., Yang, X. (2011). SUMO E3 ligase activity of TRIM proteins. *Oncogene, 30*, 1108-16. ↗

Miyauchi, Y., Yogosawa, S., Honda, R., Nishida, T., Yasuda, H. (2002). Sumoylation of Mdm2 by protein inhibitor of activated STAT (PIAS) and RanBP2 enzymes. *J. Biol. Chem., 277*, 50131-6. ↗

Editions

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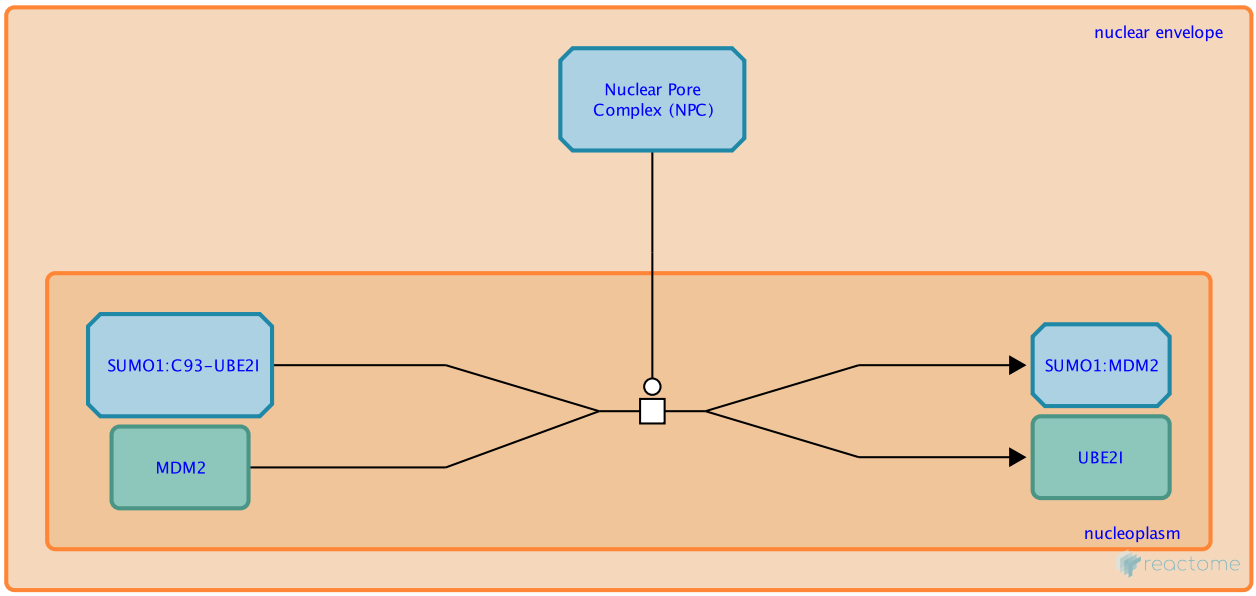
RANBP2 SUMOylates MDM2 with SUMO1 ↗

Location: SUMOylation of ubiquitinylation proteins

Stable identifier: R-HSA-5228523

Type: transition

Compartments: nucleoplasm, nuclear envelope



RANBP2 of the nuclear pore complex SUMOylates MDM2 with SUMO1 at lysine-182 (Mayauchi et al. 2002). An unSUMOylatable mutant of MDM2 accumulates in the cytosol so SUMOylation may be part of the process of nuclear import of MDM2 (Miyauchi et al. 2002).

Literature references

Miyauchi, Y., Yogosawa, S., Honda, R., Nishida, T., Yasuda, H. (2002). Sumoylation of Mdm2 by protein inhibitor of activated STAT (PIAS) and RanBP2 enzymes. *J. Biol. Chem., 277*, 50131-6. ↗

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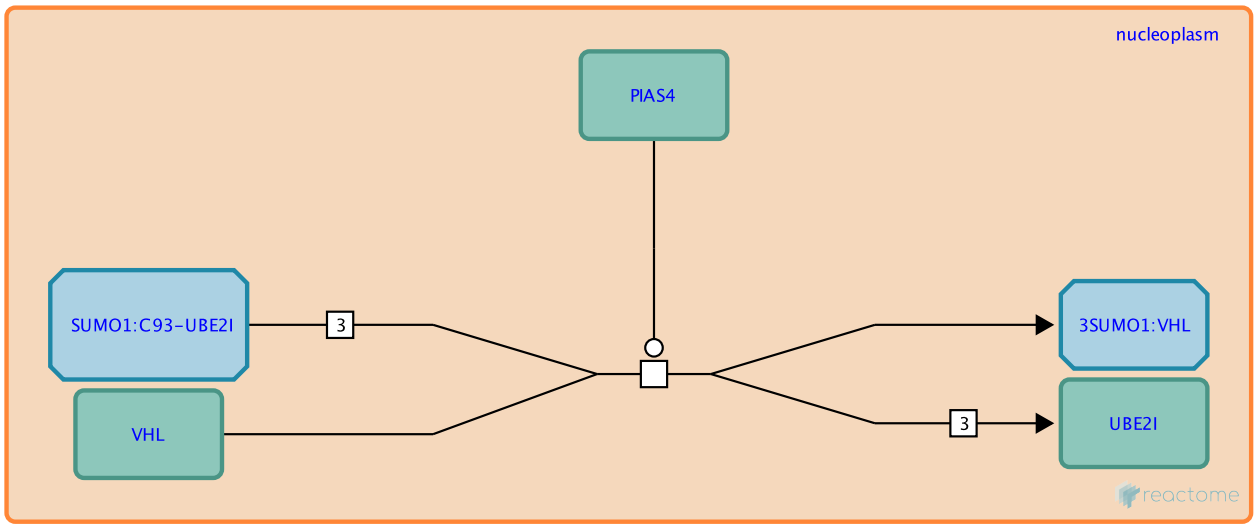
PIAS4 SUMOylates VHL with SUMO1

Location: SUMOylation of ubiquitinylation proteins

Stable identifier: R-HSA-4551721

Type: transition

Compartments: nucleoplasm



PIAS4 SUMOylates VHL at lysine-159, lysine-171, and lysine-196 with SUMO1 (Cai et al. 2010, Cai and Robertson 2010, Chien et al. 2013). SUMOylation facilitates the oligomerization of VHL, abolishes the inhibitory function of VHL on HIF1A, and abolishes the tumor suppressor function of VHL by inactivating the ubiquitinylation activity of VHL.

Literature references

Cai, Q., Verma, SC., Kumar, P., Ma, M., Robertson, ES. (2010). Hypoxia inactivates the VHL tumor suppressor through PIASy-mediated SUMO modification. *PLoS ONE, 5*, e9720.

Cai, Q., Robertson, ES. (2010). Ubiquitin/SUMO modification regulates VHL protein stability and nucleocytoplasmic localization. *PLoS ONE, 5*.

Chien, W., Lee, KL., Ding, LW., Wuensche, P., Kato, H., Doan, NB. et al. (2013). PIAS4 is an activator of hypoxia signalling via VHL suppression during growth of pancreatic cancer cells. *Br. J. Cancer*.

Editions

2013-09-13	Authored, Edited	May, B.
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