SUMOylation of transcription factors


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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


Reactome database release: 69

This document contains 1 pathway and 11 reactions (see Table of Contents)
SUMOylation of transcription factors

Stable identifier: R-HSA-3232118

Compartments: nucleoplasm

Proteins classified as transcription factors constitute a disproportionate number of SUMOylation targets. In most cases SUMOylation inhibits transcriptional activation, however in some cases such as TP53 (p53) SUMOylation can enhance activation. Inhibition of transcription by SUMOylation may be due to interference with DNA binding, re-localization to inactive nuclear bodies, or recruitment of repressive cofactors such as histone deacetylases (reviewed in Girdwood et al. 2004, Gill 2005).

Literature references


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PIAS3 SUMOylates MITF with SUMO1

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-3232162

**Type:** transition

**Compartments:** nucleoplasm

PIAS3 SUMOylates MITF with SUMO1 at lysine-289 and lysine-423 (lysine-182 and lysine-316 of the M2 isoform, Miller et al. 2005). SUMOylation reduces transcriptional activation by MITF at promoters containing multiple binding sites for MITF.

**Literature references**


**Editions**

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PIAS1,3,4 SUMOylate MTA1 with SUMO2,3

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-3465545

**Type:** transition

**Compartments:** nucleoplasm

PIAS1,3,4 SUMOylate MTA1 with SUMO2,3 at lysine-509 (Cong et al. 2011). SUMOylation increases the repressor activity of MTA1 at the PS2 promoter (Cong et al. 2011).

**Literature references**


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PIAS1 SUMOylates SP3 with SUMO1

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-3247493

**Type:** transition

**Compartments:** nucleoplasm


**Literature references**


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PIAS1 SUMOylates SP3 with SUMO2

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-6804468

**Type:** transition

**Compartments:** nucleoplasm


**Literature references**


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PIAS4 SUMOylates TP53BP1 with SUMO1

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-2997723

**Type:** transition

**Compartments:** nucleoplasm

PIAS4 SUMOylates TP53BP1 with SUMO1 in response to double-strand breaks in DNA (Galanty et al. 2009, Impens et al. 2014). Overall, like TP53BP1, SUMO1,2,3, UBE2I, PIAS1 and PIAS4 are all observed to accumulate at double-strand breaks.

**Literature references**


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https://www.reactome.org
MDM2 SUMOylates TP53 with SUMO2,3

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-2997706

**Type:** transition

**Compartments:** nucleoplasm

MDM2 in a complex with CDKN2A (p14-ARF) SUMOylates TP53 (p53) with SUMO2,3 at lysine-386 (Stindt et al. 2011, Hendriks et al. 2014, Tammsalu et al. 2014). SUMOylation decreases transcriptional activation by TP53 at some genes and decreases repression by TP53 at other genes (Stindt et al. 2011).

**Literature references**


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PIAS1,2-1 SUMOylate HIC1 with SUMO1

Location: SUMOylation of transcription factors

Stable identifier: R-HSA-4090281

Type: transition

Compartments: nucleoplasm

PIAS1,2-1 SUMOylate deacetylated HIC1 at lysine-333 (lysine 314 of HIC1 isoform 2) with SUMO1 (Stankovic-Valentin et al. 2007). Acetylation of HIC1 at lysine-333 inhibits SUMOylation. SUMOylation increases transcription repression by HIC1 (Stankovic-Valentin et al. 2007) and favors the interaction of HIC1 with MTA1 (Van Rechem et al., Mol Cell Biol, 2010) and MTA3 (Paget et al. 2016) notably during the DNA damage response (DDR) to non-repairable double strand breaks (DSBs). (Dehennaut et al. 2013). This increase of HIC1 SUMOylation during the DDR to DSBs is strictly dependent on the ATM kinase (Paget et al. 2016). SUMOylation of HIC1 is dispensable for DNA repair since the non-SUMOylatable point mutant E316A is as efficient as wt HIC1 in Comet assays which measure the repair of DSBs (Paget et al. 2016).

Literature references


Paget, S., Dubuissez, M., Dehennaut, V., Nassour, J., Harmon, BT., Spruyt, N. et al. (2016). HIC1 (hypermethylated in cancer 1) SUMOylation is dispensable for DNA repair but is essential for the apoptotic DNA damage response (DDR) to irreparable DNA double-strand breaks (DSBs). Oncotarget.

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UBE2I (UBC9), PIAS1 SUMOylate FOXL2 with SUMO1

Location: SUMOylation of transcription factors

Stable identifier: R-HSA-3968414

Type: transition

Compartments: nucleoplasm

UBC9 and PIAS1 SUMOylate FOXL2 with SUMO1 (Kuo et al. 2009, Marongiu et al 2010, Georges et al. 2011). This modification changes its cellular localization, stability and transcriptional activity (Marongiu et al, 2010). SUMOylation localizes FOXL2 to PML bodies in the nucleus. SUMOylation is required for repression of transcription by FOXL2 at the STAR promoter and reduces transactivation by FOXL2 at the PER2 promoter. Hypophosphorylation of serine-33 correlates with SUMOylation and stabilization of FOXL2, leading to enhanced transcriptional activation of TNF-R1, FAS, caspase 8, p21, and aromatase (Kim et al. 2014).

Literature references


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SUMOylation of TFAP2A with SUMO1

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-3234081

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** SUMOylation of TFAP2C with SUMO1 (Homo sapiens)

UBE2I (UBC9) interacts with TFAP2A, TFAP2B and TFAP2C, and the interaction site has been mapped to the C terminal region of TFAP2C; SUMOylation occurs on lysine-10 (Eloranta and Hurst 2002). As lysine-10 is conserved in TFAP2A and TFAP2B, SUMOylation of these factors is assumed to be on lysine-10 (Eloranta and Hurst 2002; Impens et al. 2014). SUMOylation causes a reduction in AP-2 transcriptional activation function but is required for its repressive function. A dominant negative mutant of UBC9 led to increased activation and reduced repressor function of TFAP2A and C, supporting the role of UBC9 in SUMOylation (Eloranta and Hurst 2002; Berlato et al. 2011). Isoform 1a of TFAP2A is SUMOylated, isoforms 1b and 1c lack lysine 10 and are not SUMOylated (Berlato et al. 2011). TFAP2D and TFAP2E lack lysine-10 and are thus assumed not to be SUMOylated. SUMOylation of TFAP2A blocked its ability to induce the expression of luminal genes and repression of basal genes (Bogachek et al. 2014). Disruption of the SUMOylation pathway by knockdown of SUMOylation enzymes, mutation of the SUMO-target lysine of TFAP2A, or treatment with SUMOylation inhibitors induced MET in basal breast cancers, which was dependent on TFAP2A (Bogachek et al. 2014).

**Literature references**


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SUMOylation of TFAP2B with SUMO1

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-3234084

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** SUMOylation of TFAP2C with SUMO1 (Homo sapiens)

UBE2I (UBC9) interacts with the C terminal region of TFAP2B (Eloranta and Hurst 2002). As inferred from TFAP2C, SUMOylation of TFAP2B occurs at lysine in the VKYE motif and, therefore, UBC9 is assumed to catalyze the ligation of SUMO1 to TFAP2B.

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SUMOylation of TFAP2C with SUMO1

**Location:** SUMOylation of transcription factors

**Stable identifier:** R-HSA-3234094

**Type:** transition

**Compartments:** nucleoplasm

UBE2I (UBC9) interacts with the C-terminal region of TFAP2C (Eloranta and Hurst 2002). SUMOylation of TFAP2C occurs at lysine-10 and causes a reduction in its transcriptional activation activity. A dominant negative mutant of UBC9 led to increased activity of TFAP2C therefore UBC9 is assumed to catalyze the ligation of SUMO1 to TFAP2C.

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